SECOND REVIEW

OF RECENT ADVANCES IN TROPICAL MEDICINE

ETC., ETC.

SUPPLEMENT TO FOURTH REPORT

WELLCOME

TROPICAL RESEARCH LABORATORIES

KHARTOUM

ANDREW BALFOUR, M.D.

DIRECTOR

G. Buchanan

Gordon Memorial College, Khartoum, in which the Wellcome Tropical Research Laboratories are situated

SECOND REVIEW

OF SOME OF THE

RECENT ADVANCES IN TROPICAL MEDICINE

HYGIENE AND TROPICAL VETERINARY SCIENCE

BEING A SUPPLEMENT TO THE

FOURTH REPORT

OF THE

WELLCOME TROPICAL RESEARCH LABORATORIES

AT THE

GORDON MEMORIAL COLLEGE
KHARTOUM

BY

ANDREW BALFOUR
M.D., B.Sc., F.R.C.P. EDIN., D.P.H. CAMB.
DIRECTOR
AND
CAPTAIN R. G. ARCHIBALD
M.B., R.A.M.C., ATTACHED E.A.
Pathologist and Assistant Bacteriologist

IN COLLABORATION WITH

CAPTAIN W. B. FRY, M.R.C.S., L.R.C.P., R.A.M.C., ATTACHED E.A.
Protozoologist and Assistant Bacteriologist
AND
CAPTAIN W. R. O'FARRELL, L.R.C.P. & S.I., R.A.M.C.

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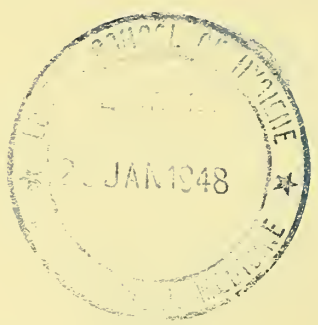

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PREFATORY NOTE

A GOOD many letters have been received testifying to the usefulness of our First Review Supplement, and expressing the hope that a Second might be forthcoming. After some hesitation it was decided to accede to these requests and, at the same time, slightly to widen the scope of the Second Review so that it might deal in a more general manner with Tropical Medicine as a whole and not merely, or mainly, with those diseases represented in the Anglo-Egyptian Sudan. In this way it was felt that it would appeal to a wider public and become a better book of reference. Happily, for such a work is a heavy undertaking, it should not again be necessary to produce a similar compilation in Khartoum. *The Medical Officer*, taking a leaf out of our book, now issues a monthly review supplement, which meets a long-felt want, and which gives an excellent résumé of current literature on bacteriology and protozoology.

The type of papers reviewed closely resembles those with which we have dealt, and now our Second Review will bridge the gap between our first publication and the first number of the above-mentioned supplement which appeared in January, 1911. Indeed it does more, for it will be found that it includes papers appearing up to the end of June, 1911. Thus an effort has been made to bring it well up to date. The existence of the admirable *Bulletins of the Sleeping Sickness Bureau* has rendered unnecessary any very exhaustive treatment of the subjects of sleeping sickness, trypanosomiasis and tsetse flies, but a certain number of papers under each receive short consideration. The fact that the Bureau is about to take the subject of Leishmaniasis under its wing constitutes another reason why this class of review work may now be abandoned at Khartoum.

The labour has been somewhat lightened by the presence of additional authors. Captain W. B. Fry, R.A.M.C., of the Laboratories' Staff, has rendered some assistance, and Captain W. R. O'Farrell, R.A.M.C., very kindly employed a large part of his spare time in carefully writing several of the sections. The presence of initials in the table of contents indicates who is responsible for each subject.

A glance at Ruge's annual catalogue [1] of papers dealing with subjects relating to Tropical Medicine will show how incomplete this Review really is, but it is quite impossible to handle all the vast number of articles which appear and to deal with them adequately in a volume of convenient size and weight. It is hoped that the most important in English and French have received due attention, and also a majority of the more authoritative which have appeared in German. Italian, Portuguese and Spanish sources have not been altogether neglected. One hopes that this Review will receive at least as favourable a reception as its predecessor, and one would take this opportunity of thanking all those who have kindly sent in reprints of their papers. When considered suitable, these have, so far as possible, been accorded notice.

Thanks are due to Dr. Bagshawe, Director of the Sleeping Sickness Bureau, Dr. Martin, Director of the Lister Institute, Sir John McFadyean, Principal of the Royal Veterinary College, Major S. Lyle Cummins, R.A.M.C., and Mr. Spencer Honeyman, the Librarian of the British Medical Association, for kindly granting facilities in connection with reference work in London. Sir Ronald Ross and Sir Lauder Brunton have been good enough to answer queries regarding incomplete references.

[1] Tropenkrankheiten in Sonder-Abdruck aus Virchow's Jahresbericht der gesamten Medizin

SECOND REVIEW

OF SOME OF THE MORE RECENT ADVANCES IN TROPICAL MEDICINE HYGIENE AND TROPICAL VETERINARY SCIENCE

Air. The question of bacterial pollution of the atmosphere by spray from the mouth has been the subject of investigation by Winslow and Robinson.[1] They employed *B. prodigiosus* and the mouth streptococci as test organisms, and found, like the German workers who preceded them, that bacteria with which the mouth has been inoculated are discharged, in the act of speaking, in large numbers and to considerable distances. Positive results were obtained as far as 7·5 metres from the speaker, and the average number of bacteria discharged over the whole surface of a room (6 × 8 metres) by 15 minutes' loud speaking was 646 per square metre. It is pointed out that a still more extensive spread of mouth spray would result from coughing and sneezing. Most of the particles are rather coarse and quickly settle out of the spray, while, in estimating aerial infection proper, it is the bacteria suspended in the air which are important, because these only could be inhaled with the inspired air. They found this was relatively small in comparison with the distribution of the heavier particles of spray. Still, they conclude that infection by mouth spray of food, or of other objects later brought directly or indirectly in contact with the mouth, is a real and important danger. At the same time, the fact that the mouth spray is a fairly coarse rain which quickly settles downwards tends, they think, to discount infection by tuberculosis or any other disease through the inspired air. They do not, however, take into consideration the question of infected dust, the influence of draughts and winds and other factors which in the Tropics, at least, doubtless play a part in disease transmission by such air. The fact that in Khartoum the incidence of tuberculosis, which is fairly common amongst our native population, falls most heavily on adults would tend to show that the infection is viâ the respiratory passages, for it is pretty generally admitted that infants and young children derive infection from infected milk by way of the alimentary tract, and tuberculosis of cattle is practically unknown in the Sudan. The way in which the native lives in crowded, dark and ill-ventilated huts or *tukls*, the way in which he expectorates, and the way in which sand and dust are blown about are factors which, to my mind, strongly suggest inhalation as a means of infection, albeit the mouth spray *per se* may only play an insignificant part.

An interesting research has been set on foot in the Philippines, and notes by Bacon on a preliminary study of the effect of tropical sunlight on the atmosphere have already appeared.[2] It is as yet too early to do more than draw attention to the institution of this work by Dr. Freer.

Amœba (*vide* **Dysentery**).

Anaplasmosis (*vide* **Piroplasmosis**).

Ankylostomiasis. For the sake of convenience one retains the old and more familiar term, but the condition is more correctly written Agchylostomiasis. An important discussion was held on this subject at the Annual Meeting of the British Medical Association in 1908.[3] Manson considered it in its relation to tropical sanitation, and pointed out that any attempt to eradicate the disease by the administration of anthelmintics to the entire population of an infected area was bound to fail. He regarded fæcal disposal as the crux of the ankylostomiasis problem. Proper disposal of fæces constituted the least expensive, the least irritating, and the most efficient method of stamping out the disease. In badly infected countries distribution of information and of anthelmintics from local post offices, as in the case of quinine in India, was advisable, while regulation of immigrants was important. Law pointed out the influence of immigration in the conveyance of infection by coolies coming from India to British Guiana, and stated that the question of prevention might be summed up in the single word "latrines." So far as the Sudan goes, one would add "inspection of certain immigrants, notably Egyptian fellaheen, at Halfa and Port Sudan," and "incinerators" to Law's watchword.

May recounted experiments with dilute sulphuric acid which, in dilutions of 0·25 to

[1] Winslow, C. E. A., and Robinson, E. A. (January 15, 1910), "Bacterial Pollution of the Atmosphere." *Journal Infectious Diseases.*

[2] Bacon, R. (July, 1910), "Preliminary Study of the Effect of Tropical Sunlight on the Atmosphere," etc. *Philippine Journal of Science, A.*

[3] Proceedings quoted in *Lancet*, September 5, 1908, and *British Medical Journal*, October 31, 1908.

Ankylostomiasis— *continued*

1 per cent. of acid, seemed to prevent the development of the ova. Sambon mentioned the three allied forms *Ankylostoma duodenale*, *Necator americanus* and *Triodontophorus diminutus*, and suggested that other forms would yet be found. He stated that it was not yet definitely proved that these parasites belonged exclusively to man, and mentioned *A. caninum*. He also cited Schaudinn's successful infection of monkeys with *A. duodenale*. He referred to the route of infection discovered by Looss, and expressed his own belief to the effect that the majority of the larvæ penetrate the lumen of the jejunum and the upper part of the ileum through the wall of the bowel. He discussed the still unsettled question as to the longevity of the parasite and, of the three views—blood-abstraction, venom secretion, secondary infection—advanced to explain the resulting grave anæmia, considered the last or microbic to be most in accord with recent investigations. Daniels drew attention to the destructive action of certain dipterous larvæ, especially those of the *Sarcophagidæ*, which live in fæces till nearly mature and destroy all thin-shelled entozoal eggs. Antiseptics are more apt to prevent these Diptera maturing than to kill the ankylostoma eggs. As regards treatment, Sandwith prefers *β naphthol* or the so-called "white mixture" (eucalyptol, chloroform and castor oil) to thymol, the latter being a dangerous drug.

Brehaut [1] made observations in Egypt on blood changes in ankylostomiasis. He found the eosinophilia was not great, a fact which he was inclined to attribute to a tolerance of the toxins which produce the eosinophilic change. The average was only 10 per cent.

A brief but interesting account of the measures adopted in Porto Rico is given in the *Journal of Hygiene* for September, 1908. Anthelmintics in the form of thymol and *β naphthol*, with sodium sulphate as a purgative, were largely used by the Commission, who also distributed cards of instruction along with the medicine. One of these is quoted :—

"Anæmia Commission of Porto Rico.

"Take one of the two purgatives given to you to-night.

"Take at six o'clock to-morrow morning half the capsules.

"Take the other half at eight o'clock the same morning.

"Take a purgative at ten o'clock.

"You should neither drink wine nor any alcoholic liquor during the time you are taking these medicines.

"Come for more medicines, until the physician says you are cured.

"Have a privy in your house. Do not defæcate on the surface of the ground, but in the privy.

"Do not walk barefooted, so that you may avoid contracting mazamorra (ground-itch) in your feet.

"Wear shoes, and you will never suffer from anæmia."

The Commission concluded that the "ground-itch" or "bunches" was not due to *Ankylostoma* but to secondary infections at the points of entrance of the larvæ. The reviewer (A. E. B.) believes this may be true as regards the boils and pustules, but that the urticarial wheals which precede such lesions are due directly to the larvæ of the worm.

In this connection it is perhaps of interest to note that Bartet has drawn attention to the association of urticaria with dracunculosis, a matter considered under the heading "Guinea-worm."

Recalling Sambon's remarks already quoted, we find that Weinberg and Leger [2] uphold the theory of secondary microbic infections as explaining the gravest or malignant forms of anæmia, and advance experimental proof in favour of their belief.

Warre [3] has recorded a case of ankylostoma anæmia of this type from the region of the Congo. The red blood corpuscles were fragile, and there was jaundice of hæmolytic origin. The etiology of the anæmia in this disease has been the subject of several papers. Whipple,[4] from a study of cases in the Canal Zone, Panama, does not believe that the hæmolysin secreted by the worm is strong or can account for the anæmia. As evidence he cites the

[1] Brehaut, A. H. (August 1, 1908), "Some Blood Changes in Ankylostomiasis." *Lancet.*

[2] Weinberg, M., and Leger, M. (April 8, 1908), "Recherches cliniques et expérimentales sur l'ankylostomiase." *Bull. Soc. Path. Exot.*

[3] Warre, H. (February 10, 1909), "Sur un cas d'anémie ankylostomiasique avec fragilité globulaire et ictère hémolytique." *Ibid.*

[4] Whipple, G. H. (May, 1909), "Ankylostomiasis." *Bulletin Johns Hopkins Hospital.*

Ankylostomiasis—*continued*

very slight hæmolysis in a blood cyst which contained an active parasite for two to three days. He believes the anæmia is probably duc to direct loss of blood and absorption from secondary foci of inflammation in the intestinal walls. The severity is stated to depend upon the number of worms and the intensity and extent of this diffuse inflammation. Siccardi [1] reviews the whole subject at length, and concludes that the anæmia is, in the main, of toxic origin. He admits that the intestinal lesions and the minute hæmorrhages are additional factors, but states that they are variable in their results. The anæmia itself is usually of a chronic nature, but may be acute, especially in the Tropics, and may assume the type of an acute or chronic dyspepsia, a pure anæmia, a jaundice, or present diverse nervous symptoms. It is to the secondary infection, due to intestinal bacteria, taking place through the minute wounds produced in the mucosa by the parasites that Castellani [2] attributes the fever which frequently accompanies ankylostomiasis. It is common in Ceylon, and the most frequent type is the *low intermittent*. The temperature rises above normal in the late morning, reaches its maximum in the evening, and falls at night between 11 p.m. and 2 a.m. The maximum seldom exceeds 101° F. The patient does not as a rule complain of feeling feverish, and indeed there are no subjective symptoms. The fever is not influenced by quinine or other antipyretics, but disappears sooner or later after energetic treatment for ankylostoma. Castellani classes the other types as *subcontinuous* or *continuous*, *irregular*, and a rare *undulant* form. The last is not unlike Malta fever. He did not find much difference between the aerobic bacterial intestinal flora of ankylostomiasis patients and that of normal individuals, but thinks it probable that under certain conditions ordinary intestinal bacteria, *i.e. B. pseudocolon*, may become virulent and pathogenic. In one case the fever was found to be probably due to a germ, *B. asiaticus*, which has not been observed in normal fæces.

Papers have appeared dealing with the spread of the disease in Natal, and its occurrence in Mexico, French Guiana, Eastern Bengal, Tunisia, the Sudan, Algeria, South Africa, Cochin China and the Philippines. Of these we may note that by Burkitt [3] on the disease and its complications in Eastern Bengal. He deals with local conditions, and points out that the more low-lying and damp the situation, the more congested with habitations, the more impure the drinking supply, the more dirty the habits of the natives, and the closer defæcation takes place to the dwellings, the greater will be the number of infected persons. The most frequent complications are noted as being amœbic dysentery and ulcerating mouth. The latter may lead to pus collections in the neck and loss of teeth. It is best treated by peroxide of hydrogen. The 10 vol. liquid is used in the strength of 1 in 3 of water made up on the spot. For the bleeding gums calcium chloride in one drachm doses every two or three hours in plenty of water is recommended. The work in the Philippines by Chamberlain [4] is of interest, because it emphasises the importance of treating mild uncinariasis, as even a slight lowering of vitality is to be deprecated in the Tropics. He believes that in the case of Americans in the Philippines, infection is more commonly by the mouth than through the skin. *Necator americanus* was found by Christopherson [5] in the case of a woman who came from the Bahr-El-Ghazal Province of the Anglo-Egyptian Sudan, and it is probable that the hook-worm is common throughout Central Africa, as it was found by Looss in the Congo pygmies, and has been reported from Uganda. The association of earth-eating with ankylostomiasis has long been known. Gobert and Catouillard [6] mention the occurrence of both in Southern Tunisia where the geophagism is apparently the cause, not the result, of the disease. They mention the arrested development of children suffering from uncinariasis. This is interesting in the light of Lemann's [7] notes on the presence of infantilism in the hook-worm disease of the Southern United States. He finds that it produces :—

(1) A general retardation of growth, symmetrical and harmonious.

(2) A simple retardation of skeletal changes.

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[1] Siccardi, P. D. (April 20, 1910), "Pathogénie de l'Anémie Ankylostomienne." *Archives de Parasitologie.*

[2] Castellani, A. (September 1, 1910), "Ankylostomiasis Fever." *Journal Tropical Medicine and Hygiene.*

[3] Burkitt, R. W. (October 30, 1909), "Observations on Ankylostomiasis and its Complications in Eastern Bengal." *Lancet.*

[4] Chamberlain, W. P. (August, 1910), "A Statistical Study of Uncinariasis among White Men in the Philippines." *Philippine Journal of Science*, B.

[5] Christopherson, J. B. (May 16, 1910), "*Necator americanus* in the Bahr-El-Ghazal Province of the Anglo-Egyptian Sudan." *Journal Tropical Medicine and Hygiene.*

[6] Gobert, E., and Catouillard, G. (December 9, 1908), "Enquête sur l'ankylostomose et les affections helminthiques dans le sud de la Tunisie et plus particulièrement dans le Djerid." *Bull. Soc. Path. Exot.*

[7] Lemann, I. I. (August, 1910), "Infantilism in Cases of Hook-worm." *Archives of Internal Medicine.*

Ankylostomiasis— *continued*

(3) A failure of development of the genitals as well as the absence of secondary sexual characteristics.

(4) A mental slowness and dullness.

(5) A general appearance which conforms neither to the Brissaud nor the Lorain type.

A paper by Christopherson,[1] mostly of the nature of a compilation, signalises the habit of earth-eating in the Anglo-Egyptian Sudan, and states that ankylostomiasis is only common in what is called the most Egyptian portion of the Sudan, which is also the region where geophagism occurs.

The question of ankylostomiasis in non-tropical countries is, of course, one of great importance, more especially as regards its occurrence in mines. Our limited space does not permit of any detailed review of this subject, but readers may be referred to an exhaustive paper by Oliver,[2] and the discussion upon it. It was stated that dogs had been infected with the human worms, but Leiper remarked that hitherto the ankylostomes of man had been found only in man. He doubted the transmissibility of human ankylostomiasis to dogs in nature. Leiper further stated that he had never been able to get larvæ to develop to a stage where their sexual characters were evident. It was impossible to differentiate the sex of the encysted larvæ. As regards the purification of mines, Oliver regarded the use of a solution of iron sulphate as probably the most promising method of disinfection. Boycott and Haldane[3] deal with the progress of the disease in Cornwall, and, in the case of English miners, uphold the value of the blood film examination with a view to detecting eosinophiles. Turner[4] found that both *Ankylostoma duodenale* and *Necator americanus* produced the disease in South Africa, and that miners there are not, as a rule, infected in the mines. He believes several factors are operative in giving this happy result, namely :—

(1) The acid reaction in many of the mine waters.

(2) The iron salts contained in some of the mines.

(3) Low temperature of some workings.

(4) Dryness of some mines.

(5) Nature of soil in the mines.

As regards the last, the finely-ground quartz of a gold mine may not be such a suitable nidus for the larvæ as the moist blue ground of a diamond mine.

Passing now to the worm itself, a very well-illustrated monograph is that by Perroncito,[5] who originally discovered the tunnel worm in Italy. Ozzard[6] has reaffirmed his belief, as the result of cultivation experiments with ova, that under certain suitable conditions the ankylostome embryo can develop outside the body into sexually mature forms. Daniels pointed out that this was a question of great importance, "because prophylactic measures that would be of value if no heterogenesis occurred would be useless if it took place." Leiper,[7] however, criticises the technique employed and opposes the idea. Apart from what has been stated, the question is rather one for zoologists, and the general reader is likely to be more interested in the method of Bass[8] for examining fæces for the ova. It is as follows :—

A quantity of fæces is well diluted with water, 1 in 10, and strained through gauze to get rid of coarse particles. This is centrifugalised, the fluid poured off, the centrifuge tube refilled and centrifugalised again, until all the diluted fæces have been used. The precipitate is rewashed several times with water as long as anything can be washed out. To know just how long to continue the centrifugalisation is the secret of success. One must learn what is the proper time for his centrifuge. It should be carried out at high speed and just long enough to throw the eggs to the bottom. Too long centrifugalisation defeats the purpose. With a centrifuge running 3,500 revolutions a minute, ten seconds at first, when there is much matter, and then four to five seconds, is

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[1] Christopherson, J. B. (January 1, 1910), "Earth-Eating in the Egyptian Sudan." *Journal Tropical Medicine and Hygiene.*

[2] Oliver, T. (February, 1910), "Ankylostomiasis, a Menace to the Industrial Life of Non-Tropical Countries." *Transactions Society Tropical Medicine and Hygiene,* Vol. III., No. 4.

[3] Boycott, A. E., and Haldane, J. S. (November, 1906), "The Progress of Ankylostomiasis in Cornwall." *Journal of Hygiene.*

[4] Turner, G. A. (February 15, 1900), "An Account of Some of the Helminthes occurring among the South African Natives." *Journal Tropical Medicine and Hygiene.*

[5] Perroncito, E. (1909), *La Malattia dei Minatori.* Turin.

[6] Ozzard, A. T. (September 18, 1909), "Life History of *Ankylostoma duodenale.*" *British Medical Journal.*

[7] Leiper, R. T. (November 6, 1909), "The Alleged Heterogenesis in *Ankylostoma duodenale.*" *Ibid.*

[8] Bass, C. C. (March, 1909), "Mild Uncinaria Infections." *Archives Internal Medicine.*

Ankylostomiasis—*continued*

usually the proper time. The centrifuge must be steady. This gets rid of most of the very small things, those having flat rough surfaces and those having a specific gravity about that of water. Now the precipitate should be centrifugated with a calcium chloride solution of a specific gravity up to 1050. This disposes of everything having a specific gravity below 1050, and the precipitate may now be examined. There frequently remains a considerable amount of material, much of which is appreciably heavier than the eggs, and of such a character that it interferes much with their recognition. This material may be removed by centrifugalising with a solution sufficiently heavier than the eggs. A solution with a specific gravity of 1250 is very satisfactory. In such a solution the eggs go to the top. With an appropriate pipette one may remove a few drops from the surface and examine, or, what is still better, pour off some of the top fluid containing eggs, dilute with water sufficiently to bring the specific gravity below 1050, and centrifuge again. The precipitate will now contain most of the eggs contained in the original amount of fæces, and may all be put on one slide and examined. One such slide contains as many eggs as could be found in several hundred ordinary slide preparations of fæces.

Passing now to the question of treatment, we find this was discussed at the meeting to which reference has already been made. Manson believed *β naphthol* to be the best drug for use on a large scale. In British Guiana, Law kept patients on a milk diet for a day or so, and then gave them a small dose of calomel followed by salts. On the following morning 20 to 30 grains of thymol in a cachet were given, and this dose was twice repeated with an interval of one hour between each dose. The salts were repeated a couple of hours after the last dose. *β naphthol* has now been largely substituted for the thymol. Nattan-Larrier has given up thymol and taken to filix mas instead, as it has given him 90 per cent. of successes. Here is his method :—

First day.—Milk diet and saline purge.

Second day.—Milk diet ; 20 capsules containing each 0·30 centigramme of oil of filix mas ; one capsule every ten minutes. One quarter of an hour after the last capsule, 8 capsules of ether, one every three minutes. After the last ether capsule, 15 grains of castor oil and half-an-hour later, 25 grains of castor oil.

Third day.—Saline purge.

Fourth day.—Examination of fæces and, if necessary, repetition of treatment.

To prevent reinfection he cautions against going about barefooted, and every six months gives 3 grains of extract of filix mas. Before giving poisonous drugs like thymol, Sandwith recommended the exhibition of strychnine, especially when combined with hypodermic injections of camphor in sterilised oil (1–10). Elliott [1] prepares the patient for thymol by giving podophyllin.

Patterson [2] in Porto Rico found thymol the best drug. In the evening magnesium or sodium sulphate (30 grains) is given. The next day the patient is kept in bed and starved. Then at 8 a.m. on the morning following, 2 grains of finely-powdered thymol are given in capsules. The dose is repeated at 10 a.m., and at 12 noon a second dose of salts is given. All solvents of thymol, such as alcohol, ether, glycerine, turpentine or chloroform are contra-indicated. The dose of thymol is regulated both by the debility of the patient and his age. He found filix mas useless, and eucalyptol both non-efficacious and dangerous. Shattuck,[3] another American physician, employs Phillips' Egyptian formula for " white mixture " as follows : he gives 30 c.c. of a mixture of oil of eucalyptus, 2·5 grains, chloroform, 3·5 grains, and castor oil 40 c.c., and repeats the dose in half-an-hour. It is preceded and followed by magnesium sulphate, and the patient fasts until the evening, treatment having begun at 6 a.m. Nicol,[4] from experience in Natal, speaks well of *β naphthol*. His formula is :—

Beta-naphthol	4 drachms
Mucil. tragacanth	1 ounce
Aq. menth. pip.	to 6 ounces

Of this mixture, 6 drachms (30 grains *β naphthol*) are given to an adult male, and 5 drachms (25 grains *β naphthol*) to an adult female for each dose. He notes that the drug does not keep well, and is very variable in quality. It should only be obtained from first-class manufacturers, should be fresh, stored in ½ lb. or 1 lb. bottles, and kept in a cool place. Brimont [5] has recently introduced a new drug which he regards as superior to eucalyptol. It is the essence of niaouli (*Melaleuca viridiflora*).

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[1] Elliott, A. M. (January 11, 1908), " Discussion on Ankylostomiasis." *Lancet.*

[2] Patterson, F. D. (1908), " Uncinariasis in Porto Rico, and its Treatment." *Therapeutic Gazette.*

[3] Shattuck, E. C. (December, 1907), " Clinical Observations on Uncinariasis." *American Medicine.*

[4] Nicol, B. (June, 1910), " Hook-worm Infection and Disease in Natal." *Transvaal Medical Journal.*

[5] Brimont, E. (1910), " Note sur le traitment de l'ankylostomiase par l'essence de Niaouli." *Ann. Hyg. Méd. Colon.*, Vol. XIII., No. 2.

Ankylostomiasis—*continued*

Additional Notes

For a good general review of the subject readers are referred to the recent *Milroy Lectures* by Boycott.[1] These are very full, but do not present much that is novel, and are very largely concerned with the disease in miners. The notes on tropical ankylostomiasis are not extensive.

A very useful illustrated pamphlet is that prepared by Byrd [2] for the State Board of Health of Florida. We quote his comparison between *Necator americanus* and *Uncinaria duodenalis*, as it is likely to be serviceable :—

Necator americanus	*Uncinaria duodenalis*
Smaller.	Larger and coarser looking.
Head small and finely tapering.	Head thicker and coarser.
Simple chitinous lips on buccal rim.	Four hooks on buccal rim.
Dorsal conical tooth projects well into mouth.	Dorsal conical tooth does not project so well into mouth.
Sexual opening in female in anterior half.	Sexual opening of female in posterior third.
Caudal bursa of male smaller.	Caudal bursa of male larger.
Dorsal lobe subdivided.	Dorsal lobe undivided.
Ova slightly larger.	Ova slightly smaller.

Of still greater value is the admirable monograph on Hook-worm Disease by Dock and Bass.[3] Every aspect of the condition is considered, though special attention is paid to the disease amongst poor whites in the Southern United States. It is not our custom to quote from books, but in this case the rule may be broken to permit the introduction of a list which the authors present. They say :—

Besides the two human species of ankylostoma and necator, there are several species of the genus uncinaria which are found in lower animals, *e. g.*—

Uncinaria canina,
Uncinaria stenocephala,
Uncinaria trigonocephala,
} in dogs.

Uncinaria (ankylostoma) tubæformis, or
Uncinaria perniciosa,
Uncinaria balsamoi,
} in cats.

Uncinaria trogocephala, in sheep.

Uncinaria radiata, in cattle.

Uncinaria lucasi, in seals (thought by Looss to be the cause of the great mortality—17 per cent.—of sucking seals on the Pribiloff Islands).

Uncinaria os papillatum, in elephants.

There is no proof that any of these infect man, and among lower animals each genus infected seems to have its own species of hook-worms. The worm supposed by Rathonyi to be a hook-worm in mine horses in Hungary has been shown to be a sclerostoma.

One must add to the above list the recently discovered *A. braziliense* found by de Faria [4] in cats and dogs at Manguinhos, South America. Several papers of interest occur in the *Transactions of the American Society of Tropical Medicine* for 1910. Of these we specially note that by Lemann,[5] who deals with the infantilism which results from ankylostomiasis, and illustrates the general changes, and more especially those in the horny skeleton. He finds that the infantilism has the following characteristics :—

(1) A general retardation of growth, symmetrical and harmonious.

(2) A simple retardation of skeletal changes.

(3) A failure of development of the genitals as well as the absence of secondary sexual characteristics.

(4) A mental slowness and dulness (not present in my patient).

(5) A general appearance which conforms neither to the Brissaud nor the Lorain type.

A good many new papers have appeared on methods for finding ankylostome eggs and larvæ in fæces. Some are given in Bass's and Dock's work (*loc. cit.*). Here we note one by

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[1] Boycott, A. E. (March 18, 25, and April 1), "Ankylostoma Infection." *Lancet.*

[2] Byrd, H. (October, 1910), "Hook-worm Disease." *Publication* 79 *State Board of Health of Florida, U.S.A*

[3] Dock, G., and Bass, C. C. (1910), *Hook-worm Disease.*

[4] De Faria, G. (April, 1910), "Contribution towards the Classification of Brazilian Entozoa." *Mem. Instit. Oswaldo Cruz.*, Vol. II., No. 1.

[5] Lemann, I. I. (1910), "A Study of the Type of Infantilism in Hook-worm Disease." *Collected Papers, American Society Tropical Medicine.*

Ankylostomiasis—*continued*

Fülleborn,[1] who figures a special filtration arrangement. It is not worth while entering into a description without the accompanying illustration, but the reference is given.

Peffer's method for eggs may be stated. He takes advantage of a stickiness which they possess :—

> Washed and sedimented fæces are put on a slide for a few minutes and then gently immersed in water ; after everything else has been washed away the eggs are still found adhering to the slide. By repeating the process numerous eggs may be collected on the same slide. This method does not apply for the eggs of ascaris, trichocephalus, or tænia.

The above is taken from a useful paper by Hall,[2] to which fuller reference is made under the heading "Parasites."

Lumsden and Stiles [3] have described what may be called a "wet privy," an ingenious apparatus for doing away with the dangers arising from the ordinary rural methods of dealing with human excreta. Briefly, it consists of a water receptacle, with an anti-splashing board, which communicates with an effluent tank. An automatic closing seat and the use of oil prevent mosquitoes breeding in it, and the effluent can be sterilised *in situ* by boiling. In short it is a little household septic tank which can serve five people, and it is likely that it will become popular and prove itself a marked and welcome advance on existing methods. A longer account of it will be found under "Sewage."

Anthrax. Since the date of our last Review Supplement there has been a case of anthrax in an English stud bull near Khartoum, and it is possible, as the Principal Veterinary Officer has suggested, that the disease exists in a mild form amongst Sudanese cattle, but proves virulent and fatal when transmitted to foreign and non-immune animals. The question of transmission and importation of infected materials is important, and will become more so as far as the Sudan is concerned. A paper by Hanna,[4] quoted in the *Journal of Tropical Veterinary Science*, gives the U.S.A. regulations, which insist on hides and hide-cuttings being dry-salted, arsenic-cured or lime-dried, after soaking for 40 days in a strong solution of lime (except those from Sweden, Norway and Britain), in all cases where the invoices are not accompanied by a proper certificate of disinfection. Wet hides are preferable to dry ones, as the possibility of dust arising is minimised. The question of anthrax being spread by the use of bone meal as a fertiliser was raised in *The Veterinary Record*, and also quoted in the above-mentioned journal.

It is interesting to note that, unlike other birds, the ostrich appears to be susceptible to anthrax, to judge by a case in South Africa recorded by Robertson.[5] The disease has been found in pigs by Bougert and Carl,[6] and it is believed that it may be a special and hitherto unknown form of anthrax. It would seem that swine, without apparently suffering from anthrax, or indeed appearing to suffer in any way, may harbour anthrax bacilli. Possibly then they may act as carriers.

M'Fadyean [7] has shown that the bacilli can occur in the milk of infected cows, but he does not consider this fact as indicating any special danger to human beings which cannot be obviated by simple precautions. "It is only necessary," he says, "to see that for a week or ten days after the last preceding case the temperatures of all the cows are taken before each milking, and to withhold the milk of every cow that has a temperature above normal, or which presents any other symptom of anthrax infection."

An important statistical paper on British industrial anthrax is contributed by Page,[8] but here we need only note, so far as Part I. is concerned, one or two of the points brought out in the summary.

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[1] Fülleborn, F. (1911), "Methode zur Anreicherung von Ankylostomenlarven." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XV., No. 11.

[2] Hall, M. C. (1911), "A Comparative Study of Methods of Examining Fæces for Evidences of Parasitism." Bulletin No. 135, *Department of Agriculture, U.S.A. Bureau of Animal Industry.*

[3] Lumsden, L. L., and Stiles, C. W. (February 1, 1911), "Preliminary Note on a Simple and Inexpensive Apparatus for Use in Safe Disposal of Night Soil." *Hook-worm Number, Quarterly Bulletin, Louisiana State Board of Health*, and also *Journal Tropical Medicine and Hygiene*, April 15, 1911.

[4] Hanna, W., "Anthrax and Imported Animal Products," quoted in *Journal Tropical Veterinary Science*, 1908, p. 402.

[5] Robertson, W. (December, 1908), "Case of Anthrax in an Ostrich." *Journal Comparative Pathology and Therapeutics.*

[6] Quoted in *Journal Comparative Pathology and Therapeutics*, March, 1909.

[7] M'Fadyean, J. (June, 1909), "Anthrax Bacilli in Milk." *Journal Comparative Pathology and Therapeutics.*

[8] Page, C. H. W. (November and December, 1909), "British Industrial Anthrax." *Journal of Hygiene.*

Anthrax—*continued*

"In all countries except Great Britain agricultural anthrax is most common, and consequently there is a close relation between the number of cases of human and animal anthrax." *Again:* "Infection may be carried in clothes or nails to people outside by workers. Anthrax spores may retain their vitality for years on hair and other material. Anthrax is common among animals all over Europe and Asia, and in most countries there is an increased incidence during the hot summer months. It is probable that in certain districts special conditions exist which make them permanent centres of anthrax infection. Here, too, hides and hair from contact with the soil may possibly become infected without the animals actually contracting anthrax."

Part II. deals with questions of bacteriology, disinfection and treatment. It is pointed out that in the bacteriological diagnosis difficulties are met with in animal inoculation owing to the presence of the bacillus of malignant œdema, which, unless special methods are used, as shown by Duncan, will often mask the presence of the anthrax bacillus altogether. When agar plates are used, three types of bacilli, one of which may be *B. subtilis*, that occur in hair and bristles and closely resemble anthrax bacilli, may lead to difficulties. Their presence, however, is to be regarded as beneficial, and Page suggests they may yet be used along with cultures of true anthrax bacilli to produce immunity. He also remarks that it may be possible to eliminate the anthrax bacillus from horsehair by increasing the quantity of an antagonistic bacillus, for example *B. œdematis maligni*. At present there is no method of absolutely destroying anthrax spores in horsehair and bristles, but the use of steam under slight pressure, 4 or 5 lb. to the square inch, greatly minimises the risk to the human subject. An intermittent sterilisation is indicated, as the spores then develop into bacilli and are killed in the latter condition. The steam must not be so damp as to injure the material or too dry to be efficacious as a germicide. Of liquid disinfectants cyllin (1 in 100) at a temperature not above 120° F. is best, though not absolutely effective.

As regards treatment, the cautery and subcutaneous injection of serum (Sclavo's or Sobernheim's) is advisable in all cases. In internal anthrax early intravenous injection of serum is essential.

Herley[1] records eight cases of human external anthrax in which Sclavo's serum was employed with benefit, and indeed one was a malignant case in which recovery was undoubtedly due to the serum.

Baldrey[2] has found in India a sporulating organism simulating *B. anthracis*, and which may be the cause of some of the gangrenous sloughing wounds so common in cattle. He compares its morphology and cultural characteristics with those of the anthrax bacillus.

Mitter[3] deals with the staining reactions of anthrax bacilli in India as compared with those in Europe. He finds a difference. Thus M'Fadyean's peculiar staining reaction with methylene blue, which consists of a deposit of amorphous granules of a more or less polychromatic character between and around the bacilli is, in India, not sufficiently marked to be diagnostic. The methods of Johne and Olt for staining the capsules were, however, found effective.

Cave,[4] who has used M'Fadyean's method in England, finds it quite reliable, but recommends dispensing with Canada balsam and a cover-glass, as when these are used the colour quickly fades. Perhaps liquid paraffin, as recommended by Coles, would make a good mounting medium.

The use of skin cultures as a means of diagnosis, especially for isolating the bacillus from putrefying cadavers, has been introduced by Ciuca and Stoicescu,[5] who conclude—

(1) That *B. anthracis* does not live longer than 48 hours in the vegetative form in the cadavers of animals dead of anthrax, owing to the putrefaction which takes place: in the capillaries of the skin it resists for a longer time, and can find the conditions necessary for sporulation there.

(2) The spores remain in a condition resistant to atmospheric conditions and common salt for a year in the skin.

(3) Diagnosis is always possible by means of cultures of the skin of putrefied carcases sent to the laboratory extended on plaques of wood and allowed to dry.

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[1] Herley, R. (December 4, 1908), "Eight Cases of External Anthrax." *Lancet.*

[2] Baldrey, F. S. H. (1910), "An Organism simulating Anthrax." *Journal Tropical Veterinary Science*, Vol. V., No. 4.

[3] Mitter, S. N. (1909), "Observations on some Staining Peculiarities of Anthrax Bacilli." *Ibid*, Vol. IV., No. 1.

[4] Cave, T. W. (December, 1908), "The Methylene Blue Staining Reaction with Anthrax Blood." *Journal Comparative Pathology and Therapeutics.*

[5] Ciuca, A., and Stoicescu, G. (1910), "The Bacteriological Diagnosis of Charbon by Cultures of the Skin." *Journal Tropical Veterinary Science*, Vol. V., No. 2; translated from *Archiva Veterinaria*, Vol. VI.

(4) This method can be used when it is not possible to make observations immediately, especially in hot weather, when, in spite of all precautions, the organs rapidly putrefy even when examined soon after death. Anthrax—*continued*

It would seem that this is a method specially applicable in the Tropics.

Turning again to questions of prevention and treatment, we find Lowe [1] detailing the method employed in an outbreak amongst horses in India. Perchloride of mercury was used as a disinfectant, carbolic acid as a drug, and Sclavo's serum 20 c.c. subcutaneously in order to produce immunity.

Experiments by Cavacini [2] seem to show that prolonged exposure of skins infected with anthrax spores to solar light is an efficient method of rendering them harmless. This is important from the tropical standpoint, but will require confirmation. The experiments were conducted in Italy, and, to judge from the results, exposure of hides to sunshine in India for 14 days before shipment would serve to render them sterile.

Barlach,[3] who has had considerable experience in treating anthrax, adopts the following methods :—

(1) Rest in bed in every case. This is absolute and rigidly enforced, since it is believed that movement favours the entrance of the bacilli into the blood stream. For the same reason all pressure on the pustule is carefully avoided.

(2) In slight cases, fomentations of aluminium acetate or sublimate, the former especially when the pustule is on the face. The author considers cases slight when the disease has remained local, the pustule being situated on an area not markedly hardened, even if there is slight redness and swelling.

(3) In severe cases the pustule is slit open, the pointed thermo-cautery is used in a ring of rather deep punctures close together, around the pustule, so that a groove results, and this groove hinders the passage of the bacilli from the pustule into the surrounding tissues. The numerous incisions formerly employed were not found to be necessary, and the author now only uses them when there is excessive tension from the œdema. Antiseptic fomentations are also used. In very severe cases, with marked œdema and severe erysipelas, Barlach finds injections of iodine to produce a surprisingly good effect. He injects one or two drops of the tincture at different points on the border of the erysipelas, about 5 to 10 cm. apart, using generally in all, about 8 minims, or in very extensive cases, up to 17 minims. This may be repeated, if necessary, in the following days. The author states, in passing, that he has found this iodine injection excellent in cases of ordinary erysipelas, especially of the wandering type. Small abscesses occasionally form at the site of the injection. Camphor injections are also given in severe cases when indicated.

Braun quoted by Creite [4] and Schwab [5] both deprecate radical measures. The former uses aluminium acetate (2 per cent.) in the form of compresses, and alcohol is given freely when the fever is high. The latter believes in sublimate fomentations combined with the use of the Italian anti-anthrax serum.

Additional Notes

The Strasburg method of diagnosis was mentioned in our First Review. This has now been perfected by Müller and Engler,[6] who searched for some porous substances on which the suspected blood might be sent with the bacilli under the most favourable conditions for sporulation. They find chalk a better substance than baked clay or the rolls of filter paper recommended by Eherle and Schüller. Fragments of flower-pots sterilised by boiling water and cooled in sterile, well aerated water can be utilised, the blood being applied to the rough side. A thin layer of blood then forms on the smooth face, and here rapid sporulation takes place. Ascoli [7] describes the diagnosis of anthrax by the precipitin method, and a translation of his paper will be found in the *Journal of Comparative Pathology and Therapeutics* for March, 1911. It has always been difficult to free foreign hides, especially those from China and India, from anthrax spores. Blood clot and the fatty cellular tissue prevent thorough penetration of disinfectants, which also tend to spoil the wool or hair. The Seymour-Jones' [8] method has surmounted both these difficulties. It consists in the combined use of formic acid and corrosive sublimate. The formic acid in 0·9 per cent. strength (1 per cent. of a 90 per cent.

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[1] Lowe, C. (1909), "Anthrax in the 34th Poona Horse." *Journal Tropical Veterinary Science*, Vol. IV., No. 1.

[2] Cavacini, V. (1909), "Sterilisation of skin infected with the spores of Anthrax by prolonged exposure to solar light." *Journal Tropical Veterinary Science*, Vol. IV., No. 1. Translated from the *Semaine Vétérinaire.*

[3] Barlach (November 1, 1908), "Milzbrand und seine Behandlung." *Med. Klin., Berl.*

[4] Creite, O. (December 25, 1907), "Traitement conservateur de la pustule maligne." *Semaine Médicale.*

[5] Schwab, O. (February 23, 1908), "Über die Behandlung des Milzbrandes." *Med. Klin., Berl.*

[6] Müller, M., and Engler, A. (October 6, 1910), "Über die Erhöhung der Leistungsfähigkeit des Strassburger Verfahrens zum Nachweis von Milzbrand." *Zeitschr. f. Infekt.-Krank. der Haustiere*, Vol. VIII.

[7] Ascoli, A. (March 6, 1911), "Die Präzipitindiagnose bei Milzbrand." *Cent. f. Bakt.*, I. Orig., Vol. LVIII., No. 1.

[8] Seymour-Jones, A. (December, 1910), *The Seymour-Jones Anthrax Sterilisation Method.* London.

Anthrax—*continued* solution) causes the tissues to swell and facilitates the penetration of the corrosive sublimate solution. It also, on account of its antiseptic power, enables the latter to be used less concentrated. The latter in 1 in 10,000, and in the presence of the formic acid, is partly absorbed in twelve hours. Four-fifths of it is absorbed in twenty hours. Practically, according to the type of hide treated, the formic acid is used in from 0·3 to 0·9 per cent. strength, and the sublimate in 1 in 5000 for a period of twenty-four hours. The swelling is afterwards reduced by immersion in saturated solution of common salt. Hides thus treated keep well, and tests on animals have shown the method to be effectual.

Bacteriology. As in the last Review, so in this, only matters of general bacteriological interest will be discussed under this comprehensive heading. Possibly as useful a subject as can be considered is the question of *Bacillus coli communis* and allied organisms. The possibility of infection of the urinary tract by *B. coli* is now recognised as a condition of great importance, and it is one which occurs in tropical and temperate climates alike. Wilson [1] investigated types of *B. coli* isolated from the urine of patients with cystitis and pyelitis, and which appeared to be responsible for these conditions. Out of 50 bacilli examined, 44 could be placed in the *B. coli communis* group, but the remaining 6 were anærogenic, *i. e.* they formed no gas in glucose media. He suggests the name *B. coli anærogenes* for bacilli of this type, and, though he cannot be certain, believes that there is absorption from the intestine through the blood capillaries or lymphatics.

A discussion [2] on the subject elicited the fact that there are three groups of infection : (1) cases with general symptoms (pyrexia and rigors) but absence of urinary symptoms ; (2) cases with irritable bladders, usually cystitis and occasionally cystic ulceration (3) cases of advanced pyonephrosis or renal abscess. It is the acute cases which appear to do best with vaccine treatment. Pollock [3] has recorded cases of bacilluria in Malta, and calls attention to the advisability of examining the urine in cases of mild pyrexia, especially when the patient complains of irritable micturition. He found that cases quickly recognised and treated speedily got well, but that those allowed to run on might prove most intractable and cause much suffering. In Malta, urotropine was found to be almost a specific, given at first in one drachm doses a day and then diminished.

Having seen a case of coli pyelitis in Khartoum one was interested to find the condition discussed by Indian physicians. McCay [4] reviews the subject, pointing out that the condition is most common in females and attacks the right kidney with greater frequency. Views differ as regards the route of infection, some upholding that from the blood stream, others believing in ascending infection from the bladder. On the whole it would seem the latter is the more likely. The following classes are tabulated: (1) Acute bacillary kidney infection, with tendency to spontaneous cure and recovery under potassium citrate treatment. (2) Acute coli pyelitis without gross injury to the renal tissue. Recovery without kidney damage if treated by urotropine, coli vaccine, or anti-colon serum. (3) Severe cases with septic implication of kidney tissue and usually requiring surgical interference, though vaccine or serum treatment should be tried.

Rogers [5] insists on the importance of the early recognition of these coli infections, so that the vaccine treatment can be speedily employed, and emphasises their being a frequent cause of fever in India both during the puerperal period and after pelvic operations. He gives some good illustrative charts, and points out that there may be no pus cells at all found in the urine even after it has been centrifuged. The urine is nearly always acid, there may be no pain on passing it, and no undue frequency of micturition. It may be quite clear, but is often slightly opalescent, and this may be all to lead one to connect the fever with a urinary infection. One has to remember that such cases may pass into acute, general and fatal coli septicæmia. Morse [6] has directed attention to coli infection of the urine, and the urinary tract in infancy. The infection is usually transparietal, but may be hæmatogenous, and in girls is usually through the urethra. It is worth noting that the irregular temperature may simulate an atypical malaria. Morse finds the alkalis more useful than urotropine in the treatment of these cases. If both fail, autogenous vaccines should be employed. This

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[1] Wilson, W. J. (September, 1908), " Bacteriological Observations on Colon Bacilli infecting the Urinary Tract, with special Remarks on Certain Colon Bacilli of the ' Anærogenes ' Class." *Journal of Hygiene.*

[2] At meeting of Bristol Medico-Chirurgical Society : quoted in *Lancet,* January 28, 1910.

[3] Pollock, C. E. (August, 1908), " Bacilluria." *Journal Royal Army Medical Corps.*

[4] McCay, D. (November, 1909), " Coli Pyelitis." *Supplement, Indian Medical Gazette.*

[5] Rogers, L. (November, 1909), " Genito-urinary Bacillus Coli Infection as a Frequent Cause of Fever in India, especially after childbirth and Gynæcological Operations." *Ibid.*

[6] Morse, J. L. (September, 1909), *American Journal Medical Science.*

Bacteriology—*continued*

question of infection in infancy and childhood has been the subject of special papers and a discussion,[1] to which the reader is referred. Here one would only quote the conclusions of Pardoe. He finds :—

(1) The acute autogenous infections with *B. coli* are less common in children than in adults. These acute infections show the same tendency to comparatively rapid and complete cure as is observed in older patients.

(2) Chronic autogenous infections in children are also more rare than in adults. They also show the same intractability to treatment.

(3) Chronic infections dependent upon, or occurring coincidently with, other conditions of the genito-urinary tract, show a much greater tendency to complete cure than is the case in adults, after the cause (that is stone, or obstruction to micturition) has been removed.

(4) Local treatment in autogenous infection is of small value.

(5) Vaccines are of little value in acute cases, but are most valuable in chronic cases.

Some general conclusions are also reached by Dick,[2] who points out that coli infection may induce erythematous rashes, states that slight cases are apt to be altogether overlooked and severe cases misunderstood, and that at present clinical observations alone are quite inadequate for diagnosis, bacteriological evidence being a *sine quâ non*.

Briscoe[3] gives some useful details regarding the condition of the urine, the technique for examination of the infected secretion, and the method of vaccine-therapy. He says :—

In the cases where pus is being passed there will be no difficulty in recognising the condition, as the cloudiness or deposit, or both, will at once arouse suspicion, but, in examining the specimen from an individual who is passing only the bacilli, the following points should be noted :—

(1) As a rule, the urine is rather paler than would be expected from its specific gravity. The specific gravity shows no peculiarities of itself, but on account of the pallor of the specimen the high urinometer reading comes as a surprise.

(2) The urine is acid in reaction, often strongly so.

(3) The specimen is not clear and translucent. A kind of haze is present throughout the whole column of the urine. In some cases a cloud, or even a small deposit, of mucus forms at the bottom of the vessel. A slight haze, such as has been indicated above, is frequently present in normal urine, and to detect these cases of bacilluria the following simple method can be adopted. A small piece of filter paper is folded in the usual manner and moistened by allowing some water to filter through it into a clean test-tube. This serves two purposes—the filter paper is rendered less pervious, and inspection of the filtrate in the tube shows whether the test-tube is clean or not. This latter point is important, as a dirty tube will give the impression of cloudiness in the contained liquid. A small quantity of urine is then filtered into the test-tube. The filter paper allows bacteria to pass through, but holds back most of the other substances which give rise to turbidity ; however, red and white blood corpuscles, fat, and occasionally certain fine precipitates, do pass through. A warning is here necessary with respect to urines which deposit urates. If such a urine is filtered while it is warm the paper will hold back the urates which are already precipitated, but as the filtrate cools more will be thrown out of solution, and will give rise to a haze in the test-tube. This is, of course, immediately dispersed by heating, but it is simpler to cool the urine before filtering as a part of the routine.

When the urine filters clear, there is no appreciable quantity of *B. coli* present. If, however, the filtrate is cloudy, the next procedure is to put a drop of the urine on a slide, apply a cover-glass, and examine with the microscope. It is not necessary to use a 1–12th oil immersion lens, for the bacilli can be easily seen by the aid of a 1–$\frac{1}{6}$th inch objective and a No. 3 eye-piece. It is advisable to cut down the light in the first instance in order to find the focus, after which as much light as is desired can be admitted. If the *B. coli* are present they will be seen either as round bodies or as short rods, according as they are floating end on or lengthwise, and they can further be seen to be moving briskly. This is in contrast to the appearance presented by cocci or other substances not endowed with the power of locomotion. In the latter case the small bodies may show some movement, but there is no change of position. Some confusion may arise temporarily from the presence of currents in the specimen, but the movement is then in one direction only, whereas the *B. coli* move continuously and in various directions. The application of a little heat will often increase the motility of the bacilli, and it will also be found that the rapidity of movement varies in different specimens. Should the haze not have been due to this condition, the cause will be discovered at the microscopic examination. Two further steps are advisable, but not essential. In the first place a large loopful of the urine may be taken by means of a sterilised platinum needle and gently rubbed over the surface of an agar tube, which is then incubated. At the end of 24 hours or less there will be a plentiful growth, which is opaque and white. The margins of this growth are usually markedly crenated in outline. The second investigation consists in making a film either from the deposit found on standing or preferably from the centrifugalised deposit. The film is allowed to dry, fixed by heat in the usual manner, and then stained by Gram's method and counterstained with carbol-fuchsin or neutral red. The *B. coli* are decolourised by Gram's method and take up the counterstain—*i.e.*, are seen to be stained red by this method. The urine is best examined as soon as possible after it is passed, directions being given that the parts should be cleansed carefully before

[1] "Proceedings of Section of Diseases of Children at the 78th Annual Meeting of the British Medical Association." *British Medical Journal*, October 15, 1910.

[2] Dick, J. S. (October 29, 1910), "*Bacillus coli* Infections, with Special Reference to their Recognition and Comparative Frequency." *British Medical Journal.*

[3] Briscoe, J. C. (October 30, 1909), "On certain *B. coli* Infections." *Lancet.*

Bacteriology—*continued*

micturition; if necessary, and more especially in women, a catheter specimen should be obtained. This method of examination of the urine is also of value in the isolation of the organism for the treatment of certain cases of infection where the discharge proceeds from some site other than the urinary tract, is obviously contaminated, and from which it would take some time to isolate the organism. . . .

As regards vaccine-therapy it is undoubtedly best to employ a vaccine prepared from the organism which is attacking the patient, and a vaccine can easily be prepared in the course of three days. Inoculations should be given every seven or eight days. The initial dose for an adult of 50,000,000 of dead organisms (estimated according to the method advised by Sir Almroth Wright) will be comfortably tolerated. The second dose should be half as much again, and so on. It is also advisable to have a fresh vaccine prepared each month, better results being obtained than when the same vaccine is employed continuously. This may be explained on one or two grounds. Either the vaccine loses some of its potency, or the organism is able to develop power to protect itself from the antibodies produced by the host as a result of the vaccination. It will be remembered that this latter occurs in the case of trypanosomes against which atoxyl is administered. Whichever explanation is correct, the fact remains that greater improvement takes place when the vaccine is freshly prepared every month.

Batty Shaw[1] states that a person with bacilluria may remain in good health, and mentions the fish-like smell the urine may acquire due to the formation of products by the colon bacillus. Cystitis is by far the commonest lesion.

Porter and Fleischner[2] deal with the infection in children, and note how it may follow fissure in ano in infants. Of special importance is their observation that the blood serum of children who have been ill for some weeks agglutinates, in high dilutions, the typhoid bacillus.

Turning now to other aspects of the activity or importance of *B. coli*, we find that von Benezur,[3] by cultivation experiments, investigated the question of the identity of *B. coli* and *B. typhosus*, but failed to confirm the observations of Tarchetti, who found the two organisms to be closely related. Lippeus[4] announces a differential reaction between the two organisms. It depends on the reducing power of *B. coli* on the hæmoglobin of the blood, a property absent in *B. typhosus*. If to a mixture of artificial serum (2 c.c.) and of washed red cells of the horse (2 drops) one adds 1 c.c. of a young broth culture of *B. typhosus* the colour of the mixture remains unchanged, but if *B. coli* be added the mixture assumes a violet colour after 8 or 10 minutes, a hue which persists for about 15 minutes.

The question of *B. coli* in its relation to drinking water will be considered under "Water," but reference may here be made to the researches by Portuguese observers[5] on *B. coli communis* in the human intestine, in the intestines of mammals and birds, and in the inferior vertebrates and cereals. They concluded that there is no means of distinguishing by morphological, biological or cultural characters *B. coli* of human origin from that derived from animals, nor did they find that the dietary had any appreciable effect on the character of the organism. Further, they decided that cereals do not form a natural habitat for the colon bacillus, and that its presence in them is to be considered accidental.

Castellani[6] examined the excreta of eleven normal individuals, nine of whom were natives, living in Ceylon, and found that the typical *B. coli communis* (Escherich) was extremely rare. The majority of the germs were represented by *B. neapolitanus*, *B. pseudocoli*, *B. acidi lactici*, and *B. para-entericus*. Details of the cultural reactions of the organisms isolated and studied will be found in the paper, which is written in English.

Burri,[7] in a short article, discusses the question of mutation amongst bacilli of the colon group. It would appear that in the strict sense of the word this cannot occur, though strains may vary in their powers to ferment sugars.

Schütze[8] has described a case of pure *Bacillus paracoli* infection. Coli-like organisms were isolated from the blood and found to differ from *B. coli* by the fact that they gave acid but no gas when grown in milk sugar and grape sugar. They gave the Widal reaction with paracoli agglutinising serum from a previously treated guinea-pig. Infection of the urine took place, but the bacilli could not be cultivated from the fæces. The complement fixation test

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[1] Shaw, H. B. (January 22, 1908), "Coli-Bacilluria." *Clinical Journal*, London.

[2] Porter and Fleischner (November, 1910), *Arch. of Ped.*

[3] von Benezur, G. (November 19, 1908), "Kleiner Beitrag zur Frage der Identität des Typhus- und Coli-Bacillus." *Cent. für Bakt.*, I. Orig., Vol. XLVIII.

[4] Lippeus, A. (January 16, 1909), "Sur une réaction différentielle du Bacterium coli et du bacille typhique." *C. R. Soc. Biol.*, Vol. LXVI.

[5] *Archiv. Real Instit. Bact. Camara Pestana*, Lisbon. (December, 1908), Vol. II., Part 2.

[6] Castellani, A. (March 19, 1910), "Note on the Intestinal Bacteriological Flora of Normal Individuals in the Tropics." *Cent. für Bakt.*, I. Orig., Vol. LIV.

[7] Burri, R. (April 6, 1910), "Zur Frage der 'Mutationen' bei Bakterien der Coligruppe." *Ibid.*

[8] Schütze, A. (June 12, 1910), *Wien. Med. Klin.*

is able to differentiate between *B. coli* and *B. paracoli*, while the symptoms caused by the latter were at first vomiting, diarrhœa and fever, passing into a general septic infection. Urotropine in doses of 30 grains a day was efficient in clearing the urine. One mentions this case at some length, as it may have an important bearing on cases of pseudo-enteric fever in the Sudan and elsewhere in the Tropics.

Wilson,[1] in a paper on variation amongst bacteria, cites a case where from a former typhoid carrier there was isolated a bacillus which formed acid but no gas in glucose media and which fermented lactose at 22° C. but not at 37° C. As it formed some gas from mannite, he likens it to his anærogenes colon bacilli which he regards as connecting links between the *B. coli* and the *B. typhosus* group of micro-organisms.

A review of several recent papers on the rôle of *B. coli* as a pathogenic agent, on intermediary and allied forms and on paracoli bacilli, will be found in the *Centralblatt für Bakteriologie, Referate*, for December 21, 1910.

I think it may now be of service to look at a few papers dealing with some of the other more important normal or abnormal bacteriological tenants of the intestinal tract. In not a few cases the more we find out about them the greater importance they would seem to assume. A paper on the "Enteritidis" group may merely be mentioned,[2] as it will be reviewed under another heading. It gives the two sub-groups into which these bacilli may be classed.

(*a*) *B. enteritidis*, type I. (Flügge-Aertryck), *B. paratyphosus.*

(*b*) *B. typhi murium*, the bacillus of hog-cholera and *B. psittacosis.*

(*c*) *B. enteritidis*, type II. and the rat-pathogenic bacteria (*page* 392).

The importance of these organisms lies in their connection with epidemics of food-poisoning.

The important question of the permeability of the intestinal wall to microbes has been the subject of considerable attention, more especially as regards the tubercle bacillus. Nasaroff[3] worked with this organism and with *B. prodigiosus* and found that the normal intestinal wall is, to some extent, permeable, but the few organisms which traverse it under these conditions perish where they remain localised in the lymphatic system. It is only when mechanical injury, toxins, etc., have produced lesions in the small vessels and thereby established a communication between the lymphatic and circulatory systems that one finds a direct passage of microbes from the intestine into the blood stream.

A very interesting research is that carried out by MacNeal, Latzer, and Kerr[4] on the fæcal bacteria of healthy men. One must be content with quoting a few of their conclusions. They found that about 70 per cent. of all the bacteria in adult human fæces are Gram-negative. Gram-positive rods are constantly present, multiplication takes place in the intestine, and there are several species of bacteria whose normal habitat is the human bowel. Free spores are constantly present, and thin flexible spirals are frequently found. Sporogenic ærobes and anærobes both exist, and *B. welchii* is a normal constituent of the fæcal flora. Death is constantly taking place amongst these intestinal bacteria, and their destruction accounts for the variation in the number of cultivable *B. coli.*

Korentschevsky,[5] elaborating the work of Metchnikoff on the intestinal flora, directs attention to the importance of *B. putrificus* and *B. perfringens.* These organisms can produce toxins capable of traversing a Pasteur-Chamberland filter, and these toxins are absorbed from the large intestine and produce the phenomena of auto-intoxication.

The intestinal streptococci are of most interest from the point of view of the water bacteriologist, but brief allusion may here be made to the work of Winslow and Palmer,[6] who find that the chief types of streptococci in the human intestine are *Strept. mitis*, which

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[1] Wilson, W. J. (December 17, 1910), "Variation among Bacteria." *British Medical Journal.*

[2] Mühlens, P., Dahm, and Fürst (October 10, 1908), "Untersuchungen über Bakterien der Enteritis-Gruppe (Typus Gärtner und Typus Flügge), insbesondere über die sogenannten 'Fleischvergiftungserreger' und die sogenannten 'Rattensehädlinge.'" *Cent. für Bakt.*, I. Orig., Vol. XLVIII.

[3] Nasaroff, J. (1908), "Études eritiques et expérimentales sur la question de la perméabilité de la paroi intestinale pour les mierobes." *Thèse.*

[4] MacNeal, W. J., Latzer, L. L., and Kerr, J. E. (1909), "Fæcal Bacteria of Healthy Men." *Journal Infectious Diseases.*

[5] Korentschevsky, V. (1909), "Contribution à l'étude de l'autointoxication gastro-intestinale." Quoted in *Bull. de l'Inst. Past.*, Vol. VII., p. 575.

[6] Winslow, C. E. A., and Palmer, G. T. (January 15, 1910), "A Comparative Study of Intestinal Streptococci from the Horse, the Cow, and Man." *Journal Infectious Diseases.*

Bacteriology— *continued*

ferments dextrose and lactose and *Strept. fæcalis*, fermenting dextrose, lactose and mannite. There is also a vigorous type of *Strept. equinus*, the characteristic streptococcus of the horse, which ferments dextrose only. In the cow, *Strept. fæcalis* is absent, but the other two are present, as is a *Strept. salivarius* which ferments dextrose, lactose and raffinose. The possible application of these facts to water work is self-evident.

A case of some interest is that recorded by Bottkey,[1] in which a fever simulating enteric and ending fatally was found to be due to an organism of the *Proteus* group.

Leaving now those intestinal bacteria which are amongst the most important micro-organisms, so far as tropical diseases are concerned, we propose to consider very briefly some general bacteriological subjects which experience has shown to be of interest and importance both in the Tropics and elsewhere. A long review might be written on these subjects alone. Here we can only pick and choose and trust the notes made may be of service to laboratory and other workers. We avoid, more or less, those matters adequately dealt with in the text-books.

In these days of vaccine manufacture staphylococci are much to the fore, and hence a paper by Dudgeon [2] on their differentiation deserves notice. He experimented with many strains derived from normal and abnormal conditions, but capable of classification into three main types. (1) *Staphylococcus aureus.* (2) Staphylococci between albus and aureus and *S. citreus.* (3) *S. albus* and *Micrococcus neoformans* (Doyen). As a result of cultural and agglutination tests, and the estimation of the opsonic index, he concluded that there appeared to be sufficient evidence for regarding all staphylococci as members of one species. In these days of division and species-making this is a very comforting result, and one which it is hoped may be confirmed. Dudgeon, however, is careful to point out that it would seem that *S. aureus* produces the suppurative and severe inflammatory affections and *S. albus* the mild and often conservative processes.

Taking now the allied streptococci we find Hollick [3] recording three epidemics of "septic" sore throats as due to these organisms combined with staphylococci. The symptoms were not unlike those of diphtheria and the microbes lingered in the affected throats and tended to cause adenitis, constitutional disturbance and anæmia. Anti-streptococcic serum was used in some of the cases. It is interesting that in connection with these epidemics a tonsillitis, a case of erysipelas, and one of scarlet fever occurred respectively. For work in connection with streptococcal immunisation and the effects of injection of homologous streptococci, papers in the *Journal of Infectious Diseases* for 1908 may be consulted.

Other investigations into the relationship of streptococci and sore throats will be found in papers by Harrison [4] and Kennedy.[5] The former found that he could not distinguish streptococci isolated from normal throats from those isolated from sore throats, and that cultural tests are unreliable as a means of classification. The latter examined streptococci from cases of follicular and suppurative tonsillitis, and found the brevis, medius, longus and conglomeratus types present, associated in some cases with diplococci and staphylococci. From the throat to the eye is no long journey. The question of ophthalmia falls for review later, but some points regarding the bacteriology of eye conditions may be noted here.

Brons [6] deals with Gram-negative cocci found on the conjunctiva, and records a case of xerosis of both eyes and infantile diarrhœa where the conjunctival secretions showed at first pneumococci and a few meningococci. The latter greatly increased while the former well-nigh disappeared. Other cases in which the *Micrococcus catarrhalis* was found are mentioned, and the author insists on the necessity of isolating Gram-negative diplococci of the conjunctiva, of cultivating them in sugar media, and of testing their agglutinative reaction with meningococcus serum. He points out that *M. catarrhalis* ferments neither glucose nor maltose, the gonococcus only glucose and the meningococcus both glucose and maltose.

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[1] Bottkey, C. V. (April 21, 1910), "Über eine unter dem Bilde des Typhus abdominalis verlaufende Proteusinfektion mit tötlichem Ausgang." *Deutsche Med. Woch.*

[2] Dudgeon, L. S. (January, 1908), "The Differentiation of the Staphylococci." *Journal Pathology and Bacteriology.*

[3] Hollick, J. O. (December 19, 1908), "Streptococcal ('Septic') Throats." *Lancet.*

[4] Harrison, L. W. (November, 1909), "The Streptococci of Normal and of Sore Throat." *Journal Royal Army Medical Corps.*

[5] Kennedy, J. C. (November, 1909), "An Investigation into the Micro-organisms present in Normal and Pathological Throats, with Special Reference to their Reactions to Gordon's Tests for Streptococci." *Ibid.*

[6] Brons, C. (1908), "Weitere Mitteilung über gramnegative Diplokokken der Bindehaut, besonders über einen Fall von echten Weichselbaumschen Meningokokken." *Cent. für Bakt.*, I. Orig., Vol. XLVIII.

In this connection Martin's [1] recent work deserves notice. He finds that though variations occur, cultural characteristics are of considerable service in the differentiation of these three organisms. As he says :— Bacteriology—*continued*

The following features are all highly characteristic of the *gonococcus*. Delicacy of growth and its comparative restriction to serum media of a particular reaction; a greyish-bluish-white moist appearance of surface colonies which are radially plicated and concentrically striated, and have granular centres and scalloped margins; and poor growth (slight granular deposit) in serum bouillon.

The *meningococcus* gives a more luxuriant and more rapid growth. It grows well on a wide variety of media and forms a uniform turbidity, with deposit later, in serum bouillon. Its colonies are comparatively undifferentiated greyish-white, but the delicate, almost invisible margins of young colonies are very typical.

The *Micrococcus catarrhalis* is the most opaque and active grower of the three, it being the only one which grows on gelatin at room temperature. In serum bouillon it gives a scum and granular deposit without turbidity. Its colonies have an opaque white varnished appearance; later their centres become raised and their margins crenated.

As regards fermentative activities he found that the gonococcus fermented dextrose (glucose) with the production of acid but not of gas, and dextrose alone of nineteen alcohols and saccharides and glucosides tested. The meningococcus fermented maltose in addition (acid and gas). The catarrhalis strains varied, four types being isolated. The typical fermented neither dextrose nor maltose, but some of the others were positive. It will be seen that these results agree with those of Brons, just quoted. The immunity reactions obtained were interesting, and the results are here tabulated.

(1) Normal sera may be bactericidal towards gonococci and meningococci. Of those tested (guinea-pig, rabbit, cat, human), cat's serum has proved most active on both organisms.

(2) A normal serum may be distinctly bactericidal towards meningococci, and yet have practically no effect on gonococci, *e.g.* guinea-pig and human sera.

(3) The serum of a normal rabbit may vary within short periods of time, on one occasion being actively bactericidal towards meningococci, while on another almost without action. Simultaneous observations on gonococci showed comparatively little variation in the serum.

(4) From rabbits inoculated with living cultures of gonococci and meningococci, bacteriolytic immune-bodies have been obtained which can be reactivated by feebly acting normal sera, a marked bactericidal action resulting. These immune-bodies are relatively specific; thus a reactivated rabbit *v.* gonococcus serum which has a marked bactericidal effect on the gonococcus has only a slight effect on the meningococcus.

Martin's final conclusions are that the terms *Gonococcus*, *Meningococcus* and *Micrococcus catarrhalis* not only stand for fairly definite pathogenic entities, but that they are representative of types of organisms which, though closely similar, can be differentiated by a summation of characters observed in a study of their conditions of growth, cultural appearances, fermentative properties and serum reactions. So that given, from a human source, a Gram-negative organism of appropriate morphology, it is possible to identify it by bacteriological laboratory methods. As has been shown, the vast majority of these pathogenic Gram-negative organisms conform to fairly distinct types, although within each type considerable variations occur. Occasional variants are, however, met with which deviate further from the mean than usual, and to which there is difficulty in allocating definite names. The very existence of these borderland organisms invalidates, in the eyes of some, the claim of the above types to specific rank, and hence to distinctive names; but in the present state of knowledge, until systematists are more agreed as to what exactly constitutes a species, it is a great practical convenience to retain the names, more particularly as borderland organisms are only very rarely encountered in practice.

The paper enters into useful particulars as regards the preparation of sugar media, and gives an excellent list of references. In the *Referate* of the *Centralblatt für Bakteriologie*, 1909, Vol. XVII., p. 670, will be found lists of organisms associated with pathological states of the conjunctiva. Diplo-bacilli, and especially those of Morax-Axenfeld, play an important part, as do staphylococci and, to a less extent, pseudo-diphtheritic bacilli and the Koch-Week's bacillus. It is perhaps worth noting that a case of streptococcal conjunctivitis in a new-born infant has been recorded. In the last review some notes on the bacteriology of the common cold found a place, and this complaint, not infrequent in tropical countries, may again claim brief attention.

Allen [2] gives an account of its pathology and treatment, considering also the bacterial flora of healthy throats and noses. The technique employed for the bacteriological examination is given in detail, and very interesting accounts of vaccine-therapy are submitted. The summary may well be quoted as follows :—

(1) It has been shown that there are at least five organisms capable of the production of an attack of acute nasal catarrh—*viz.*: (1) the *bacillus influenzæ*; (2) the *bacillus septus*; (3) the bacillus of Friedländer; (4) the *micrococcus catarrhalis*; and (5) the *micrococcus paratetragenus*.

(2) These may be present in the naso-pharyngeal space in a certain percentage of cases which exhibit no pathological features; increase of virulence and lowered resistance of the tissues may then light them up into activity. In other cases the infection is one from without.

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[1] Martin, W. B. M. (July, 1910), "The Isolation of the Gonococcus and its Differentiation from Allied Organisms." *Journal Pathology and Bacteriology*, Vol. XV.

[2] Allen, R. W. (November 28 and December 5, 1908), "The Common Cold; its Pathology and Treatment." *Lancet*.

Bacteriology— *continued*

(3) Each organism produces its own type of cold, and a differential diagnosis of the organism is possible from a consideration of the clinical features; this is more difficult should the infection be a multiple one.

(4) This differential diagnosis is of considerable value both in prognosis and in treatment.

(5) Chronic nasal catarrh is probably always due to infection by the bacillus of Friedländer, unless the Eustachian tube and middle ear be involved by the *Micrococcus catarrhalis;* chronic tracheal catarrh to infection by the *Micrococcus catarrhalis* or *Micrococcus paratetragenus* to which secondary infection by staphylococci, streptococci, pneumococci, and other pathogenic organisms may be superadded.

(6) For infection local defect of opsonin, and for cure increase of opsonin, are probably necessary conditions.

(7) By means of the injection of the corresponding bacterial vaccines an attack of acute cold due to any given organism or organisms can be considerably shortened and complications be probably prevented.

(8) In a similar manner chronic infections may be cured.

(9) By injection of the vaccines of the several organisms in appropriate doses and at appropriate intervals, considerable if not complete immunity against future attacks of acute cold may be secured. In those who are very susceptible and fall victims to every epidemic that may occur, the best procedure probably is systematic immunisation every four to six months against all the "cold" organisms, and special immunisation against the particular organism or organisms which may be responsible for the appearance of subsequent epidemics against which protection is desired.

Benham[1] has also returned to the subject. He mentions *M. catarrhalis*, *M. paratetragenus*, *B. septus* and *B. friedländer* as causative organisms, while *B. influenzæ* and the pneumococcus may also play a part. The first named is usually associated with a very irritable cough, accompanied by scanty and viscid pharyngeal expectoration. Kühn's views on the prevention of cold are quoted in the *British Medical Journal*, November 20, 1906.

He seems to think that a cold is not usually caught from another person, but that a chill affords to microbes already in the nose, throat, or mouth the conditions favourable to their activity. This it does by producing an alteration in the cutaneous circulation, and indirectly modifying the usual resistance against infections. He adduces evidence in support of the lessening of bactericidal power in an organ in which the quantity of blood is diminished by contraction of the vessels. From an examination of the conditions in which cold is applied for a short or long time, he concludes that if short exposure to cold is followed by a reactionary dilatation of the vessels it never produces the state favourable to infection, the fortifying effect being due to the flushing of the part with blood in the reaction stage. In dealing with plans for hardening the body to resist the noxious influences of cold he utters a word of warning against exaggeration. The body must be kept warm, and this is particularly true in the case of children. He does not approve of cold-water hardening for very young children, but advises the gradual resort to cold bathing at a later age. Throughout his articles he preaches moderation, and advises the use of cold water, fresh air, exercise in the open air, and so on, in such measure as the individual can easily tolerate without feeling a sensation of coldness or discomfort.

A later note by Allen[2] deals in greater detail with the pneumococcal variety. As the pneumococcus is a frequent cause of illness in badly-constructed prisons and barracks in the Sudan and elsewhere, this subject may be considered a little more fully than usual. The author says :—

This pneumococcal cold is clearly differentiated from the other varieties. It would appear to begin with slight cough, located in the upper part of the trachea. This extends within two to three days both downwards into the bronchi and upwards in the larynx; later the bronchioles and naso-pharyngeal space are also involved. Malaise is pronounced, the temperature may rise to 102°–103° F., there may be slight frontal headache, the cough becomes very bad and may be pronouncedly paroxysmal, and the secretion of mucus, which is clear, viscid, and jelly-like at the beginning and later, perhaps, of a bright yellow colour, is very profuse. Hearing, taste, and smell may be very markedly impaired, the former from extension to the Eustachian tube, the latter from that to the turbinal bones. The inferior meatus of the nose may completely escape involvement, with the curious result that, despite copious nasal secretion and pronounced engorgement of the mucosa of the nasal septum and that of the middle and superior turbinal bones, nasal respiration may be comparatively free. The subacute stage may be prolonged into several weeks, during which the nasal and bronchial secretion may continue very profuse and blood-stained, and hearing, taste and smell remain much impaired. The mixed infection by means of the *M. catarrhalis* and *M. paratetragenus* may complicate the clinical picture. Treatment upon general lines is rather unsatisfactory, and the response to vaccine-therapy not so prompt as in the other varieties of the "common cold." Due attention must, of course, be paid to the various organisms in the cases of mixed infection. The dose of pneumococcus should not exceed 50,000,000 for a first injection, but may be combined with 50–75 millions of *M. catarrhalis* or *M. paratetragenus*. Ten days later a dose of double this amount may be safely given. In this way the duration of even a severe attack may be confined within 14 to 17 days or less.

An interesting paper on draughts and colds is that by Macfie,[3] who admits that draughts may occasionally play an auxiliary part in the production of colds, but thinks they are easily deprived of their dangers and should be favoured rather than feared. As he points out, an endeavour to escape draughts only favours the growth of bacteria and renders dangerous a draught that otherwise might be quite harmless. He is the enemy of stuffy rooms and stuffy churches, and believes the skin is meant to be exposed to moving air currents and to vicissitudes of heat and cold.

Blood culture work is becoming more and more important both in temperate and

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[1] Benham, C. H. (August 28, 1909), "The Bacteriology of Common Colds." *British Medical Journal.*

[2] Allen, R. W. (February 13, 1909), "The Present Epidemic of Common Colds." *Lancet.*

[3] Macfie, R. C. (January 14, 1911), "Draughts and Colds." *British Medical Journal.*

Bacteriology—*continued*

tropical countries. While the subject will be considered in its relation to enteric and other fevers, some mention of it may here be made. Lafforgue[1] records a new method whereby the blood is added to citrate of soda solution in the proportion of 1 drop of the citrate solution to one-fifth up to 1 c.c. of blood. The mixture is then centrifuged and the clot only placed in broth. Thanks to the absence of serum the quantity of broth employed may be greatly reduced (10 to 20 c.c. to 2 c.c. of blood clot). It is said that growth always occurs in cases of human septicæmias, being slow in the case of fragile organisms like the pneumococcus and rapid and active in the case of *B. typhosus*, *B. coli*, etc. The supernatant liquid is generally sterile, but in certain cases is charged with microbes.

A still more recent method is that of Meyerstein and Rosenthal,[2] who, in order to keep the blood fluid, thus preventing the loss of organisms in the fibrin clot and yet at the same time preventing any deleterious action upon them by the addition of citrates or oxalates, advocate the admixture of the blood with common salt. In practice they use small, sterilised Ehrlenmeyer flasks or Schottmüller bottles containing each 0·5 gramme of powdered NaCl. To each is then added 10 c.c. of blood obtained by venesection.

What would seem to be a useful routine method for the bacteriological and cytological examination of sputum has been described by Eckenstein[3] as follows: "Films are carefully made from recent sputum, precautions being taken to avoid crushing; they are stained with carbol-fuchsin and gently heated in the usual manner. Decolorisation is effected by means of 20 per cent. sulphuric acid, and the specimen is washed in 95 per cent. alcohol and in distilled water. It is counterstained for one or two minutes in a solution of the precipitated stain of Giemsa dissolved in methyl-alcohol, then a few drops of distilled water are added and the specimen is shaken for about a minute, and then washed in distilled water. The stains of Jenner, of May and Grünwald, and of Leishman give similar results, and they may be combined with ordinary Giemsa stain diluted to 1 in 20. By this means the various cells, such as lymphocytes, polymorphonuclear leucocytes, and epithelial cells, found in sputum, can be differentiated and their percentage determined. Mucus is stained violet, fibrin greenish, and albuminous exudates bluish, while tubercle bacilli are stained red and other organisms blue. The same process may be applied to other pathological exudates and fluids."

Considerations of space forbids a much lengthier view under the comprehensive heading "Bacteriology," but some notice may be taken of recent work on the relation of bacteria to certain foodstuffs. A paper which is certainly of practical interest is that by Lange,[4] who appears to have proved that coli, typhoid and paratyphoid bacilli, *B. enteritidis* (Gærtner) and *B. botulinus*, can pass through the intact shells of eggs and even get into the yolk. The power of penetration appears to depend to some extent upon the intensity of the motion of the bacilli themselves.

Pennington[5] has found that eggs may harbour microbes. Of 57 eggs examined 7 were sterile, in 18 the yellow showed most germs, in 11 the white was most contaminated, and in 21 the distribution was approximately similar. In 100 eggs examined 36 microbic species were isolated, amongst which streptothrices and even yeasts were present.

Poppe[6] deals with the same subject in more detail. He finds eggs laid by non-fecundated fowls more often sterile than those laid by fecundated birds. *M. albus* is the most frequently found organism both in the yellow and the white, and streptococci are not uncommon. The author believes the more motile bacilli, *i.e. B. paratyphosus B*, may penetrate the shell, and also points out how this organism, which resists desiccation and may remain living for 35 days in dried excrement, may possibly contaminate eggs which become soiled.

The question of bacteria in meat will be found discussed under "Food."

Work by Sartory and Fillassier[7] has shown the great number of micro-organisms which is found adhering to raisins, strawberries, and other fruits as exposed for sale in the ordinary way and when hawked about by vendors. It also demonstrates how greatly they are reduced

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[1] Lafforgue, M. (October 24, 1908), "Un procédé économique d'hémoculture." *C. R. Soc. Biol.*

[2] Meyerstein, W., and Rosenthal, L. B. (July 5, 1910). *Münch. Med. Woch.*

[3] Eckenstein, K. E. (February 7, 1909), *Gaz. Hebd. Sci. Méd. de Bordeaux.*

[4] Lange, R. (1908), *Arch. f. Hyg.*, Vol. LXII., quoted in *Journal Royal Institute Public Health*, Vol. XVI.

[5] Pennington, E. (January, 1910), "A Chemical and Bacteriological Study of Fresh Eggs." *Journal Biological Chemistry.*

[6] Poppe, K. (June 2, 1910), "Zur Frage der Übertragung von Krankheitserregern durch Hühnereier. Zugleich ein Beitrag zur Bakteriologie des normalen Eies." *Arb. a.d. Kais. Gesundheitsamt.*

[7] Sartory A., and Fillassier, A. (October 30, 1909), "Les fruits porteurs de microbes." *C. R. Soc. Biol.*

Bacteriology—*continued*

by washing. It might be interesting to see the effect of tropical conditions on such infections. Remlinger and Nouri [1] have answered in the negative a question which is sometimes asked, *i.e.*, "Can pathogenic microbes from the soil penetrate into the interior of vegetables?" Other experiments by the same authors [2] show that such organisms may, under certain conditions, gain a lodgment on the stems or leaves, but this is not of much practical importance in ordinary cultivation.

Auche [3] has carried out experiments which go to show that bread properly baked is to be regarded as an aseptic article of diet. This, at least, applies to a loaf one kilogramme in weight and to the smaller bread preparations, rolls, etc.

An interesting investigation [4] into the possible existence of infectious bacteria upon telephone mouthpieces has recently been conducted. After fifty separate examinations, with entirely negative results as regards bacilli of diphtheria and tuberculosis, it is stated that

> As the method pursued was also likely to detect other pathogenic bacteria, but failed to do so, it may be concluded that the telephone mouthpieces did not, or at least did not conspicuously, harbour infectious microbes.

One cannot end this section better than by making reference to Houston's [5] address on the bionomics of pathogenic organisms and its bearing on the spread of disease. He lays stress on the living storehouses and factories of pathogenic bacteria, and a few points may well be quoted. He says: "The danger of a polluted soil and subsoil rests, in my opinion, almost solely on the possibility of water or food becoming accidentally infected therefrom." Again, as regards air infection, he says: "In diseases of proved microbial origin, apart from the setting free of 'droplets' of saliva and the detachment perhaps of particles of scurf, it is difficult to see how a patient can continuously produce an infective atmosphere even in his immediate environment." His fiat on that ancient bogey, sewer air, is decisive, for he states: "If sewer air, then, were charged with *B. coli*, the occasional accompanying presence of specific bacteria might be conjectured. But knowing that it is not, I can only regard the attributing of *direct* pathological significance to sewer air as a fetish of the past." As regards the part played by water, the fact that pathogenic bacteria do not multiply in this medium, but tend fairly rapidly to lose their vitality, is emphasised. As regards solid foods he cites contamination from flies and the dangers of uncooked vegetables and raw shell-fish, the latter being "concentrators" of pollution. It is noted, however, that "whatever be the infection conveyed to solid food it is probably limited to the actual dose of infective material, for the reason that it is unlikely, generally speaking, that multiplication takes place." In liquid foods, however, multiplication can take place, and milk is cited as a good example of an agent which, if infected, may greatly increase the danger of a widespread infection.

Additional Notes

Willett [6] makes the following interesting remarks on the vaccine treatment of coryza:—

> My experience of the vaccine treatment of coryza is eminently satisfactory—marked and rapid improvement in symptoms, and gain in weight especially. A careful bacteriological examination of the nasal discharge is all-important. If the predominant organism can be isolated and pure vaccine made so much the better; but if two or more organisms are found in anything like equal amounts, a mixed vaccine is advisable containing them all, so as to provide for the varying resistance of a patient, which seems to fluctuate at different dates. I am of opinion that far more important than merely subduing the symptoms is the getting rid of the toxæmic state which these cases so often show, and which I for one have never till quite lately fully apprcciated. The damage to the general health produced by constant nasal catarrh seems out of all proportion to the condition itself, and is, to my mind, the greatest argument in favour of vaccine treatment. The rapid production of immunity is the object to be aimed at (tinkering with ineffective doses is so much waste of time); begin with a small dose, and double it every three days till either a reaction of some sort is produced (for example, rise of temperature) or the highest advisable doses of the particular organism have been reached. Should *M. catarrhalis* be present, the immunizator will very likely notice marked attacks of low spirits and melancholy after the injections; but this is to be regarded as the surest sign that he is on the right track, and that success is at hand.

Many of the recent papers on streptococci and streptococcal diseases will be found reviewed in the *Centralblatt für Bakteriologie, Referate*, for March 11, 1911 (Vol. XLVIII., No. 25), while

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[1] Remlinger, P., and Nouri, O. (1910), "Les microbes pathogènes du sol peuvent-ils pénétrer à l'intérieur des végétaux?" *C. R. Soc. Biol.*

[2] *Idem.* "Les microbes pathogènes du sol peuvent-ils être entraînés à la surface des végétaux?" *Ibid.*

[3] Auche, B. (February 1., 1910), "De la destruction par la cuisson des agents pathogènes contenus dans le pain. Le pain est un aliment aseptique." *Réunion biol. de Bordeaux.*

[4] *Report Government Bureau of Microbiology for* 1909. New South Wales, Sydney.

[5] Houston, A. C. (November 12, 1910), "Discussion on Recently Acquired Knowledge concerning the Bionomics of Pathogenic Organisms and its Bearing on the Spread of Disease." *British Medical Journal.*

[6] Willett, G. (February 25, 1911), "Vaccine Treatment of Coryza." *Ibid.*

Bacteriology—*continued*

Gordon's [1] latest views on the value of his differential tests is worthy of attention. He deals with Walker's criticism, upholds his tests, and points out that—

in carrying out the tests it is essential that—

(1) The sugars, etc., should be pure. I procure mine from either Merck or Kahlbaum, for the products of English manufacturers are, I regret to say, not to be relied upon in this sense.

(2) It is essential that the streptococcus should be an absolutely pure culture, *i.e.* derived from a subculture of a single colony.

(3) Convincing evidence of growth is necessary before marking a reaction as negative. In testing the characters of streptococci in this way it is essential to inoculate the medium profusely. Streptococci, as all who have worked with them on a large scale must know, are very delicate organisms, and are exceedingly liable to die out. So much is this the case that more constant results will be obtained if, when preparing a subculture for testing, this subculture be made in broth, and the inoculations made by using a sterile 1 c.c. pipette instead of the platinum loop, and by allowing a drop of the broth culture to fall into the "sugar" tube by this means. Occasionally a delicate streptococcus, recently isolated from the blood or tissues, does itself more justice in the tests if the tubes contain a little sterile diluted ascitic fluid or blood serum (Hiss).

Bacteriologists will find a paper by Penfold [2] on variability in the gas-forming power of intestinal bacteria useful, but it is rather too technical for review here. An important paper on the classification of the *B. coli* group is furnished by Jackson.[3] As it is not written merely from the aspect of the water bacteriologist his suggestive conclusions may find a place. He says :—

(1) A study of this classification shows that 13 out of 17 known varieties of *B. coli* have been isolated from fæces or diseased conditions, and that 7 of these varieties have been isolated from water. Of the 7 varieties isolated from water, 4 would conform to so-called "typical" *B. coli*, in spite of the fact that they are here grouped under three distinct species, *B. communior*, *B. communis*, and *B. acidi-lactici*. It is evident that the so-called "typical" *B. coli* does not exist as such, but that the entire group is typical of fæcal contamination when water or milk examinations are to be considered.

(2) All the known members of this group give positive gas tests with lactose bile, while no other known species gives such a test except *B. welchii*, a pathogenic bacterium also of fæcal origin. This may be readily distinguished from the *B. coli* group by its appearance under the microscope after growing in lactose bile, when long strings of bacteria considerably larger than those of the *B. coli* group are shown. Also unlike all members of the *B. coli* group, *B. welchii* gives a negative test with esculin solution. It usually gives more rapid and active gas production in lactose bile than does *B. coli*. It is also distinguished by being obligate anærobic.

(3) The importance of this classification from a medical point of view is shown by the fact that a vaccine made from *B. communis* B was not effective in cases of urethritis and cellulitis when the infection was from *B. ærogenes* A2. It is evident that different members of the *B. coli* group may not be used indiscriminately for the production of vaccine, but that the variety of the *B. coli* causing the infection should be known, and should be the one chosen for this purpose. The above classification readily facilitates the identification of any specific variety.

(4) The classification of bacteria into main groups according to motility widely separates the most closely allied forms. Winslow has discarded this classification for the Coccaceæ, and called attention to the fact "that this property is not correlated with any other character—arising independently in forms exactly resembling non-motile forms in every other respect." Classification by motility would widely separate three of the varieties of *B. ærogenes* herein given from the other two known varieties, whereas their description shows an unusually strong natural relationship. A classification based first on form and grouping of cells, second on the relation of their growth to air, third on their fermentive characteristics and, finally, on general cultural and morphological characteristics and biochemical reactions, would bring allied species and varieties into closely related groups. Carrying out this idea the next group to be classified would be the facultative anærobic bacilli which ferment dextrose with gas production but do not produce gas in lactose. Then would follow a classification into groups of those facultative anærobic bacteria which produce acid but no gas when grown in the various sugar media. Just as in qualitative chemistry allied elements are brought together into groups by the reactions which they produce, so in qualitative bacteriology species and varieties having natural relationship may be brought together into groups by a classification based on their fermentive characteristics.

What Jackson has done for the *B. coli* group Glenn [4] has, to some extent, done for the *B. proteus* group. His observations, however, are more in the direction of a study of acid and gas-producing powers in sugar media, and of the ferments produced. The paper is written in English though it appears in a German journal. Cameron [5] contributes what is, in the main, a clinical paper on the persistence of disease germs in the human body. It is full of interest, and indicates how streptococci, staphylococci, *B. typhosus*, the tubercle bacillus, *Treponema pallidum* and *Amœba histolytica*, may all lurk in the infected body and, under

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[1] Gordon, M. H. (1911), "The Differentiation of Streptococci." *Journal Pathology and Bacteriology.*

[2] Penfold, W. J. (February, 1911), "Variability in the Gas-forming Power of Intestinal Bacteria." *Proceedings Royal Society of Medicine*, Vol. IV., No. 4.

[3] Jackson, D. D. (March 6, 1911), "Classification of the *B. coli* group." *Journal Infectious Diseases.*

[4] Glenn, T. H. (May 18, 1911), "Variation and Carbohydrate Metabolism of Bacilli of the Proteus Group." *Cent. für Bakt.*, I. Orig., Vol. LVIII., No. 6.

[5] Cameron, H. C. (April 29, 1911), "Persistence of Disease Germs in the Human Body." *British Medical Journal.*

Bacteriology— *continued*

certain conditions, awake to activity. He might have added the bacillus of tetanus to the list, for it has been found that tetanus spores can exist in the body in cases where the primary infection gave rise to no symptoms. These spores, however, retain their virulence (*see page* 360). In the case of protozoa the infective granules, which doubtless many of them shed, may play the same rôle as bacterial spores, while the occurrence of granules in bacteria may possess a special significance in this direction. Hence the value, apart from other considerations, of a recent paper by Dobell [1] on the cytology of the bacteria. The great pathogenic importance of *Bacillus pyocyaneus* in the Tropics is well brought out in a paper by Minett and Duncan,[2] who give a formidable list of the serious conditions with which they have found it associated. All of them were of a suppurative nature. For those familiar with German a reference is given to a paper by Klodintzky,[3] which is of the nature of a review of the blood examination methods for the bacteriological diagnosis of the infectious diseases. The methods applicable both to the living and dead body are described.

Beri-Beri. In the First Review Supplement one wrote : " The vexed question of the precise etiological factor determining this disease still remains unsettled." So rapid is the march of events in tropical medicine that, if this statement cannot now be absolutely contradicted, there are good grounds for believing that it is no longer true. This, in large measure, is due to the researches of Fraser and Stanton,[4] a brief consideration of which leads us to review those papers which deal with what may be called the " rice " aspect of beri-beri.

Working on lines originally suggested by Braddon, carrying out feeding experiments on fowls and observations on gangs of coolies and on rice grains in the Federated Malay States, they issued in 1909 the following summary of their work :—

(1) Beri-beri is a disorder of nutrition, and, as it occurs in this country, is associated with a diet in which white rice is the principal constituent.

(2) White rice as produced in the mills here commonly makes default in respect of some substance or substances essential for the maintenance of the normal nutrition of nervous tissues. These substances exist in adequate amount in the original grain and in superabundant amount in the polishings from white rice.

(3) The estimation in terms of phosphorus pentoxide of the total phosphorus present in a given rice may be used as an indicator of the beri-beri-producing power of such rice when forming the staple of a diet in man. The prevention of beri-beri in this country will be achieved by substituting for the ordinary white rice a rice in which the polishing process has been omitted, or carried out to a nominal extent, or by the addition to a white rice diet of articles rich in those substances in which such white rice now makes default. One such article which is cheap and may readily be obtained is the polishings from white rice.

The use of parboiled rice (rice treated by soaking, steaming, drying and milling, but which still retains fragments of pericarp), as suggested by Dr. Braddon, will achieve a like result, provided that the polishing process is not carried beyond the limited extent now customary.

The later researches and conclusions of these authors [5] are of additional interest and importance, especially as a deficiency in fat in the dietary had been advanced as a cause of the disease. They state that—

(1) White polished rice, when forming the staple of the diet in man, has been shown to cause beri-beri.

(2) Such white polished rice when fed to fowls produces in them a disease closely analogous to beri-beri in man. This reaction has been taken in this, and previous researches, as a test of the beri-beri-producing power of a given rice when it forms the staple of a diet in man.

(3) The addition of rice polishings to a diet of white rice is an effective preventive of the development of polyneuritis in fowls. Rice polishings comprise from 8 to 10 per cent. by weight of the original grain.

(4) The substances contained in polishings which are effective in preventing polyneuritis are soluble in 0·3 per cent. hydrochloric acid, and are not precipitated from the solution on the addition of 95 per cent. alcohol in quantity sufficient to make the resulting mixture of proof-spirit strength. These substances comprise 16 per cent., or less, by weight of rice polishings, or 1·6 per cent., or less, by weight of the original unpolished rice grain.

(5) The fats which are contained in rice polishings in comparative abundance have been proved of no importance in preventing polyneuritis.

(6) Phosphorus compounds equal to 85 per cent. of the total phosphorus content have been proved to be unimportant in preventing polyneuritis.

Evidence is forthcoming in favour of this view, but by far the most elaborate piece of research in this connection is the large monograph by Schaumann.[6] Apart from anything

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[1] Dobell, C. C. (April, 1911), " Contributions to the Cytology of the Bacteria." *Quarterly Journal of Microscopical Science.*

[2] Minett, E. P., and Duncan, W. J. (June 1, 1911), " The Pathogenicity of *Bacillus Pyocyaneus* in British Guiana." *Journal Tropical Medicine and Hygiene.*

[3] Klodintzky, N. (April 19, 1911), " Die Methodik der bakteriologischen Blutuntersuchungen bei Infektionskrankheiten." *Cent. für Bakt.*, I. Orig., Vol. LVIII., No. 4.

[4] Fraser, H., and Stanton, A. T. (1909), " The Etiology of Beri-Beri." *Studies from Institute for Medical Research, Federated Malay States.*

[5] *Idem.* (December 17, 1910), *ibid. Lancet.*

[6] Schaumann, H. (December, 1910), " Die Ätiologie der Beriberi unter Berücksichtigung des gesamten Phosphorstoffwechsels." *Arch. f. Schiffs-und Tropen-Hyg. Beihefte,* 8.

Beri-Beri—*continued*

else, the literature of the subject is most fully dealt with in this publication, and the various theories considered in some detail. His earlier conclusions were mentioned in the *Indian Medical Gazette* for November, 1909, which at the time commented on their great importance in view of the epidemic dropsy (probably wet beri-beri) prevailing in Calcutta at that season. These conclusions were that nucleo-proteids are absolutely necessary for the organism, and that their absence gives rise to degeneration of the nerve fibres, polyneuritis, etc. Moulds have a great avidity for phosphorus, and in order to obtain it they break up the nucleo-proteid molecules. Schaumann insists on the greater phosphorus content of "cured," *i.e.* ordinary rice made from paddy, compared with "uncured" rice like Burma rice, which has its entire endocarp removed during husking. He believes the ordinary rice is much less apt to cause beri-beri than is Burma rice. His later work extends and confirms his observations, though he is careful to state that absolute proof of the correctness of his theory is not yet forthcoming. He traces a relationship between tropical beri-beri, ship beri-beri, scurvy, Barlow's disease, pellagra, osteomalacia and rickets, and enters very fully into the question of the phosphorus content of the human body and of divers aliments. He supplies an elaborate bibliography of the subject, and the second part of the paper is illustrated by admirable photographs of his experimental animals and birds. Any one studying beri-beri must have recourse to this standard work on the subject.

Braddon's views are well known. He believes the disease to be due to an intoxication, the toxic substance being found in stale uncured rice, which therefore must be avoided. In his latest paper [1] he states that cured rice *never* produces beri-beri, however much of it be eaten, however old, stale, broken, and even decomposed it may be. He gives a good general account of the disease, and lauds atropin in its treatment, as he believes it neutralises the effects of the toxin, which resembles muscarin in its action. He believes strychnine, arsenic, mercury and digitalis to be actually prejudicial. Although Braddon's final conclusions as regards etiology may not be correct, he has the credit of first directing attention to the rôle of rice in beri-beri, and leading the way to the later and possibly more exact researches.

Mine [2] went fully into the question of rice and beri-beri. He cited the Japanese views, that of Takaki, who believes in a poisonous principle due to fermentation in husked rice, and that of Hirota and Sakurai, who find that children of mothers who are suffering from the disease develop the symptoms, and lose them whenever they are suckled by healthy mothers or get other forms of nourishment. According to him the disease occurs where no rice is eaten. This, of course, is not against the phosphorus starvation theory.

Van Andel,[3] besides supporting the rice theory, though apparently more from the point of view of the results following unhygienic handling, mentions the frequency with which the cardiac palpitations of beri-beri are simulated by malingerers, and warns the physician in Java and the Malay States to be on the lookout in consequence.

A very excellent paper is that by Fletcher [4] who, apparently, independently arrived at the view held by Fraser and Stanton, although he did not realise that white polished rice meant phosphorus starvation. He gives the diagnostic tests employed in the Kuala Lumpur Lunatic Asylum, and some of these may be quoted :—

(1) *The gait* of the patient, if he be strong enough to walk at all, is of the usual "steppage" type common to all forms of polyneuritis where there is foot-drop. In a healthy man, as the "unemployed" foot is swung forward in walking the toes are extended in order that they may clear the ground. The beri-beric is, by reason of his paresis, unable to extend his toes. Consequently, in order to avoid scraping them along the ground he has to raise his feet higher, and he walks as though he were continually stepping over objects obstructing his path. He brings his foot down to the ground not heel first as a healthy man does, but the ball of his foot and his toes reach the ground first.

The gait of the tabetic is quite different; inco-ordination is apparent, and the heel is brought down first and with a bang, as if the patient intended to "make his mark" upon the floor. The extensor muscles are affected earlier and to a greater extent than the flexors. Many a beri-beri patient can stand and even walk so long as he keeps his legs straight; but as soon as he attempts to put any weight on them while they are flexed they collapse under him. This method of walking and the loss of tone in the muscles leads to hyperextension at the knee.

(2) *The Jongkok Test*, so-called from the Malay word "jongkok," signifying to squat down. This is a crucial test for beri-beri. The patient places both hands on the top of his head, and slowly squats down on his heels and

[1] Braddon, W. L. (1909), "Beri-Beri, its Cause, Symptoms, Diagnosis, Treatment, Pathology and Prevention." *Transactions Bombay Medical Congress.*

[2] Mine, N. (September, 1908), "Untersuchungen über den Einfluss des Reises bei Beriberi." *Arch. f. Schiffs-u. Tropen-Hyg.*

[3] Van Andel, P. (March 1, 1909). "A Contribution to the Etiology and Treatment of Beri-Beri." *Journal Tropical Medicine and Hygiene.*

[4] Fletcher, W. (May 1, 1909), "Rice and Beri-Beri." *Ibid.*

Beri-Beri—*continued*

then rises up again. If the patient be suffering from beri-beri the extensors are early affected, and it soon becomes impossible for him to perform this exercise.

(3) *Foot-drop Test.*—Put the patient in a sitting position, the leg at right angles to the thigh, and the foot flat upon the floor. Place the hand on the thigh a little above the knee, and tell the patient to extend the foot and toes. If there is much weakness of the extensors he will be unable to do so.

(4) *Wrist-drop Test.*—The forearm is bent at right angles to the arm. The elbow and wrist are kept upon the table by the pressure of the examiner's hand, and the patient is instructed to extend his hand. Weakness in the upper extremity usually appears later than in the legs. In the hand the first evidence of paresis is often manifested by an inability to extend the last joint of the thumb.

(5) *Knee Reflexes.*—These are best tested by sitting the patient on a table with the thigh well supported, reinforcement being employed if necessary.

A pleximeter or small hammer is more satisfactory as a striker than the fingers of the examiner. The loss of knee-jerks is among the earliest signs of beri-beri. The reflex is often increased for a short time before it gradually diminishes, and is then lost entirely. It is probably safe to say that the knee-jerks are absent in every case of beri-beri.

Bréaudat[1] has advanced his views as to the relationship of rice and beri-beri in a series of papers. He regards the initial cause as a vibrio allied to the *B. septicus* of Pasteur. This vibrio, he says, flourishes in hot countries, and is found in swamps and rice-fields, where it is the chief agent in producing putrefaction of the stubble. He believes that it sets up a fermentation due to butyric and propionic acids in rice, etc., in the digestive tract. He believes, further, that certain portions of the envelopes of rice have a preventive action or protective action, a view put forward by Eykmann. He regards the cause of death both in man and experimental animals as due to an insufficiency of utilisable nutritive elements and to an intoxication. Save for his views regarding the vibrio and its fermentative actions, this author's beliefs are not unlike those of Schaumann and the observers in the Malay Peninsula.

Fraser and Stanton's paper, above reviewed, will be found with illustrations in the *Philippine Journal of Science*, B., for February, 1910, and in the same number are confirmatory papers by De Haan,[2] and by Aron [3] and by Aron and Hocson.[4] The former states that the constituents necessary for the normal nutriment of the peripheral nervous system, and which are lost during the cleaning of the rice, are neither salts nor nucleins. Their character is unknown. The conclusions of the latter are so interesting that they may be quoted in full :—

(1) It is highly probable that living for an extended period on a one-sided, almost exclusively vegetable diet, which is characterised by its poverty in phosphorus and protein, may result in beri-beri.

(2) The process of polishing rice removes a fine skin and the outer layers (bran); this rice bran is rich in phosphorus, especially in its organic soluble form (phytin); the content of phosphorus of the rice is considerably reduced by the removal of the bran.

(3) Polished rice, poor in phosphorus, may cause beri-beri in man if it is the main constituent of the food; but it is harmless if sufficient other nourishment, rich in phosphorus and protein, is taken. The same polished rice causes a polyneuritis in chickens. White bread, a food of similar chemical composition as regards phosphorus and protein, cannot sustain monkeys in normal health if it forms the entire diet.

(4) The addition of phytin (the organic phosphorus compound from rice bran) considerably reduces the deleterious effect of white rice on chickens.

(5) Metabolism experiments show that a diet such as is described in this paper, which contains about 40 calories per kilo, and which supplies less than 0·2 gramme of nitrogen and 0·032 gramme of P_2O_5 per kilo of body weight, cannot meet the need of a normal man for phosphorus and protein. If phosphorus in the form of phytin or rice bran is added, a part is stored and a favourable influence on the nitrogen metabolism can also be observed.

(6) Metabolism experiments on a beri-beri patient in a fairly advanced stage of the disease show that the capability of the man to utilise the nitrogen and phosphorus in the food is reduced; he demands a higher intake of nitrogen and phosphorus than a normal person to attain nitrogen and phosphorus equilibrium. It is especially to be noted that the capability of utilising additional doses of phytin is considerably less than in that of a normal man under like conditions.

(7) While it is certain that phosphorus and nitrogen starvation cause a certain and probably a great number of diseases which we term beri-beri, there must be other factors, especially when the œdematous form is observed.

They recommend that where beri-beri is likely to occur the people should be given a large supply of fresh meat (to yield phosphorus and protein) or, in the Philippines where this is not available, a sufficiency of the native bean. The use of the rice bran itself is indicated, 50 to 100 grammes being cooked with the rice daily, as a protective or medicine. This is the cheapest and most natural supply of phytin, the organic phosphorus compound itself being much too expensive for practical use. More recent work goes to show that phosphorus starvation alone is not the cause of the disease.

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[1] Bréaudat, L. (January 12, February 9, March 9, and May 11, 1910), "Origine alimentaire et traitement du béribéri." *Bull. Soc. Path. Exot.*

[2] De Haan, J. (February, 1910), "On the Etiology of Beri-Beri." *Philippine Journal of Science*, B.

[3] Aron, H. (February, 1910), "Phosphorus Starvation, with Special Reference to Beri-Beri," I., *Ibid.*

[4] Aron, H., and Hocson, F. (February, 1910), "Phosphorus Starvation, with Special Reference to Beri-Beri," II., *Ibid.*

Beri-Beri—*continued*

In connection with the recommendation of the Philippine native bean, it is interesting to note that Pol[1] states that true beri-beri can be cured by the administration of *Katjangidjo* of the Dutch East Indies. This is *Phaseolus radiatus*, L. He recommends 150 grammes a day of the cooked beans together with sugar.

Fink[2] reports feeding experiments on young parrots, which confirm the work of Fraser and Stanton. Feeding with boiled, white milled rice produced a polyneuritis which the addition of rice polishings to the diet cured.

Interesting confirmatory observations on a large scale amongst conscripts for the Bangkok police are given by Highet in his report on the health of Siam, and referred to in the *Journal of Tropical Medicine and Hygiene* for November 1, 1910.

It is of interest to be able to refer the reader to a review[3] of a useful paper by Hooper on the composition of Indian rices. The milling processes are described, and analytical tables presented.

Passing now to papers dealing with other aspects of the disease, we find Noe and Brochard[4] drawing attention to the presence of abundant yellow pigment in the spleens and livers of persons dying from beri-beri. It is not always of malarial origin, and may be dependent upon the presence of ankylostomes in the intestine. Its abundance in certain cases of beri-beri points to a very active hæmolytic degeneration. Weinberg believes it has a double origin, *i.e.* from red cells destroyed by ankylostome toxins and by those of an unknown microbe, the cause of beri-beri. Leger believes the condition has nothing to do with beri-beri, and is solely dependent on the accompanying ankylostome infection.

Verrall[5] has recorded a case in which apparently the incubation period was at least two months. The period is generally put down as unknown. Hamilton Wright put it at from ten to fifteen days.

Le Dantec[6] has drawn attention to the presence of cigar-shaped, starch-fermenting bacteria in the fæces of beri-berics. He believes they play a part in the disease. Mathis and Leger[7] examined the stools of ten beri-berics, but failed to confirm this observation.

Bréaudat, already quoted, has recently[8] been examining the urine and blood of beri-beri cases. He finds a deficiency of organic matter in both, and reaffirms his previous contentions as to the factors causing the disease. He and Deiner in the same bulletin confirm the value of the bran of rice as a preventive and curative agent.

A paper of great interest is that by M'Laughlin and Andrews[9] on what they have named infantile beri-beri. They find that in the Philippines a large number of infants die from a disease like moist beri-beri, the etiology of which is still obscure. Post mortem, a dilated and hypertrophied right heart, congestion of all the internal viscera and anasarca were the chief features, while the symptoms were said to be chiefly dyspnœa, cardiac trouble and general œdema. These infants were almost all breast-fed, and rice was never found in their stomachs. It would seem that the wretched condition of the native mothers plays a part in the production of this curious disease, though the possible rôle of an ultra-microscopic organism cannot be excluded.

The relationship of beri-beri to scurvy has been mentioned. Monteith[10] gives a graphic account of an Australian epidemic of the former which showed scorbutic symptoms. As noted in our last Review I have seen just the reverse in the Sudan. Monteith also likens beri-beri to post-anæsthetic poisoning and fatty acid intoxication. Some interesting notes on this subject, embracing also ship beri-beri, and founded on Holst's work, will be found

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[1] Pol, J. H. (June, 1910), "Beriberi-Forschungen in den Niederländisch-Ostindischen Kolonien, besonders inbezug auf Prophylaxis und Heilung." *Archiv. f. Schiffs-u. Tropen-Hyg., Beihefte*, 3.

[2] Fink, L. G. (August 15, 1910), "Beri-Beri and White Rice; an Experiment with Parrots." *Journal Tropical Medicine and Hygiene.*

[3] In *Indian Medical Gazette*, July, 1910.

[4] Noe, F., and Brochard, V. (July 8, 1908), "Sur la présence du pigment ocre dans les organes des sujets morts de béribéri." *Bull. Soc. Path. Exot.*

[5] Verrall, P. J. (February 19, 1910), "Long Incubation in Beri-Beri." *British Medical Journal.*

[6] Le Dantec, A. (February 9, 1910), "Présence de bactéries amylozymes dans les fèces des béribériques." *Bull. Soc. Path. Exot.*

[7] Mathis, C., and Leger, M. (June 8, 1910), "A propos de la présence des bactéries amylozymes dans les fèces des béribériques." *Ibid.*

[8] Bréaudat, L. (November 9, 1910), "Sur les urines et sur le sang des béribériques." *Ibid.*

[9] M'Laughlin, A. J., and Andrews, V. L. (July, 1910), "Studies on Infant Mortality." *Philippine Journal of Science*, B.

[10] Monteith, J. (October 3, 1908), "The Relationship of Beri-Beri to Scurvy." *Lancet.*

Beri-Beri—*continued*

in the *Journal of Tropical Medicine and Hygiene* for May 2, 1910. It is asserted that any interference with Nature's method of supplying food, be it by boiling, aeration, drying, or the addition of preservatives, tends to the deterioration of the article and a diminution in its nutritive value. This, however, save in a restricted sense, seems certainly open to question.

Convy[1] cites an epidemic of beri-beri in Mauretania, where a prior scorbutic state appeared to favour the onset of the beri-beric condition. While the latter was due to faulty rice, the former seemed to be occasioned by the drinking of a water heavily charged with chlorides and salts in solution.

The relationship of beri-beri to epidemic dropsy will be found mentioned under the heading "Dropsy" (*page* 79).

Additional Notes

Recently Bréaudat and Denier[2] of Saigon have described cases occurring in an epidemic. They enter specially into the preventive and curative treatment by means of the bran of rice. They find it does not provoke any digestive trouble. A dose of 40 grammes a day exercises a protective action, but this dose will not act as a preventive in cases already showing symptoms of the disease. Forty grammes and upwards act as a curative agent, and this without any necessity for changing the diet. It is therefore a means at once simple, cheap, and readily accessible. The *Lancet* for March 25, 1911, has an interesting article on beri-beri in ships at British ports, in the course of which it is stated that—

> on the sailing ships the crews of which are Europeans, and where little or no rice is consumed, it was until lately more difficult to account for the appearance of beri-beri. These ships, owing to their slower progress, remain at sea for long periods, during which no fresh meat or vegetables can be obtained. Their dietary is of necessity made up largely of preserved food, much of it tinned. There has been brought forward recently, evidence to show that in some of the processes employed for preserving these kinds of food, the organic phosphorus is extracted or destroyed, and also that the growth of certain moulds on long-stored food-stuffs robs them of a proportion of their phosphorus. So that it appears that beri-beri may be produced by the same cause, not only among coolies in the East and Asiatic sailors aboard steamships, but also among European seamen on sailing vessels during long voyages. The deficiency of the necessary amount of organic phosphorus in the dietary produces wasting of nerve tissue which needs a certain amount of that element for its normal nutrition.

For those who are working up the literature of the subject a paper by de Jonge[3] is likely to be useful, for he reviews the various works on beri-beri published in the Dutch East Indies, and which naturally cannot be easily consulted by British workers. Mathis and Lever[4] have contributed to our knowledge of the hæmatology of beri-beri. They find an increase of the lymphocytes, and a diminution of the eosinophiles to be characteristic of well-established cases. A recent German monograph is that by Glogner.[5]

Beverages. This subject need not long detain us. Owing, however, to the custom, even more prevalent in the Tropics than in temperate climates, of beginning the day with a cup of tea, reference may be made to a short article in the *Lancet* of April 3, 1909, entitled "Tea, Veniente Die," where it is pointed out that, apart from its beneficial, stimulating properties, the morning cup may do harm. This may be so if taken strong and without milk on an empty stomach for prolonged periods, a chronic gastric catarrh being induced. A more cogent argument against the homely habit is the possibility of the tea washing down into the stomach the septic potentialities which have accumulated in the mouth overnight, and which may set up a poisoning process and a catarrhal condition. The mouth and teeth should certainly be well cleansed before any food, and more especially any warm drink, is taken. Attention may be drawn to extracts of the Proceedings of the Second International Food Congress which appeared in the *Journal of the Royal Institute of Public Health* for February, 1910. A finding as regards wine was that while pure wine could only be described as the product of the complete, or incomplete, fermentation of the juice of fresh grapes, yet the addition of foreign substances such as sulphurous acid and pure alcohol derived from malt is allowable. In the case of coffee, however, the addition of chicory in any shape or form, or the extraction of caffeine, were declared to be sophistications, and were prohibited. The use of alkali in cocoa manufacture was tolerated, but the question was referred to a Commission.

In countries like the Sudan, aerated waters are frequently tinted with colouring matters derived from coal-tar. Some of these are harmless, some poisonous, some innocuous in small

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[1] Convy, L. (December 14, 1910), "Scorbut et béribéri à Akjoucht (Mauritania)." *Bull. Soc. Path. Exot.*

[2] Bréaudat, L. and Denier (February 25, 1911), "Du son de Paddy dans le Traitement Préventif et Curatif du Béribéri." *Ann. de l'Inst. Past.*

[3] de Jonge, G. H. K. (April 12, 1911), "Note sur les travaux publiés aux Indes néerlandaises sur l'étiologie et la pathogénie du béribéri." *Bull. Soc. Path. Exot.*

[4] Mathis, C., and Lever, M. (May 10, 1911), "Contribution à l'hématologie du béribéri et du scorbut." *Ibid.*

[5] Glogner, M. (1910), "Die Ätiologie der Beriberi und die Stellung dieser Krankheit im nosologischen System." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XV., No. 8.

doses but deleterious when taken in a larger quantity. A reference, therefore, to the latest legislative work on the use of these dye-stuffs may be useful. Chassevant [1] has a paper on the subject from the French standpoint. A list of those colours which it is proposed to permit in food and drink is given. It is too long to quote here, but as beverages are usually rose, red, yellow or orange, the approximately harmless dye-stuffs of these colours may be mentioned which are recommended to be permitted for use with certain reservations. Beverages—*continued*

Rose.—Eosine, Erythrosine, Rose bengal.

Red.—Bordeaux B. Ponceau crystallised (this is used in making "Roman," a pomegranate beverage in the Sudan). Bordeaux S. New Coccine, Solid Red. Ponceau R.R. Scarlet R. Acid Fuchsin.

Orange.—Orange I., employed for making orangeades.

Yellow.—Naphthol Yellow S. Chrysïne, Auramine O.

The chemical names of these substances are given in the paper.

Bilharziasis (*vide* **Schistosomiasis**).

Blackwater Fever. I think that most of those with practical experience of this condition are now agreed that it is a manifestation of malarial infection. Certainly most of the recent work tends to confirm this view, as, for example, that of Deeks and James.[2] Plehn,[3] who states that the tendency of the European to sicken with blackwater fever depends on the length of his sojourn in the fever district, maintains that a preceding malarial infection is the indispensable previous condition of the tropical hæmoglobinuric condition. He believes, further, that the tendency must be present if the malarial poison is to be effective. This tendency, he says, is created by latent malaria in the system. The negro races are not immune. Apart from the question of avoiding malarial infection by the various measures which may be employed, he sums up prophylaxis as consisting in *systematic quinine prophylaxy*. As regards treatment, he gives quinine if parasites are found in the peripheral blood, not otherwise. In cases where a microscopical diagnosis is impossible he advises the physician to wait at least until the third day of the attack before employing quinine-therapy, because, as a rule, all parasites will have disappeared of themselves by this time, and it is well to avoid quinine if possible. As regards symptoms, he recommends for vomiting Doring's method of washing out the stomach with weak soda solution. The sucking of ice where the latter is available also does good. Hot packs for chills, lukewarm sponging for pyrexia, and, if necessary, morphia for restlessness, are all indicated. Cold sponging and antipyretics are dangerous. So is alcohol, shock of any kind, and especially all excitement.

Free flushing, the exhibition of diaphoretics and copious enemata are of value. As we are on the subject of treatment, Bellet's [4] ideas may be quoted. Following Vincent (*vide* First Review), he advocates calcium chloride in a dose of 4 to 6 grammes per ounce, or 1 to 2 grammes in normal saline subcutaneously to check the loss of hæmoglobin. He also gives it as a preventive after the administration of quinine. It is dispensed in syrup of bitter oranges and an infusion of *Filia europœa*. If the stomach is irritable, saturated chloroform water is added to the mixture. In cases with persistent vomiting the drug should be administered *per rectum*, 6 to 8 grammes in 24 hours. He reports favourably on its use, and mentions two very grave cases where 100 to 200 c.c. of the following solutions injected subcutaneously two or three times in the 24 hours appeared to cause marked benefit :—

℞	Calcii chloridi	4–5 grammes
	Sodii chloridi	10 grammes
	Aq. destill.	1000 grammes

Calomel, he says, irritates the kidneys, and castor oil or citrate of magnesia are indicated as purgatives. Dry cupping over the liver and kidneys and absolute rest are indicated, together with milk and diuretic mixtures, while the action of the skin should be encouraged by rubbing with warm vinegar or alcohol solutions, followed by dry friction. Bellet gives quinine in doses of about half a gramme, checking its deleterious action by the calcium chloride. He

[1] Chassevant, A. (June, 1910), "Colorants dont l'emploi peut être autorisé pour la fabrication des Produits Alimentaires." *L'Hygiène Générale et Appliquée.*

[2] Deeks, W. E., and James, W. M. (1911), "A Report on Hæmoglobinuric Fever in the Canal Zone." *Department of Sanitation.*

[3] Plehn, A. (October 1, and November 2, 1908), "The Cause, Prevention, and Treatment of Hæmoglobinuric Fever in Warm Countries." *Journal Tropical Medicine and Hygiene.*

[4] Bellet, E. (July 8, 1908), "Du traitement de la fièvre bilieuse hémoglobinurique des paludéens." *Bull. Soc. Path. Exot.*

Black-water Fever— *continued*

employs the hydrochlorate, and gives it in smaller doses daily during convalescence. This employment of the hydrochlorate is shown to be on correct lines by the work of M'Cay,[1] who has investigated the action of quinine salts on the osmotic pressure of the blood plasma. The sulphates lower this, and *pari passu* that of the red cells, whose envelopes therefore tend to burst. As in malaria the erythrocytes are already injured, hæmolysis is all the more likely to occur if quinine sulphate is given. Chlorides have the opposite effect to sulphates, so that quinine hydrochloride with common salt is indicated.

Celli,[2] owing to its absence of toxicity, speaks highly of quinine tannate in cases of malaria complicated by hæmoglobinuria. It is worth noting that he has seen this condition follow immediately on the administration of quinine hydrochloride. This does not support the observations just quoted, nor does the lengthy and very complete research conducted by Christophers and Bentley[3] in the Indian Duars. According to them it is solely a question of repeated attacks of, or infections by, malaria, the condition being a poisoning due to a hæmolysin acting under special conditions. Quinine in itself, they say, is innocuous, and its consistent use by a community may even diminish the incidence of blackwater fever by reducing the liability to malarial infection. There is a great deal more in their report, but it must be studied in detail. Here we have only recorded the more practical deductions from their results. A very precise account of the treatment of a severe case in West Africa from its commencement to its favourable termination is given by Queely.[4] It is a helpful kind of paper for anyone to have at hand who has to treat his first case of blackwater fever, though some would object to the administration of champagne and of calomel. Broad principles are all very well, but in a severe and acute disease like blackwater fever it is the *minutiæ* which count for so much—when to give food, when to sponge, when to give a saline injection, etc., and the details supplied appear to be on the whole sound and practical. Hearsey's well-known mixture was given.

May,[5] believing that the calcium content of the blood may be increased, treated cases successfully by citric acid—10 grains every two hours or smaller doses, and the anuria by saline enemata.

MacGilchrist[6] is opposed to M'Cay's views, for amongst other things he has found the sulphate and hydrochloride of quinine to possess about equal hæmolytic power. He thinks there may be a diminished alkalinity of the blood.

Hearsey,[7] who is an authority on the disease, and whose method of treatment by perchloride of mercury and bicarbonate of soda, has in the hands of many proved most successful, does not believe in the presence of any gross kidney lesion, and makes the following observations on the inter-relation between tropical malaria, blackwater fever, and the influence of quinine :—

(1) Malignant tertian infections in adult aborigines very rarely have a fatal termination; the mortality among Europeans and Asiatics, on the other hand, is equal to, and in some years exceeds, that resulting from blackwater fever.

(2) No case of blackwater fever has yet been recorded in a native in this country (Nyasaland), though large numbers are annually treated in the various mission hospitals for malaria.

(3) Blackwater fever is always preceded by attacks, usually several, of malaria; persons who have not had malaria do not get blackwater fever.

(4) In residential localities, where anophelines are most numerous and where malaria is most intense, blackwater fever is most common.

(5) At plantations and outlying stations where separate native locations are not always provided, malaria is more frequent, and the incidence of blackwater fever is relatively greater. And conversely, where natives are strictly segregated at a distance from European dwellings, residents enjoy comparative immunity from both malaria and blackwater fever. These points (4) and (5) are borne out by the monthly sick returns.

(6) As blackwater fever always commences like an ordinary malarial attack, it is very seldom that quinine has not been taken before the onset of hæmoglobinuria.

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[1] M'Cay, D. (1908), "Preliminary Note on Quinine Sulphate as a Factor in the Causation of Blackwater Fever." *Glasgow Medical Journal.* Also "Hæmoglobinuria and Quinine Sulphate." *Indian Medical Gazette.*

[2] Celli, A. (November 21, 1908), "Quinine Tannate for Hæmoglobinuria." Quoted in Epitome, *British Medical Journal.*

[3] Christophers, S. R., and Bentley, C. A. (1908), "Blackwater Fever." *Scientific Memoirs of the Government of India*, No. 35.

[4] Queely, J. G. H. G. (April 15, 1909), "Some Notes on Blackwater Fever." *Journal Tropical Medicine and Hygiene.*

[5] May, A. W. (August 2, 1909), "Blackwater Fever—A Suggestion for Treatment." *Ibid.*

[6] MacGilchrist, A. C. (June, 1909), "Blackwater Fever, Hæmolysis and Quinine." *Indian Medical Gazette.*

[7] Hearsey, H. (September 1, 1909), "Blackwater Fever." *Journal Tropical Medicine and Hygiene.*

(7) During the treatment of a malignant infection (clearly ascertained), blackwater fever has supervened, and the only presumptive disturbing factor has been the administration of quinine.

Blackwater Fever—*continued*

(8) After the urine has cleared during the course of a blackwater fever, hæmoglobinuria has again occasionally developed on the administration of the first small dose of quinine; the hæmoglobinuria in these instances, however, being of comparatively shorter duration.

These facts appear to indicate :—

(i.) That natives do not suffer from blackwater fever, because they have survived the malarial infections of infancy, and thereby acquired some degree of immunity, as evidenced by the relative infrequency of malarial infections among adult natives, and especially by the insignificant mortality from malignant tertian attacks.

(ii.) That as malarial infections always precede an attack of blackwater fever, there appears to be no ground for the assumption that the latter is other than a virulent form of malaria. It can hardly be a disease *sui generis*, for it occurs only after a residence of some duration in the country, in intimate association with malaria, and does not attack newcomers, which on the contrary hypothesis it would occasionally be expected to do.

(iii.) That while quinine and blackwater fever cannot rigidly be regarded as in the nature of cause and effect, yet quinine undoubtedly does appear to act as the provocative factor in a large majority of cases, as clinical experience has shown. In order to explain why malaria and quinine, alone or in association, fail to produce hæmoglobinuria in some countries where both these factors coexist, I think it may not unreasonably be surmised that in these localities the parasite does not attain the same degree of virulence as in those geographical areas where blackwater fever prevails, and where possibly the infections are more severe. And severity is, after all, a relative term, for an attack from which a native may recover without treatment may prove fatal to a new arrival.

Barratt and Yorke,[1] of the Liverpool School, carried out a lengthy investigation chiefly with the view of finding out the cause of the hæmoglobinuria. They regard the fever as malarial in origin, show that quinine would have to be given in toxic doses in order to have any direct hæmolytic action on the red cells, and that in blackwater fever the latter are not more susceptible to its action than in health. They do not find that a hæmolysin is operative at all, but believe the hæmoglobinuria to result from an accompanying hæmoglobinæmia, though they could not decide where the blood is actually destroyed. Quinine may act either by initiating or aggravating the process. Anuria, they state, is due entirely to mechanical causes, to a plugging of renal tubules by fibrin and coarsely granular casts. Their illustrations bear this out, and they enter fully into the morbid histology of the kidneys in the disease. This is a very important monograph, and is in keeping with the more recent lines of thought and treatment.

Fisher[2] cautions against the use of Hearsey's bipalatinoids (hydrarg. perchlor. and sod. bicarb.) by those unable to obtain medical help. He has seen mercurial poisoning result, and believes more in general treatment and careful nursing than in the use of drugs. He washes out his patients by the mouth and the rectum, and gives bismuth and soda to allay the gastric irritability. He also believes in calomel and quinine, and reports good results.

Cleland[3] has advanced an interesting theory, asking if the disease may not be the expression of anaphylaxis to the malarial parasite. Such a view, as he points out, would explain much that has been puzzling in the past. An article in the *Indian Medical Gazette* for January, 1910, criticises this view adversely, and may be studied for the arguments which can be advanced against it.

Turner[4] gives a useful résumé of the literature, mentioning Yersin's unconfirmed discovery of a bacillus in cases of Madagascar, and giving a good account of native African remedies, especially of *Cassia beareana*. He also mentions the methylarsenate of soda treatment, to which reference will shortly be made.

Marshall[5] gives an interesting account of a case occurring in Scotland in a patient recently returned from Africa. He believes in giving quinine if parasites are found in the blood, and of special interest is the fact that persistent vomiting was speedily checked by the application of *liquor epispasticus* over the line of the vagus on the left side of the neck. This, too, after the ordinary remedies had been tried in vain.

Harford,[6] commenting on this case, a type far from uncommon, asks what is its moral, and replies as follows :—

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[1] Barratt, J. O. W., and Yorke, W. (1909), "An Investigation into the Mechanism of Production of Blackwater." *Annals Tropical Medicine and Hygiene*, Vol. III.

[2] Fisher, W. (October 15, 1909), "Blackwater Fever." *Journal Tropical Medicine and Hygiene.*

[3] Cleland, J. B. (October 15, 1909), "Is Blackwater Fever the Expression of Anaphylaxis to a Malarial Plasmodium?" *Ibid.*

[4] Turner, G. A. (January, 1910), "A Résumé of the Literature of Blackwater Fever." *Transvaal Medical Journal.*

[5] Marshall, D. G. (May 14, 1910), "A Case of Blackwater Fever." *Lancet.*

[6] Harford, C. F. (May 28, 1910), "A Case of Blackwater Fever." *Ibid.*

Black-water Fever—*continued*

(1) That the only way to keep malaria in check by those who are liable to infection, or who show by the occurrence of attacks of malaria that they have been infected, is to take quinine.

(2) That quinine must be taken regularly or it is useless, perhaps worse than useless, for it is the erratic taking of quinine which is most likely to produce unpleasant results.

(3) That 5 grains of quinine a day is probably the best system, as any less regular system is not very likely to be rigidly carried out.

(4) That the most important time to take quinine is on return to England, and for at least three months after, especially if the weather is cold, and for an even longer period if fever develops in England.

(5) That whilst it probably is sound practice not to give quinine whilst the blackwater symptoms are present, yet quinine should be commenced in small gradually increasing daily doses immediately after. It may be added that it is the opinion of Professor Koch that if any one will do this he will not suffer from blackwater fever or malaria again.

(6) It should therefore be clearly understood that in a person who has been infected by the malignant malarial parasite there is one, and only one, prophylactic, and that is quinine regularly and persistently taken. If only this were acted upon we should hear very little of blackwater fever.

As regards the question of return to the Tropics after blackwater fever, this depends entirely upon the severity rather than the frequency of the attacks, and each case must be decided on its merits. It is certainly not the case that a man is immune after three attacks, and it is almost equally a mistake to say that "the chances of recovery from a second or third attack are . . . slight."

Frere [1] records two somewhat similar cases, agrees in the main with Harford, and states that not only is alcoholic stimulation not contra-indicated, but that it is often imperative.

Cardamatis,[2] from a result of experience in Greece and from a study of records of cases, is of opinion that quinine should on no account be given in bilious hæmoglobinuric fever. A very instructive account of cases with careful clinical observations and temperature records is given by Mayor.[3] It is worthy of study, as it gives those details and *minutiæ* to the value of which we have already spoken.

Nightingale [4] gives as predisposing factors—(1) A chill. (2) The taking of quinine—not always injudiciously. (3) Exposure to the tropical sun. He pins his faith to Hearsey's mixture, his stock prescription being :—

℞	Liq. hydrarg. perchlor.	½ drachm
	Sodii bicarb.	10 grains
	Aquæ	ad 1 ounce

Sig. Every two hours for the first 24 hours, and then every three hours till the urine clears.

At the same time he gives one grain of sodium dimethylarsenate thrice daily till the temperature is below normal for 24 hours. This soothes the gastric irritation and clears the urine "like a charm." He suggests the use of pituitary gland extract in cardiac failure, and employs stimulants if necessary, in heroic doses. In the same journal Garin [5] advocates the use of cholesterin, first introduced by Grimm in the Cameroons on account of its anti-hæmolytic action. Two to four doses of 1 gramme each are given at intervals of four to six hours. The drug has no taste and is readily absorbed. It is best given in suspension in cream or thick milk. Where there is much gastric intolerance it may be given as an intramuscular injection in oil. The author has also used it as a preventive. It is best dispensed in powder form, as it is not soluble in water and does not decompose readily. It is, however, rather expensive. The same drug forms the subject of a paper by Külz,[6] who treated a severe case by it, administering it in olive oil by Reicher's method. He thinks the method of administration is immaterial, but Grimm does not agree with him, as it is possible that cholesterin is not well absorbed when given as a powder by the mouth. The question, however, would appear to be still *sub judice*.

Additional Notes

At the beginning of this section one stated that there tended to be a consensus of opinion as to the association of blackwater fever and malaria. Recently, however, there have not been lacking papers seeking to prove that blackwater fever is a

[1] Frere, J. E. (June 18, 1910), "Two Cases of Blackwater Fever." *Lancet.*

[2] Cardamatis, J. P. (February 9, 1910), "Quelques mots sur l'étiologie et la pathogénie de la fièvre bilieuse hémoglobinurique. Devons-nous la traiter par la quinine ?" *Bull. Soc. Path. Exot.*

[3] Mayor, J. F. G. (August 1, 1910), "Blackwater Fever." *Journal Tropical Medicine and Hygiene.*

[4] Nightingale, P. A. (July, 1910), "Blackwater Fever : Further Observations." *Transvaal Medical Journal.*

[5] Garin, H. (July, 1910), "Notes on a New Remedy for Blackwater Fever." *Ibid.*

[6] Külz, L. (1910), "Beitrag zu einer Cholestearin-Therapie des Schwarzwasserfiebers." *Archiv. f. Schiffs-u. Tropen-Hyg.*, Vol. XIV., No. 23.

disease *sui generis*. Of these the most important is that by Craig.[1] Whatever may be thought of his arguments his paper makes very interesting reading, and he presents a formidable array of statements against the malarial theory, concluding as follows :— Black-water Fever—*continued*

That hemoglobinuric fever is not due to malaria I believe to be proved by its geographical distribution; by the fact that it occurs in individuals who have never suffered from malaria; and by the fact that, in many instances, neither before, during, nor after an attack can plasmodia be demonstrated in the blood, while, even at autopsy, no trace of malaria can be found.

That the disease is not due to quinine is proved by the fact that it occurs in individuals who have never taken the drug, and that in many regions where the drug is extensively used the disease is unknown.

For the following reasons I believe that it is due to a specific organism: Its geographical distribution; its numerical disproportion to malaria wherever it occurs; its occurrence in epidemics; the character of the pathological lesions; its symptomatology; the lack of conclusive evidence that it is due to malaria; and its analogy with other well-known infectious diseases.

Like Sambon, he believes it to be probably tick-borne and due to a small piroplasma. One good point he does make is to emphasise the fact that very little experimental work on animals has been carried out in this disease, and he urges very wisely that the experimental method which has led to so many valuable discoveries should be applied in hæmoglobinuric fever. Brem [2] suggests a new classification as follows :—

Type 1.—Pernicious malarial fever with hemoglobinuria. The etiology is known, and it is better that the condition or symptoms of hemoglobinuria should not receive a more prominent place in the diagnosis.

Type 2.—Erythrolytic hemoglobinuria. Our knowledge of the etiology of this type is incomplete, and until an etiologic terminology can be rationally applied, it would seem best to use one based on the mechanism of production, and on the most prominent feature of the symptom-complex.

He believes that quinine should never be given, at least in the second type. There can be no doubt there is a great deal of confusion about cases of so-called blackwater fever, and from the little I have seen of the disease I would be inclined to lay stress on the presence or absence of jaundice. If jaundice is not present the disease is unlikely to be true blackwater, or what Brem calls erythrolytic hæmoglobinuria. A good account of the pathology of the latter comes from the pen of Whipple.[3] He mentions specially the large spleen with purplish, velvety pulp, and very opaque, sharply outlined Malpighian bodies. He also speaks of the necrosis which may be a striking feature in the spleen, and the focal necrosis met with in the liver. All these points I have noted in the few blackwater autopsies I have performed or attended. Gaston and Dufougère [4] advocate the use of quinine, and record a case where, though no malarial parasites could be found by ordinary blood examination, yet after centrifugation sexual forms of *Plasmodium præcox* were discovered. One has not heard before of the use of the centrifuge in malaria or blackwater fever, and it would seem advisable to employ this method wherever possible.

A general discussion of the subject following a paper by Cardamatis [5] will be found in the same number of the French journal. Cardamatis absolutely condemns the use of quinine whether parasites are or are not present in the peripheral blood. A peculiar case which was very carefully studied is recorded by Ross, Thomson, and Simpson.[6] No other parasites besides *plasmodia* were present, and these disappeared at the onset of the blackwater. There was a peculiar relapse without hæmoglobinuria or detectable *plasmodia*. The concluding paragraphs of the paper may be quoted :—

The enlargement of the liver and the bilious vomiting might suggest derangement of the hepatic system, but they may also represent the hyperæmia of extreme activity. The fact that the liver eliminated, in its usual manner, such an enormous amount of blood pigment tends to confirm the latter hypothesis.

In conclusion, we would remark that hæmoglobinuria seems to be merely a small overflow of the freed hæmoglobin which the liver has not been able to deal with; and that some other cause other than the toxin of the *plasmodia* seems to produce both the special hæmolysis and the special fever associated with it.

Rodenwaldt [7] has recently recorded a case of blackwater in a seven-year-old child in

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[1] Craig, C. F. (1910), "Is Hæmoglobinuric Fever a Manifestation of Malaria or a Disease *Sui Generis?*" *Collected Papers American Society of Tropical Medicine.*

[2] Brem, W. (1910), "Studies of Malaria in Panama." II. "Treatment of Blackwater Fever." *Ibid.*

[3] Whipple, G. H. (1910), "The Pathology of Blackwater Fever." *Ibid.*

[4] Gaston, P., and Dufougère (May 10, 1911), "Paludisme et fièvre bilieuse hémoglobinurique." *Bull. Soc. Path Exot.*

[5] Cardamatis, J. (May 10, 1910), "Traitement de 115 cas d'hémoglobinuria chez les paludéens." *Ibid.*

[6] Ross, R., Thomson, D., and Simpson, G. C. E. (December 20, 1910), "A Case of Blackwater Fever followed by a Peculiar Relapse without Hæmoglobinuria or Detectable *Plasmodia*." *Annals Tropical Medicine and Parasitology*, Vol. IV., No. 3.

[7] Rodenwaldt, E. (1911), "Schwarzwasserfieber ohne Malariafieberanfall." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XV., No. 11.

Black-water Fever—*continued*

German East Africa. There was absolutely no evidence of a malarial attack immediately prior to the onset.

Blood. As in the last Review, this *résumé* will be limited to a few papers dealing with medico-legal work, morphology, and clinical technique.

Cowie [1] describes a method for detecting small blood-stains which is said to be very sensitive, and applicable to fresh and dry stains alike :—

The part of the cloth on which the blood spot occurs is cut out, moistened with 2 to 10 drops of water, according to the size of the stain, and rubbed with a glass rod; 2 to 10 drops of acetic acid are now added and carefully mixed, and then 1 or 2 c.c. of ether; to the ethereal liquid are added a few fragments of guaiacum resin and 20 to 30 drops of oil of turpentine. If the spot be blood a blue colour develops which persists for five minutes and then slowly vanishes. It is necessary to avoid adding too much water or ether, in order that the hæmoglobin should not be excessively diluted.

Deléarde and Benoit [2] describe a new chemical test.

Twenty grains of anhydrous potash are dissolved in 100 c.c. of water, 2 grains of phenol-phthalein added, and the whole boiled with 10 grammes of zinc dust until a perfectly colourless liquid is obtained, the solution being filtered whilst hot. It should be protected from air by a layer of liquid paraffin. The presence of blood in any liquid is shown by the production of a red colour when 2 c.c. of the liquid are placed in a test-tube and 1 c.c. of the reagent, together with 2 or 3 drops of hydrogen peroxide (12 volumes strength) added in this order without shaking. The test depends upon the presence of an indirect oxidizing enzyme in blood, which has the power of oxidizing the reduced phenol-phthalein. It is very delicate, and, though urine reduces its delicacy 1 in 10,000, gives a distinct reaction.

Delsart's [3] method of detecting blood in urine and fæces is as follows :—

Crystalline guaiacol 5 cgm. is dissolved in about 1 c.c. of alcohol, to this 2 c.c. of hydrogen peroxide (10 volumes) is added, then 4 to 6 mils. of the urine. On shaking the mixture, a bright reddish-brown colour indicates the presence of blood. The colour is completely soluble in chloroform, and on shaking out with that solvent the aqueous solution is decolourised, the chloroform becoming tinted. Fæces should be treated with a little water filtered and the filtrate made faintly acid before the test is applied.

Piorkowsky [4] mentions a simple method for differentiating human blood. If his work is confirmed it will be of great value, as the ordinary precipitin test is troublesome, and should only be conducted by one with experience, owing to the fallacies which may occur.

Into a test-tube about 6 cm. long and 8 mm. in diameter, 1 c.c. of hydrocele fluid or human blood serum (preferably the former) is introduced. In another vessel a drop of the fresh blood to be examined is diluted with 10 to 50 drops of water. This latter liquid is carefully poured into the test-tube containing the serous liquid in such a way as to form a layer. If the blood is of human origin there is formed in about half-an-hour a faintly red coloured precipitate of coagulated blood, while the supernatant liquid remains clear. Operating in the same way with the blood of any of the lower animals, no precipitate is formed, and the liquid is coloured red. Dry blood is first dissolved in physiological salt solution before applying the test.

It is interesting to note that Uhlenhuth and others [5] have applied the precipitin reaction for the purpose of determining the origin of blood found in the alimentary tract of blood-sucking insects. They have had good results in the case of bed-bugs (recognition 14 days after injection), fleas, lice, ticks and mosquitoes. They suggest its application to tsetse flies for the purpose of determining the habitual hosts of the latter. A good general account of the precipitin test as used in medico-legal work is given by M'Weeney.[6] The technique and necessary precautions are well described. So much for blood tests. We pass to the consideration of new or simplified methods of blood enumeration. Such is Loewenberg's.[7]

Dilute the blood 1 to 400, take up a drop on a round object glass, and press a cover-glass on it. Examine under the microscope, and count the number of corpuscles in the field. As two circles are proportional to each other according to the squares of their radii, the total number of corpuscles on the object glass may be computed by this formula. If the radius of the microscopic field is 0·5 mm., and of the object glass 10 mm., the object glass field thus represents 400 of the microscopic fields, and if 25 corpuscles are counted in one field, it is easy to compute the number in a cubic centimetre. If, for example, 5 c.c. of blood diluted to 400 were used, the 400 multiplied by 400 and divided by 5, and then multiplied by the number of corpuscles observed in the microscopic field, would give

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[1] Cowie, D. M. (1907), "A Comparative Study of the Occult Blood Tests, etc." *Physician and Surgeon*, Detroit and Ann Arbor.

[2] Deléarde and Benoit, A. (1908), "De la recherche chimique du sang dans les sécrétions organiques." *C. R. Soc. Biol.*

[3] Delsart, *L'Union Pharm.* Quoted in *Pharmaceutical Journal*, March 27, 1909.

[4] Piorkowsky (June 1, 1909). *Gaz. Medicale de Paris.* Quoted in *Pharmaceutical Journal*, August 14, 1909.

[5] Uhlenhuth, P., Weidaug, O., and Angeloff, I. I. (1908), "Über den biologischen Nachweis der Herkunft von Blut in blutsaugenden Insekten." *Arb. a. d. Kais. Gesundheitsamt.*

[6] M'Weency, E. J. (June 18, 1910), "The Precipitin Test in Medico-Legal Work." *Lancet.*

[7] Loewenberg, M. (March 19, 1908), "Eine neue Methode der Blutkörperchenzählung." *Deut. Med. Woch., Berl.*

the correct number of corpuscles in a single cubic millimetre. The dilution to 400 is made by mixing 10 cubic mm. of blood with 4 c.c. of a 3 per cent. salt solution.

Albert [1] has a useful paper on the technique in blood examinations. We quote in full the account of his method for counting leucocytes, both the total and the differential count in blood films at one and the same time.

It is at once evident that a method of determining the leucocyte count by a direct examination of the slide preparation, to be of value, must consist either of counting all of the cells of the spread, or of making a spread which is uniform and the various cells evenly distributed. The former would be a very tedious procedure—the latter may be quite satisfactorily accomplished by making spreads on slides by means of narrow strips of tissue paper such as may be conveniently obtained in the form of cigarette paper. Not all cigarette paper is equally well adapted for this purpose. It must not be too absorbent, nor too oily or stiff. An ordinary piece is cut in two lengthwise. The slide, which must be perfectly *clean*, is made to touch by its surface near one end a *small* drop of *freshly*-oozing blood; one end of the strip of paper is then laid on it and immediately drawn over the slide while held in a position almost horizontal to its surface. If the drop is too large, the spread will be entirely too thick. One about the size of the head of a match is about right. Experience, however, is a better guide. The spread is then stained, preferably by some method which causes the nuclei of the white cells to be clearly recognisable. For such, I prefer the use of an eosinate of methylene blue dissolved in methyl alcohol, such as Wright's or Jenner's stain. Staining with hematoxylin and eosin following fixation with methyl alcohol is also very satisfactory. We now have a spread of blood in which the spread is uniform and the various cells are quite evenly distributed. The counting of the white cells by fields, without the actual enumeration of the white cells, is liable to give very misleading results. I have, therefore, had prepared a micrometer eye-piece consisting simply of a circular piece of glass which may be dropped into the ordinary eye-piece of a microscope. This eye-piece is so ruled that it divides the visible field of the microscope into 100 equal squares. We are now ready for making the counts with the object of determining not only the relative number of leucocytes but also the differential leucocyte count. For counting, I prefer to use the one-sixth objective, and preferably a No. 2 eye-piece, although a No. 1 eye-piece may be used with as great satisfaction. The number and kind of leucocytes in a given field may be determined by a mere glance.

The following table illustrates the method of keeping a record of the counts made :—

Red Corpuscles	Leucocytes	Polymorphonuclear neutrophile leucocytes	Lymphocytes	Eosinophiles	Etc.*
300	1	1	—	—	
700	3	2	1	—	
1100	—	—	—	—	
1550	5	3	2	—	
1920	6	4	—	—	
2210	7	—	3	—	
2600	9	5	—	1	
2940	11	7	—	—	

* Etc., until one hundred leucocytes are counted

The number of the red cells of the field may be quite accurately determined by counting five of the average squares and multiplying the figure by 20. If the entire spread is very uniform it will be necessary to count the number of red cells in only several of the fields and by comparison be able to make a very good guess of the number of red cells in the other fields. The count of each field is added to the preceding count until 100 leucocytes have been counted. The percentage of the various kinds of white cells is represented by the number of cells that have been counted, and the proportion of white cells to the red cells may be determined by dividing the red-cell count by 100. Going on the supposition that the number of red cells in a cubic millimetre of a person's blood is 5,000,000, the number of white cells may be determined by dividing 5,000,000 by the figure which represents the proportion of red cells to each white cell.

It is, of course, true that we cannot be certain without an accurate count that the individual has 5,000,000 red blood corpuscles per cubic millimetre. This method does not therefore give an accurate idea of the number of white cells in anæmic individuals. On the other hand, we must recognise that it is not the single leucocyte count that is of so much value, especially in inflammatory processes, but rather the comparison of a number of blood counts made at short intervals. When such is all that is necessary, this method gives us a very accurate idea of any increase or decrease in the number of leucocytes that may be taking place, even better than the use of the hemocytometer, because the accurate use of that instrument requires an accurate manipulation, without which gross errors are liable to creep in.

As advantages, then, of determining the leucocyte count by a direct examination of the microscopical slide as proposed, over the use of the Thoma-Zeiss hemocytometer, it may be urged—First, that the method is much more

[1] Albert, H. (March, 1908), "On the Technique of Blood Examination." *Bulletin State University, Iowa*, New Series, No. 182.

Blood— *continued*

simple. The technique necessary for making this count is the same as that which is necessary for making the ordinary differential leucocyte count, and it is possible to avoid the use of the diluting pipette, mixing, spreading of the blood on the special slide and the counting of such as is necessary with the Thoma-Zeiss instrument. Second —It is more accurate in the hands of the majority of practitioners who have not received any special training in the making of blood examinations. When observing the simple precautions of having a clean slide, using freshly drawn blood and the proper kind of paper for making the spread, it is almost impossible to make a mistake as far as technique is concerned. With the use of the hemocytometer, however, errors may creep in by improper dilutions, improper mixing, obtaining the blood in an improper way from the pipette, and improper spreading on the counting slide.

I have compared the two methods in a large number of cases, and find that as far as comparative results are concerned I am able to obtain them just as well by the direct method as by the use of the hemocytometer. In the hands of students who have had but little experience in blood examinations, I have found that they obtain much more uniform and accurate results by the method of making the count directly from the stained slide as described. For accurate work or for determination of the absolute number of white cells per cubic centimetre, this method will of course never take the place of diluting pipette, but for practical work I believe it has distinct advantages.

Carruthers [1] describes another simple method of counting leucocytes. His account of it shows it to be more complicated than that of Albert, so reference to it must suffice. It would seem to be useful and not fatiguing. The simple method of Seguin and Mathis [2] for carrying out a differential leucocyte count merits mention. I have tried it, and now employ it as a routine measure. It consists simply in having 500 glass beads or balls and a sufficient number of Petri dishes each marked to represent a form of leucocyte. Then, when counting, one throws a bead or ball into the Petri dish representing the type of leucocyte encountered. One cannot overshoot the count, as one uses up all the beads. Then count the beads in all the dishes save that representing polymorphs. Divide each count by 5, you get the percentage. That of polymorphs is finally obtained by subtraction. Yakimoff [3] has modified this method by using a mechanical counter. He believes in counting 1000 cells.

Stitt [4] has devised a method of performing differential leucocyte counts on wet preparations. We quote what he says about it, but Captain Archibald, who tried it here, was not very favourably impressed by it. It seems, however, to have points which recommend it.

By employing the ordinary technique for making a count of the white blood cells, with the exception that I use a diluting fluid made by adding five drops of Giemsa's stain to 5 cubic centimetres of 2 per cent. formalin, I also am able quickly and, I am convinced, accurately to make a polymorphonuclear percentage count, or a complete differential count in addition to that of the leucocytes.

Another advantage is that blood parasites are also perfectly stained, are shown distinctly, and by reason of the larger amount of blood visible in each field, the finding of them is far less tedious than where a stained, dry film is used.

In preparing the Giemsa stain I use the original method by dissolving 0·08 gramme Azur II. and 0·3 gramme Azur II. eosin in 25 centimetres of glycerine at 60° C., then adding 25 cubic centimetres of methyl alcohol, allowing the whole to stand overnight and then filtering.

The ordinary commercial formalin and distilled water are used in preparing the 2 per cent. formalin solution.

Better results are obtained when the Giemsa solution is added to the formalin just prior to using. The staining power of the mixed formalin and Giemsa begins to diminish after a few hours, therefore it is better to drop the Giemsa solution from a dropping bottle into the formalin in a watch glass at about the time the blood count is to be made. The best results are secured when the mixing in the pipette bulb is done immediately after taking up the blood and diluent.

The usual technique in making the hæmocytometer preparation is employed, a Türck ruling being used. I count the leucocytes in the 3 upper or lower square millimetres, divide by 3 to obtain an average per square millimetre, multiply by 10 for the content of a cubic millimetre, and then by 20 for the dilution. (Blood to 0·5, diluent to 11.) This can be done mentally, and requires no calculation on paper. Having counted the leucocytes I again go over the same portion of the ruled surface and determine the polymorphonuclears and estimate the percentage of these to the total leucocytes.

It is unnecessary in such counts to have an assistant record the results. Of course, in making a complete differential count it is preferable to have some one tabulate them, or laboriously to do this personally.

Price Jones [5] points out that by employing Toisson's fluid for counting red cells fallacious results may be obtained unless a control with Hayem's solution be simultaneously made. The reason is that in cases of anæmia pale red cells may be found which have a refractive index

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[1] Carruthers, V. T. (December 18, 1909), "A Simple Method of Counting Leucocytes." *British Medical Journal.*

[2] Seguin and Mathis, C. (1910), "Procédé pour la détermination rapide de la formule leucocytaire." *Ann. Hyg. et Med. colon.*

[3] Yakimoff, W. L. (September, 1910), "Procédé pour la détermination rapide de la formule leucocytaire." *Fol. Hæmat.*, Vol. X., No. I.

[4] Stitt, E. R. (July, 1910), "A Quick, Simple, and Accurate Method of Making Differential Blood Counts in Wet Preparations, and Its Advantage in the Diagnosis of Surgical and Tropical Diseases." *Philippine Journal of Science*, B.

[5] Price Jones, C. (June 4, 1910), "A Source of Fallacy in Counting Red Cells." *British Medical Journal.*

identical with that of Toisson's fluid, and hence are invisible. They may be new formed cells and indicate a regenerative process. Blood—*continued*

Balfour [1] has a paper on blood fallacies and puzzles, especially such as occur in tropical countries. They may be divided into Internal or Autogenetic and External or Adventitious, and further subdivided into those met with in fresh preparations and those encountered in stained films. Information, will be found regarding Jolly's bodies, Ferrata's plasmosomes, Kurloff's bodies, Maraglianos, altered red cells and leucocytes, hæmoconia, the changes induced in blood when it is heated, pseudo-parasites, the *corps-en-anneau*, and *corps-en-pessaire* of French writers, centrosomes and other matters of interest to workers at tropical medicine. It is hoped that, as it is fairly exhaustive, it will be found useful, especially by students and beginners. Reference to this paper may perhaps permit one to dispense with reviews of all the papers to which it refers.

As regards hæmoconia, however, reference may be made to a paper in the *British Medical Journal* for November 20, 1909, while in the *Epitome* of the same number is an interesting quotation on the subject of basophilic granules in red cells with the latest views regarding them. Jolly now believes these are due to hydration of the stroma or corpuscular membrane of the red cell. The variation in the size of red blood cells is the subject of a paper by Price Jones.[2] He shows that the association of a raised colour index with increased diameter of red cell is connected with the formation of large nucleated red cells in the marrow. These are known as metrocytes or mother cells, are not found in normal animals, and divide to form megaloblasts. Free nuclei found in the marrow seem to be megaloblast nuclei, and this suggests a derivation of the large red cells from the metrocytes.

Polychromasia, so commonly met with in the blood of rodents, is regarded by Ward [3] as being due to the existence of certain differences in red cells, congenital in origin, not of necessity pathological, but capable of being aggravated by conditions inimical to normal hæmogenesis.

An interesting paper is that by Tunnicliff [4] on the anti-infectious power of the blood of infants. She concludes :—

(1) That at birth the opsonic power of the blood serum toward streptococci, pneumococci, and staphylococci is a little less than that of adult serum. It falls still lower during the first months of life, and does not equal the opsonic power of adult serum until about the second year.

(2) That the phagocytic activity of the leucocytes of infants toward streptococci, pneumococci, and staphylococci follows a course similar to that of the opsonic indices. The leucocytes at birth are a little less active than adult leucocytes. Their activity diminishes considerably during the first months of life, and does not reach that of adult leucocytes until about the third year.

(3) The phagocytic power of the whole blood of infants drops decidedly during the first and second months of life, and does not reach that of adult blood until about the third year.

(4) During the first and second years of life the anti-infectious power of the blood, as measured by the opsonic power of the serum and the phagocytic power of the leucocytes, is far below that of adult blood.

Of value from a clinical standpoint is Austrian's [5] paper on blood viscosity in health and disease. He finds the viscosity of the blood reduced in anæmia, either primary or secondary. In malaria the viscosity of the blood is usually normal or subnormal, rarely above normal. That of the plasma is normal or increased, the last as a result of hæmoglobinæmia. In typhoid fever the viscosity varies with the anæmia, is increased by hydro-therapy, and is apparently uninfluenced by diet. In pneumonia it is generally increased owing to cyanosis and salt retention.

The discovery of X bodies in the blood, by Horrocks and Howell, was mentioned in our first Review. These have now been found in a case of urticaria in the Sudan by Balfour,[6] who was unable to come to any definite conclusion regarding them, but was inclined to think they might be derived from the skin, and hence be accidental contaminations.

Additional Notes

Those studying the morphology of the blood will find the *Folia Hæmatologica*

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[1] Balfour, A. (1911), "Fallacies and Puzzles in Blood Examination." *Fourth Report, Wellcome Tropical Research Laboratories*, Vol. A.

[2] Price Jones, C. (November 5, 1910), "The Variation in the Sizes of Red Blood Cells." *British Medical Journal.*

[3] Ward, S. R. (November 5, 1910), "Polychromasia and the Pathology of Hæmatomata." *Ibid.*

[4] Tunnicliff, R. (October 25, 1910), "Observations on the Anti-Infectious Power of the Blood of Infants." *Journal Infectious Diseases.*

[5] Austrian, C. R. (January, 1911), "The Viscosity of the Blood in Health and Disease." *Bulletin Johns Hopkins Hospital.*

[6] Balfour, A. (February 4, 1911), "X Bodies in Human Blood." *Lancet.*

Blood— *continued* for April, 1911, a specially useful number, as it contains papers on Cabot's rings, on polychromatophilia, and other changes in the red cells. Mention must also be made here, as elsewhere ("Fevers") of an excellent paper by Robertson. In this place, however, one would only mention the fact that Robertson,[1] in contradistinction to Rogers, makes his differential count by counting across the smear *at different points*, leaving out the two ends *and not counting the edges*. Rogers believes only one part of the film can be relied upon, and he counts the cells at the edges. Personally one follows Rogers, but it would be well if some observer with time, patience, and the necessary experience, would decide if the one method is as good as the other, for to a busy man in a hot country, the edges come as a boon, especially in cases of leucopenia.

Bubo. Under this heading reference may be made to a paper by Ley,[2] wherein he describes three cases of a tropical form of adenitis occurring in soldiers in England who had recently served in Burma and Northern India. According to the author the features of the disease are: (1) that it may be latent for a long time (months at any rate), and thus cases may appear to develop in temperate climates; (2) that the glands attacked are those of the groin and popliteal space, thus pointing to infection from the soil; (3) that animals are susceptible and possibly infect human beings. The situation of the glands and the chronicity are the most marked characteristics. This is the chronic non-venereal bubo of India and the far East, and so far, according to the *Lancet* of June 12, 1909, there is no evidence to prove it connected in any way with plague, *i. e.* that it is *Pestis minor* of Cantlie. Knox,[3] however, believes that a European inoculated with a small dose of not very malignant plague bacilli may develop adenitis or *Pestis minor*, a not uncommon affection amongst laboratory workers in tropical areas where plague occurs.

A discussion on Climatic Bubo took place at the Sixteenth International Medical Congress, Budapest, and will be found recorded in the *Lancet* for September 18, 1909. Most of the speakers agreed that the bacteriology of the condition and its true nature remained unknown. Staphylococci are found when suppuration occurs. Malaria can be excluded as a cause. There was a hesitancy to regard the condition as absolutely unconnected with plague, but chiefly because, by so doing, cases of true plague might be missed. Ruffer pointed out that the climatic bubo is quite distinct from the plague bubo, clinically, pathologically and bacteriologically. The gland is painless, the process is slow, and the duration of the affection prolonged. It is common in ship's stokers. The bacteriological findings vary, strepto-staphylococci, the *B. pyocyaneus*, and other organisms having been found. When suppuration occurs it is in the form of small foci in the gland itself, not in the periglandular tissue as in plague. Stoney[4] in an earlier paper also mentions this point, and recommends early excision as the best treatment.

Probably the most important recent work is to be found in an illustrated paper by Letulle and Nattan-Larrier.[5] They mention the abnormal elements found either in cells or in capillaries, and which have been considered as possibly parasitic. These bodies are refringent, contain chromatin granules and are difficult to distinguish from the nuclear debris of phagocytes. They find that the histo-pathology consists of a dislocation of the glandular tissue, an increase in plasma cells, diffuse and insular, and an insular necrosis of the reticular tissue. Finally, they state that their work supports the view of those who regard the condition as a specific entity, and goes to show that it is absolutely distinct from plague.

Calabar Swellings. Manson[6] has reported an interesting case wherein, by puncture of the swelling, he obtained two drops of serum which, on staining and examination, were found to contain microfilariæ with all the characters of *Microfilaria loa*. The patient was one whose blood harboured this parasite and also a few *Microfilaria perstans*. This observation goes a long way to prove Manson's hypothesis that these peculiar swellings are due to the periodical and normal emptying of the contents of the uterus of the gravid female worm into the connective tissue of the host, but there is the fallacy, as he himself points out, that

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[1] Robertson, A. W. (May, 1911), "Hæmateikona. The Significance of the Blood Picture in Disease." *Indian Medical Gazette.*

[2] Ley, R. L. (June 5, 1909), "A Tropical Form of Adenitis, apparently due to an as yet unrecognised Organism." *Lancet.*

[3] Knox, E. B. (June 26, 1909), "Tropical Adenitis and Plague." *Ibid.*

[4] Stoney, W. W. (March 10, 1908). *South African Medical Record.*

[5] Letulle, M., and Nattan-Larrier, L. (December 14, 1910), "Étude histologique du Bubon climatérique." *Bull. Soc. Path. Exot.*

[6] Manson, P. (March, 1910), "On the Nature and Origin of Calabar Swellings." *Transactions Society Tropical Medicine and Hygiene.*

they might have been derived from the small quantity of blood obtained along with the serum. He suggests repeating the little operation on a patient with no microfilariæ in his blood, at the same time taking care to see that the swelling is recent, and on the increase, that the exploration be made as near as possible to the point of origin of the œdema, and that when aspiration is made the needle-point lies in the œdematous tissue. Leiper, in criticism, said that the only crucial experiments which could set aside Manson's theory would be the discovery of male sex in a worm that caused a Calabar swelling, and not whether there were embryos in the blood.

Calabar Swellings—*continued*

Cancer. Our Review must naturally be limited to points similar to those discussed in the previous volume. Bentall[1] summarises 1700 cases coming under his observation in Travancore, South India. He comments on the frequency of buccal cancer and its possible association with the habit of "betel chewing," and concludes that—

(1) The younger age incidence of cancer in Travancore is suggestive of some definite cause early in life.

(2) Frequency of cancer of the buccal cavity and absence of it in the rest of the alimentary canal is suggestive of a local cause for the former, but absence of digestive causes in the latter.

(3) The inveterate habit of "betel chewing" from childhood is suggestive of the cause, either by mechanical irritation or a medium suitable for the growth of a possible cancer germ.

Amongst other interesting matter in the *Third Report of the Imperial Cancer Research Fund* is a paper by Seligmann[2] on the frequency of new growths in the natives of New Guinea. He finds that, whether benign or malignant, they are rare. When malignant new growths do occur, they are, on the evidence then available, sarcomata. He further points out that chronic, irritative processes *per se* are not sufficient to produce new growths in Papuasians, that they and the Melanesians are predominantly vegetable feeders, but that this cannot explain their immunity from new growths, as these are rare amongst Australian natives, who make no gardens and are hunters. Lastly, and this is important, he finds that where malignant disease does occur among Melanesians, its incidence seems to be associated in some obscure way with the adoption of a mode of life which approximates to that of the white man, while there is proof that there is nothing in the environmental conditions in British New Guinea capable of preventing the development of new growths in aliens resident in the country.

Seidelin[3] cites his experiences in Yucatan. He met with benign tumours and sarcomata, but carcinoma was distinctly rare. He advances as a reason the fact that carcinoma is a disease of advanced life, and that in the Tropics, where the mortality is high, few individuals attain the "cancer age." A suggestive paper is that by Renner,[4] who investigated the spread of cancer among the descendants of the liberated Africans or Creoles of Sierra Leone. His observations, so far as they go, tend to show that those races which have not been in contact with Europeans, and those who, though they have been in contact with the white man, have yet markedly resisted European civilisation, are but little liable to malignant disease. He mentions the people of the Gold Coast in this connection and the aborigines, while the Creoles are an example of people who have become deeply tinged by European customs and habits, and are subject to cancer and other malignant growths. His arguments are supported by Casalis,[5] who mentions similar conditions in South Africa.

Randle[6] criticises Renner's paper freely, pointing out that Renner's premises are at fault, though he admits the interest of the question raised. The two papers are worth reading by any one working out cancer statistics in dark races, as is a very ingenious essay by Watkins-Pitchford[7] on the genesis of cancer to which one cannot do justice here, and also, from the mathematical side, an article by Maynard[8] on cancer death-rates.

Neve[9] records the occurrence of epithelioma in Kashmir, due to irritation from the constant application of heat by means of the portable fire basket or Kangri which is carried

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[1] Bentall, W. C. (November 7, 1908), "Cancer in Travancore, South India." *British Medical Journal.*

[2] Seligmann, C. G. (1908), "On the Occurrence of New Growths among the Natives of British New Guinea." *Third Report, Imperial Cancer Research Fund, London.*

[3] Seidelin, H. (November 15, 1910), "Experiences in Yucatan." *Journal Tropical Medicine and Hygiene.*

[4] Renner, W. (July 15, 1910), "The Spread of Cancer among the Descendants of the Liberated Africans or Creoles of Sierra Leone." *Ibid.*

[5] Casalis, G. A. (January, 1911), "The Incidence of Cancer in South Africa." *Transvaal Medical Journal.*

[6] Randle, J. (October 15, 1910), "Cancer among the African Creoles." *British Medical Journal.*

[7] Watkins-Pitchford, W. (1909), *Light, Pigmentation, and New Growth.* Durban, Natal.

[8] Maynard, G. D. (April, 1910), "A Statistical Study in Cancer Death-rates." *Biometrika.*

[9] Neve, E. F. (September 3, 1910), "One Cause of Cancer, as Illustrated by Epithelioma in Kashmir." *British Medical Journal.*

Cancer—*continued* by the people under their clothes. He thinks the facts he adduces favour the trophic theory of cancer. Ortholan [1] reviews the whole subject of cancer in tropical countries, and confirms the view of its rarity in coloured races.

One had intended quoting from some of the more recent papers dealing with the supposed parasitic origin of the disease, and more especially the question of the rôle played by skin parasites, such as *Demodex folliculorum* in the transmission of certain cancers, a view advanced by Borrel, but such papers are easily found by those interested, and one's limited space is better devoted to other aspects of parasitology.

Cerebro-spinal Fever. In the first instance we consider papers dealing more especially with the bacteriology of the disease. Wilson [2] found a Gram-negative diplococcus in the fæces of three cases of cerebro-spinal meningitis. This, though it had a superficial resemblance to Weichselbaum's organism, was proved to be distinct from it, but the author suggests that the true meningococcus may yet be found in the intestine, and then it would be necessary to distinguish it carefully from his organism and also from others of the *Micrococcus catarrhalis* class. For this reason he describes the cultural characteristics, and deals with the pathogenicity of these morphologically similar cocci.

In a later paper the same author [3] considers the use of the Drigalski-Conradi medium for differentiating purposes, and concludes that in the lumbar puncture fluid of certain cases of cerebro-spinal meningitis, Gram-negative diplococci may be found which differ from Weichselbaum's and Still's cocci as regards their morphology and capacity for growth on this medium. Amongst other things they had a tendency to grow in chains. At a time when cerebro-spinal fever was epidemic in Belfast, Symmers and Wilson [4] isolated from Belfast tap water a bacillus closely resembling *B. fæcalis alkaligenes*, and which they named *B. grosvenor*. While performing the Widal test in cases of supposed enteric fever they found that one of the blood samples clumped this bacillus, a fact which led to an interesting research, and the conclusions that—

(1) The blood of patients suffering from epidemic cerebro-spinal meningitis is in practically all cases agglutinative to *B. grosvenor*.

(2) If the patient lives long enough, the reaction can be obtained in dilutions of 1 in 2000.

(3) Occasionally the blood is agglutinative to *B. typhosus* and *B. coli* in comparatively high dilutions.

(4) The opsonin and agglutinin acting on *B. grosvenor* are quite distinct from those acting on the *Meningococcus*.

In 1908 there was a very important discussion at the meeting of the British Medical Association in which questions of bacteriology and serum treatment were chiefly to the fore. Owing to more recent advances the results then announced need not be detailed, but an account of the proceedings will be found in the *British Medical Journal* for October 31 of that year. One point brought out, however, may be mentioned, namely, that in very acute infections and also in cases which are chronic from the outset there are no agglutinins in the blood. In the *Bulletin of the Pasteur Institute* for 1908 a good many papers are reviewed. Amongst others is one by Ruge,[5] who describes an enrichment method for finding the meningococcus in the fluid obtained by lumbar puncture. He recommends placing 6 to 8 drops of the fluid on a slide and allowing them to dry at laboratory temperature. While one is more likely to find the organism, the necessary delay in examination is against this procedure. The employment of the centrifuge is probably better.

A very useful paper on the bacteriology of the disease is one by Hislop.[6] Amongst other matters which he mentions is the use of a special probe turned up at the end for the purpose of taking swabs from the naso-pharynx in the case of "contacts." The swabbing has to be done carefully, as if bleeding results it is unlikely that further examination will be permitted, *i.e.* in the case of a family of children. Hislop gives the sugar-fermenting formula for the meningococcus as—

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[1] Ortholan, A. J. O. J. (1909), "Les cancers dans les pays tropicaux." *Ann. d'Hyg. et de Méd. Colon.*

[2] Wilson, W. J. (June 13, 1908), "A Contribution to the Bacteriology of Cerebro-Spinal Meningitis." *Lancet.*

[3] *Idem.* (June 20, 1909), "Differentiation of certain Gram-Negative Cocci occurring in Cases of Cerebro-Spinal Meningitis by their Morphology and Power of Growth on the Drigalski-Conradi Medium." *Ibid.*

[4] Symmers, W. St. C., and Wilson, W. J. (June, 1908), "Agglutination of Bacilli of the Alkaligenes, Colon and Typhoid Groups by the Blood Serum of Cases of Cerebro-Spinal Fever." *Journal of Hygiene.*

[5] Ruge, R. (September 8, 1908), "Erleichterung der Meningokokkendiagnose." *Cent. f. Bakt.*, I. Orig., Vol. XLVII.

[6] Hislop, J. A. (December, 1908), "The Bacteriological Aspects of Cerebro-Spinal Fever." *Journal Royal Institute Public Health.*

Glucose + Maltose + Lactose + Galactose + Mannite—Saccharose — Raffinose—Inulin—Salicin ; and summarises as follows :— Cerebro-spinal Fever—*continued*

(1) Bacteriological examination can alone determine the specific cause of a cerebro-spinal meningitis.

(2) The number of meningococci present appear to have no direct relation to the purulent nature of the cerebro-spinal fluid.

(3) Vitality of the organism in first cultures depends probably more on the strain of the meningococcus than on the composition of the medium.

(4) There appears to be a fatal form of cerebro-spinal meningitis associated with a Gram-positive diplococcus.

(5) The whole respiratory tract probably affords a portal of entry for the meningococcus.

(6) Buchanan's method has much simplified the separation of the meningococcus from other Gram-negative organisms.

(7) Cerebro-spinal meningitis is probably a septicæmia, with secondary localisation on the cerebro-spinal meninges as the seat of election.

(8) The blood serum appears to have a bacteriolytic effect on the meningococcus.

Buchanan's method above mentioned consists in making Petri plates with Lœffler's blood serum, containing 1 per cent. of glucose, and adding neutral red in the proportion of ·5 in 10,000 as an indicator. Streak cultures are made on these plates from all Gram-negative cocci found on the original plate, and from the subcultures, colonies resembling the meningococcus are finally confirmed by means of glucose, maltose, galactose, and saccharose blood serum slants, to which neutral red 1 in 10,000 has been added.

Workers in the Tropics will find a good account, given by Horn,[1] of the disease as it occurs on the Gold Coast. He draws attention to the fact that epidemics occur during the dry and dusty season, and that children and young adults are chiefly affected. In the Sudan, on the contrary, older adults seem most liable. He classes the cases seen as : (1) malignant, (2) ordinary, (3) atypical. The last are those in which there were complications such as periarthritis and pneumonia. He found Kernig's sign of great importance, though often absent in mild cases, and mentions that though the knee jerk is frequently difficult to obtain in natives, if it is exaggerated in one or both legs, it is worthy of consideration, in conjunction with other symptoms, as confirmative evidence. Siriasis is one of the diseases with which sporadic cases are liable to be confounded.

Reviews of a large number of papers appeared in the *Bulletin of the Pasteur Institute* for 1909. It is impossible to refer to these here, but mention must be made of an important article by Dopter,[2] in which he considers the whole subject. He points out that there can now be no doubt as to the meningococcus of Weichselbaum being the sole pathogenic cause of the disease, and that it multiplies in the naso-pharynx before gaining access to the meninges. He gives the following table of cultural reactions in sugar media both for the meningococcus and for certain allied organisms.

Organism studied	Lævulose	Dextrose	Maltose	Galactose	Mannite	Dulcite	Lactose	Saccharose
Meningococcus	0	+	+	0	0	0	0	0
M. cinereus	0	0	0	0	0	0	0	0
M. catarrhalis	0	0	0	0	0	0	0	0
Dipl. pharyngis flavus I.	+	+	+	0	0	0	0	0
„ „ II.	+	+	+	0	0	0	0	0
„ „ III.	0	+	+	0	0	0	0	0
Dipl. siccus	+	+	+	0	0	0	0	0
Dipl. crassus	+	+	+	+	0	0	+	+
Gonococcus	0	+	0	0	0	0	0	0

[1] Horn, A. E. (December 1, 1908), "Reports on an Investigation of Cerebro-Spinal Fever in the Northern Territories of the Gold Coast in 1908." *Journal Tropical Medicine and Hygiene.*

[2] Dopter, C. (November 30, and December 15, 1909), "Les Données Nouvelles sur la Méningite Cérébro-Spinale Épidémique et son Agent Spécifique." *Bull. de l'Inst. Past.*

Cerebro-spinal Fever—*continued*

These are sufficiently constant to serve for differentiation, but it will be noted that *Diplococcus pharyngis flavus III.* reacts like the meningococcus. If, however, the duration of complement test be applied, the former can be excluded, as specific amboceptors are present. As other proofs of specificity he mentions the agglutination reaction, and the fact that the blood serum of patients is bactericidal for the meningococcus. The precipitant test in itself does not suffice to differentiate, but if the saturation of precipitins be established, additional proof is obtained. There undoubtedly exists, however, what may be termed para-meningococci. They do not give the sugar reactions, but give the Bordet-Gengou reaction, thus being easily separated from the so-called pseudo-meningococci. He mentions Vincent and Bellot's test, which consists in centrifuging 50 to 100 drops of the cerebro-spinal fluid to be tested until it is quite clear and limpid, adding to it 1 to 5 drops of blood serum from the patient and incubating the mixture at 37° C. to 55° C. A cloudiness indicates meningitis if a control tube remains clear. Proceeding, he deals with the pathogenesis of the infection and the question of carriers, and concludes that it is really a rhino-pharyngitis which constitutes the epidemic, an epidemic complicated at times by meningitis. Certainly, in view of the curious way in which a solitary case will crop up and the difficulty of finding any source of infection, this seems a very reasonable view to take. What, however, is the element of virulence which sometimes leads to many persons developing the meningitis ? Perhaps there is no question of special virulence, but the epidemic of rhino-pharyngitis is so widespread that a number of persons who happen to be susceptible to cerebral invasion are affected.

He concludes with notes on prophylaxis and sero-therapy, speaking very highly of the latter and giving references, but not entering specially into details.

Bochalli [1] gives an interesting account of a regimental epidemic, in the course of which the following points are mentioned :—

(1) During epidemic times there are probably ten or twenty times as many contacts as actual cases.

(2) The cocci usually disappear quickly from the naso-pharyngeal mucus, but may remain four weeks.

(3) They are most numerous and virulent during the first week of their settling in the throat.

(4) They are little resistant to the sun's rays.

Those specially interested in the bacteriological aspect of the question may also be referred to a paper by Symmers and Wilson in the *Journal of Hygiene* for 1909. It is very useful, and gives the formula for the special fluid medium of Gordon, in which the sugar reactions can conveniently be tested. One can scarcely, however, review it here, as its virtue consists in details.

Under the heading "Bacteriology" will be found a reference to a paper by Martin giving an account of the more recent methods for the differentiation of the *Meningococcus*, the *Gonococcus* and the *Micrococcus catarrhalis*.

Mention must be made of the work of Elser and Hunton [2] in New York, who found that

the meningococcus is transmitted directly through the medium of the air, from individual to individual. The most important part in the dissemination of this disease is played by the so-called meningococcus carriers. During an epidemic their number greatly exceeds the number of those who actually acquire the disease. The occurrence of adult germ carriers, and the fact that the majority of individuals are naturally immune to infections with this organism explains many of the peculiarities of the disease. The almost constant presence, and the early appearance of the meningococcus in the respiratory passages of individuals suffering from this disease, indicate that they gain access to the body by these channels. The fact that repeated examination of the naso-pharynges of individuals occupying wards harbouring cases of meningitis (children) failed to reveal a single germ carrier, may be mentioned in support of the relative innocuousness of children actually suffering from the disease. The experiments designed to determine whether the organisms were excreted by way of the naso-pharynx yielded negative results. The question concerning the paths selected by the meningococcus in reaching the brain cannot be definitely answered, although all the evidence is in favour of a hæmatogenous origin of the disease. Concerning the relationship of other bacteria to epidemics of meningitis, the authors arrived at the conclusion that only one other organism is capable of producing epidemics of this disease, namely, the encapsulated streptococcus of Bonomé.

Any one who has worked with the meningococcus knows the difficulties of getting a first culture growth of the organism, hence the method of Bruyonoghe [3] is likely to prove of interest. He adds to a broth tube a given quantity of the patient's cerebro-spinal fluid, and incubates the mixture at 37° C. for 24 hours. When the result is positive the meningococci are soon found on the surface of the fluid. After 24 hours the growth is visible to the naked eye,

[1] Bochalli (1908), "Zur Verbreitungsweise der Genickstarre." *Zeitschr. für Hygiene u. Infekt.*, Vol. LXI.

[2] Elser, W. J., and Hunton, F. M. (1909), "Studies on Meningitis." *Journal of Medical Research.*

[3] Bruyonoghe, R. (September 26, 1910), "Einfaches Verfahren zur Züchtung der Meningokokken." *Cent. f. Bakt.*, I. Orig., Vol. LVI.

and can be seen even when the fluid contains a considerable amount of pus. When, however, this is the case it is well to sediment or centrifuge and use only the supernatant fluid. The process is said to answer in chronic as well as in acute cases, and is not suitable for cases of mixed infection or when the fluid has become polluted. Cerebro-spinal Fever—*continued*

A valuable paper to which, unfortunately, only passing allusion can be made is that by Mott[1] on the cerebro-spinal fluid, more especially the second part dealing with its pathology. Another article dealing with the cytology of the fluid is that by De Lepinay.[2] He finds that in cerebro-spinal fever, on centrifuging and sometimes even merely on standing, large numbers of polymorphs with neutrophile granules are deposited. Some are altered and stain badly. The alteration is said to indicate an unfavourable prognosis. In addition mononuclears, lymphocytes, red blood corpuscles and some endothelial cells are found. In subacute and chronic forms a lymphocytosis may be predominant. This author also mentions a clinical test less well known than Kernig's sign, and called the *signe de la nuque*. To obtain the reflex the neck is bent forward and it is found that the lower limbs at the same time become flexed at the knees and on the abdomen. This sign is said to be present in 97 per cent. of cases. As regards treatment the author speaks highly of the serum method, giving 15 c.c. to a very young child, 20 to 30 c.c. to one above two years, and 30 to 40 c.c. to an adult. The dose is repeated on each of three or four successive days. He is inclined to think it advisable to give the serum in any case where the fluid is turbid without waiting for the laboratory report.

Dow[3] made routine examinations of the blood in a large number of cases, and came to the following conclusions:—

(1) That cases of epidemic cerebro-spinal meningitis are always accompanied by a leucocytosis, whether the attack is acute, abortive, mild or chronic. (2) That the character of the leucocytosis is practically the same in all instances, both in adults and children, and is the result mainly of an increase in the number of the polymorphonuclear cells. (3) That, nevertheless, a lymphocytosis may be very occasionally observed in infants and young children. (4) That there is a relative decrease of the large mononuclear elements alike in fatal and non-fatal cases, though less marked in the chronic type. (5) That in the first three groups there is sometimes an absolute decrease of the large mononuclear elements and occasionally total absence of these cells. In the chronic group absolute decrease, like relative decrease, is little marked. (6) That eosinophile corpuscles in acute fatal cases are always absent, although present in varying degree in all the other groups.

Probably as good an account of the disease as is to be obtained occurs in Ker's[4] excellent volume on the Infectious Diseases. It is specially useful as regards symptoms and complications. Salebert and Thubert[5] have found that the condition of the urine differs from that in other acute febrile disorders. During the acute stage urea and phosphates are much in excess of normal, while the chlorides are greatly diminished. The total amount of urine passed is markedly increased. If the urea remains high when the temperature falls and the symptoms have improved, the amelioration is only apparent and serum injections should be continued. An account of the sequelæ is given by Colin.[6] Hydrocephalus may occur, also various pareses; headache is not uncommon, and atrophic conditions may result.

Deafness, owing to labyrinthine affection, has been noted.

The question of "carriers" is, of course, one of primary importance. The most extensive work on this subject is that by Mayer[7] and his collaborators, who examined more than 9000 soldiers of the Munich garrison. They found that when no cerebro-spinal fever was present 1·93 per cent. of coccus carriers existed among 9,111 healthy persons (each once examined); 2·46 per cent. among 1,911 persons (many times examined). This means about 2 per cent. in 11,022 healthy persons. As a result of their labours these authors advance somewhat heterodox views. They believe the sick exercise the chief rôle in the spread of the disease, more especially the mild cases, and they do not think cultural detection of coccus carriers necessary.

Most writers, however, appear agreed that it is necessary to treat the contacts, as will be seen by reference to Purves Stewart's review of the subject in the *Medical Annual* for 1910. He mentions Setler's case, where a man who had been infected three months before, returned

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[1] Mott, F. W. (July 2 and 9, 1910), "The Cerebro-Spinal Fluid." *Lancet.*

[2] De Lepinay, C. E. M. (March 4, 1910), "La méningite cérébro-spinale épidémique." *La Clinique.*

[3] Dow, W. (March 20, 1909), "An Investigation into the Leucocytosis of Epidemic Cerebro-Spinal Meningitis." *Lancet.*

[4] Ker, C. B. (1909), *Infectious Diseases.*

[5] Salebert and Thubert, quoted in *Medical Annual,* 1911.

[6] Colin, L. (1909), "Über Folgen der Erkrankung an Zerebrospinalmeningitis." *Berl. Klin. Wochenschr.*

[7] Mayer, G., and Others (July 26, 1910), "Über Genickstarre, besonders die Keimträgerfrage." *Münch. Med. Woch.*

Cerebro-spinal Fever—*continued*

convalescent to his regiment with meningococci, however, still present in his naso-pharynx. Seven days after his arrival ten men out of thirty in his part of the barracks were found to have become carriers.

In the first Review, chlorine water and menthol were stated to have been used for disinfecting carriers. Vincent and Bellot have since introduced a mixture of 60 per cent. alcohol, 100 parts; iodine, 10 parts; guaiacol, 1 part; and thymol, $\frac{1}{8}$ part. The solution is evaporated, and the vapour slowly sniffed up the nose for three minutes at a time on four or five occasions daily. The fluid is evaporated by placing it in a small porcelain dish within another vessel filled with hot water. In addition the tonsils and pharynx may be swabbed with iodized glycerine 3 per cent., and frequent gargling with oxygenated water 10 per cent. carried out. Under these measures the organisms are said to disappear within four days. Pyocyanase has also been recommended. The following are the detailed instructions for the disinfection of the naso-pharynx and mouth issued for the French army and quoted along with other useful regulations in the *Journal Royal Army Medical Corps* for October, 1910 :—

All carriers must have the naso-pharynx, mouth and tonsils carefully disinfected by antiseptic inhalations and swabbing.

Inhalation.—The following mixture is recommended :—

Iodine	12 grammes
Guaiacol	2 ,,
Thymol	25 centigrammes
Alcohol, 60 per cent.	200 grammes

Note.—In order to dissolve the iodine, 6 grammes of iodide of potash should be added to the above.

This mixture is put in a porcelain dish, which is floated in a basin of boiling water. The patient is directed to sit with his head bent over this at a few inches distance and inhale the fumes, breathing slowly through each nostril; the sitting should last for two or three minutes, and should be repeated five times in twenty-four hours.

Disinfection of the Pharynx.—This should be carried out by swabbing with glycerine containing 3 per cent. of iodine; the swabbing is to be done most carefully morning and evening.

Disinfection of the Mouth.—The gargle recommended is 20 parts of peroxide of hydrogen (10 vols.), distilled water 180 parts, the mixture being supplied in a separate corked bottle to each man.

We pass now to the all-important question of treatment, but can only deal with some of the very latest papers on the subject. The chief measure now employed is, of course, the injection of anti-meningococcic serum, but as in the Tropics this is often not available other alleviative methods will be mentioned. Taking first the question of serum. A very good account of its administration and the beneficial results recorded is given by La Fétra of New York in the *Medical Annual* for 1909. We quote what he says about technique and dosage in the case of the Flexner and Jobling serum which does not contain carbolic acid (0·4 per cent.) like that of Kolle and Wassermann :—

When the serum is to be injected, the patient should be lying down, with head extended, in order to facilitate the entrance of the fluid. The serum should be warmed and injected slowly, at least as much being used as the amount of fluid withdrawn, often somewhat more. Warming the fluid is important, since the patients experience a good deal of pain if the serum is employed cold. Very little force should be used with the syringe.

Dosage.—From 30 to 40 c.c. is the initial dose in moderately severe cases. It is to be repeated in twelve hours if there is no improvement, and after that daily. Frequently a single dose is enough. It is not necessary that it be given during the first twenty-four hours of the disease, but by far the best results have been obtained when the injections were begun during the first three days. The doses should be repeated until the symptoms improve.

The following are the instructions issued by the French War Office in 1909, and quoted in the *Journal Royal Army Medical Corps* for September, 1909 :—

(1) It will be injected into the arachnoid cavity, and not subcutaneously, under the strictest antiseptic precautions.

(2) The puncture is made in the middle line of the spinal column in the lumbar region, at a point where the horizontal line between the crests of the ileum intersects it, corresponding to the space between the third and fourth lumbar vertebræ.

(3) A quantity of cerebro-spinal fluid, slightly in excess of the amount of serum to be injected, is withdrawn, and the serum injected from tubes kept in water at a temperature of 38° C.

(4) After injection the patient's head is lowered and the hips raised; he is kept in this position for about two hours to enable the serum to be diffused.

(5) The dose varies from 20 c.c. to 40 c.c. in an adult.

(6) In severe cases the higher doses are injected daily for three or four days. Subsequent doses will be determined by the results.

(7) In slighter cases the smaller doses (20 c.c. to 25 c.c.) will be sufficient to relieve the symptoms; but if they return after twenty-four hours the injection will be repeated, and also on subsequent days if necessary.

Cerebro-spinal Fever—*continued*

Dopter,[1] already quoted, has a special article on the subject, and insists on the facts that the dose must be sufficient, must be repeated with sufficient frequency, and must be judiciously administered. Even in children large doses are indicated.

Merle[2] uses either Flexner's or Dopter's serum, giving 20 c.c. for the first three days and continuing if the temperature or meningeal symptoms indicate further treatment. In cases where the meningococcus is present in large quantities he recommends subcutaneous injections as an adjuvant, and mentions a prolonged case with persistent fever where this plan proved highly successful. He also describes a case which developed rose spots like those of typhoid. That the serum treatment is not wholly free from danger is shown by the increasing literature on the occurrence of anaphylaxis in cases wherein it has been employed. Thus Netter and others caution against the dangers of too large or too prolonged injections of serum. In all cases a careful investigation of the cerebro-spinal fluid and the recognition of polynuclear and meningococcic cells must be made before resort is had to further injections of serum. One cannot enter further into this subject here. Papers on it will be found reviewed in the *Bulletin of the Pasteur Institute* for 1910 and 1911.

As regards other therapeutic measures Larkins[3] says that hot applications to the nape of the neck tend to relieve pain. Hot baths do good, the patient being placed for ten to fifteen minutes in a bath at 107° to 110° F. three times a day. They are specially valuable in chronic cases. Sponging with hot water twice daily is also useful. Of drugs, morphia in full doses is of great service, and during convalescence potassium iodide is indicated.

Additional Notes

Dopter[4] has recently shown that if a mixture of anti-meningococcus serum, and of an emulsion of meningococci be introduced into the jugular vein of a guinea-pig, there is an immediate and profound effect and rapid death, which he attributes to the serum destroying the cocci and liberating a toxin. By the saturation test he has shown this action to be specific. The same author[5] has also introduced a technique like the Pfeiffer test for cholera in order to distinguish the meningococcus from other organisms. To a guinea-pig of 250 grammes, 1 c.c. of a non-heated meningococcic serum is given intraperitoneally. Twenty-four hours thereafter one-sixth of an agar culture, *i. e.* a non-lethal dose of meningococci, is given by the same route. The exudate is withdrawn and the meningococci are found to be breaking up. They finally disappear. The method would seem to be of value in differentiating para and pseudo-meningococci. Moussons and Rocay,[6] dealing with the symptoms and diagnosis—

refer to Brudzinski's signs, of which there are two. The one is called the *reflex contro-lateral identique*. In this, the patient being supine with both legs extended, it is found that, on flexion of the leg and thigh of one side upon the abdomen, the moment the thigh touches the abdominal wall the other leg follows suit. If this is not obtainable, the second of them, the *reflex contro-lateral réciproque*, may be found. In this case, one leg and thigh being flexed as before and the other extended, it is found that when the flexed limb is lowered to the extended position the opposite limb undergoes, in turn, flexion on thigh and abdomen.

The absence of Babinski's sign is said to be due to anæmia of the cord caused by hypertension of the cerebro-spinal fluid. They describe herpetic and purpuric rashes, and discuss articular manifestations, various complications and sequelæ, and state that Vincent's precipito-reaction is an almost certain means of diagnosis.

An account of a case treated by Jochmann's polyvalent serum is given by Schepelmann.[7] He believes in large doses, 40 c.c. intraspinally for an adult, and thinks one large dose better than several small ones, both from the point of view of a rapid effect and that of possible anaphylaxis.

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[1] Dopter, C. (February 25, 1910), "La Sérothérapie Antiméningococcique." *Ann. de l'Inst. Past.*

[2] Merle, E. (October 15, 1910), "Statistique de 9 cas de méningite, cérébrospinale traités en 1909–10," etc. *Ann. Méd. et Chir. Inf.*

[3] Larkins, F. E. (1909), "Cerebro-Spinal Fever." *Practitioner*, Vol. I.

[4] Dopter, C. (December 10, 1910), "Action bactériolytique comparée du sérum antiméningococcique sur le méningocoque et les germes similaires." *C. R. Soc. Biol.* Also "Le pouvoir lytique du sérum antiméningococcique est-il spécifique ?" *Ibid.*

[5] *Idem.* (December 24, 1910), "Différenciation du méningocoque et des germes similaires par l'épreuve du péritoine." *Ibid.*

[6] Moussons, A., and Rocay, C. (July 31, August 7, and 14, 1910), "Méningite cérébro-spinale chez l'enfant; symptômes; moyens de diagnostic." *Gaz. héb. des Sci. Méd.* Quoted in Epitome, *British Medical Journal*, April 22, 1911.

[7] Schepelmann, E. (1911), *Wien. Klin. Woch.*, No. 4. Quoted in Epitome, *British Medical Journal*, June 17, 1911.

Chicken-pox. One has not personally accumulated many references to varicella during the past three years, and a glance at the volumes of the *Index Medicus* shows that there has been no great literature upon it. Mention must, however, be made of a leading article in the *Indian Medical Gazette* for September, 1908, on Tropical Chicken-pox.

It is chiefly concerned with a criticism of the views put forward with regard to the well-known Trinidad outbreak, an epidemic of eruptive fever which Scheult considered as a mild and irregular small-pox, and described as follows :—

> Essentially this eruptive fever and small-pox are alike; they differ in degree rather than in kind. The almost entire absence of constitutional symptoms in comparison with the abundance of the eruption, the absence of secondary fever, the fact that many unvaccinated people had mild or abortive attacks, while some of the vaccinated suffered severely, the frequency of recurrences, the bulbous character of eruptions in some severe cases, the appearance of the rash in successive crops in many instances, the apparently slight infectivity of the disease, its slow spread among the black community, largely leavened with unvaccinated immigrants, the occasional vaccinal reaction during convalescence or after recovery, the extremely low case mortality, are facts difficult to explain in association with small-pox.

There were not wanting those who regarded the condition as a specific entity allied to, but distinct from, varicella and variola. The writer of the article in the *Indian Medical Gazette* regarded the condition as undoubtedly chicken-pox which, be it noted, may be a very different disease in the Tropics from the familiar childish ailment of temperate climates. As he says very truly :—

> Chicken-pox in the tropics is an adult's disease; it recurs with almost unfailing regularity in the spring, say, February to March. It disappears with the onset of the hot weather (we speak, of course, only of our own experience in Bengal). An epidemic is made up of a great variety of cases: the majority are very mild, some even have only a few typical spots, many are severe, a few are extremely severe, and death may occur in confluent cases or in the rarer bulbous cases. The rash almost always comes out in crops, and " pitting " is seldom or never seen.

From what I have seen of the disease in the Sudan, I should say it answers to the Indian type, though I have never met with the very severe forms. It is certainly largely a disease of adults, though children may be attacked. Smallpiece [1] has recorded the case of a child who was inoculated against chicken-pox with the contents of a vesicle from a boy who had passed through rather a severe attack. A mild attack followed, and the eruption was so modified as to show no likelihood of pitting, while the incubation period was apparently much shortened. Hoyle [2] criticises this paper, pointing out that there are reasons for supposing that the inoculated child possessed a certain amount of natural immunity, and deploring the absence of a control. He admits, however, the possibilities of such a procedure.

Bertarelli [3] has studied the etiology of the condition. He finds that varicella cannot be transmitted from man to man with the same facility as variola. Indeed, he obtained negative results with the contents both of vesicles and pustules, while he was unable to inoculate a macacus monkey, the dog, or the guinea-pig. He was, however, successful in the case of the rabbit's cornea. Attempts at culture proved negative, as did blood culture. He describes and figures some fine granulations in the base of the epithelial cells of the infected cornea of the rabbit, but thinks they are merely the products of a specific karyolysis. If one admits the allied nature of varicella and variola, then these granules might be regarded as initial stages of a *Cytoryctes*, arrested in their development.

A recent paper by Magnan and La Riboisière [4] signalises the constant presence of a special bacillus in the vesicles. The bacilli have rounded ends, form characteristic little masses, and two are often united to form a V. They are most abundant one or two hours after the eruption appears, and diminish in number after the third day. They are Gram and Ziehl negative. Animal inoculations have not proved successful. The authors refrain from expressing any opinion as regards the rôle of this organism.

Additional Note

Armstrong [5] records a case with a certain incubation of twenty-two days and a probable one of twenty-seven days. It is important to bear in mind these lengthy incubation periods, as the usual three weeks' quarantine may now and then not prove sufficient.

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[1] Smallpiece, D. (July 31, 1909), " Inoculation for Chicken-Pox." *British Medical Journal.*

[2] Hoyle, J. C. (August 14, 1909), " Inoculation for Chicken-Pox." *Ibid.*

[3] Bertarelli, E. (1909), " Beitrag zur Atiologie der Windpocken." *Cent. f. Bakt.*, I. Orig., Vol. I., No. 2.

[4] Magnan and de La Riboisière (March 10, 1911), " Sur la présence constante d'un bacille particulier dans les vésicules de la varicelle." *C. R. Soc. Biol.*, Vol. LXX.

[5] Armstrong, H. G. (May 20, 1911), " The Infection of Chicken-Pox." *British Medical Journal.*

Chigger. This insect seems to have been somewhat neglected of late, save for a well-illustrated paper by Fülleborn.[1] Photographs of the male and female *Sarcopsylla penetrans* are shown, and of sections of infected epidermis. He mentions that Schilling proved that the chigger had not to become free before laying her eggs, but laid them *in situ*. This was done by covering a chigger embedded in the skin with plaster. On the day following, the insect was found to have laid eggs. This agrees with Wellman's statement quoted in the last Review.

Cholera. Lack of space forbids any extensive review of work dealing with the bacteriology of cholera, but a few recent papers may be cited.

Dold[2] has pointed out that the so-called "fish in stream" arrangement, which was supposed to be characteristic of cholera vibrios in smears, is merely the mechanical result of the spreading of the mucus in which the bacteria are embedded, and is of no diagnostic importance whatever.

Zlatogoroff[3] has shown that along with true cholera vibrios there may exist in water other forms which give Pfeiffer's reaction and the complement deviation test, but fail to agglutinate with cholera serum. Possibly these are cholera vibrios which have lost some of their biological characteristics.

A paper of practical interest is that by Fürbringer and Stietzel[4] on the vitality of cholera vibrios in latrine drains, *i.e.* the open channels from native latrines which carry off the more fluid portion of the dejecta, together with water used for lavage, etc. This kind of drainage was collected in bottles and infected with cholera cultures, the bottles being placed uncorked in the tanks into which the drainage flowed. For the first week cholera vibrios were found in enormous numbers, then they steadily diminished, but could be detected even after 106 days. If air was excluded their vitality greatly diminished.

It would seem advisable to give the method of preparing Dieudonné's[5] blood-alkali-agar medium, as it has come largely into notice.

To defibrinated ox blood an equal quantity of normal KOH solution is added. This gives rise to a lake-coloured blood solution, which is then sterilised in the autoclave. Of this sterilised solution 3 parts are added to 7 parts of agar that has been prepared in the usual way and rendered neutral to litmus paper. On this mixture, which contains about 0·6 per cent. free alkali, as may be revealed by titration with sulphuric acid, the vibrios grow luxuriantly, but *B. coli* grows but feebly, if at all. Consequently stroke cultures from normal fæces give no growth, whereas the agar that has been prepared by the addition of 30 per cent. of a 10 per cent. solution of crystallised sodium carbonate allows a strong growth of *B. coli* to appear. Ordinary agar that contains 0·6 per cent. KOH is not a culture medium for cholera vibrios, therefore we must conclude that it is the albuminate of potassium that is favourable to their growth in Dieudonné's agar.

This blood alkali-agar is poured into Petri dishes, which are dried for several days at 37° C., or kept for five minutes at 60° C. The material for examination is streaked on the surface of the agar with a glass rod.

Several German papers testify to the usefulness of this medium. The blood of a pig or horse is said to be better than that of cattle, while Laubenheimer[6] states that this medium exercises an unfavourable influence on the morphological and tinctorial properties of *V. choleræ*, and on its agglutinability.

Wretowski,[7] who has used this medium for the cultivation of other vibrios, both saprophytic and pathogenic, and of pathogenic intestinal bacilli, concludes that while it may sometimes render useful service it will neither serve for the differentiation nor the diagnosis of *V. choleræ*, and is unable to replace the peptone water method. Neufeld and Woithe,[8] on the

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[1] Fülleborn, F. (1908), "Untersuchungen über den Sandfloh." *Arch. f. Schiffs-u. Tropen-Hygiene, Beiheft* 6, Vol. XII.

[2] Dold, H. (August, 1909), "Artificial 'Fish in Stream' Arrangement of Bacteria." *Journal Royal Institute of Public Health.*

[3] Zlatogoroff, S. J. (January 8, 1909), "Zur Frage der Diagnostik der Choleravibrionen." *Cent. f. Bakt.*, I. Orig., Vol. XLVIII.

[4] Fürbringer and Stietzel, W. (1908), "Über die Lebensdauer von Cholera-und Typhusbakterien in Spülgruben." *Zeitschr. f. Hyg. u. Infekt.*, Vol. LXI.

[5] Dieudonné, A. (1909), "Blutalkaliagar, ein Elektivnährboden für Choleravibrionen." *Cent. f. Bakt.*, I. Orig., Vol. L.

[6] Laubenheimer, K. (1909), "Der Dieudonnésche Blutalkaliagar als Elektivnährboden für Choleravibrionen." *Ibid*, Vol. LII.

[7] Wretowski, J. (1910), "Sur le diagnostic bactériologique du vibrion cholérique." *Gazeta lekarska*, Vol. XXX., No. 10, quoted in *Bull. de l'Inst. Past.*, Vol. VIII., 1910.

[8] Neufeld, F., and Woithe (February 3, 1910), "Über elektive Choleranährböden, inbesondere den Dieudonnéschen Agar." *Arb. a. d. Kais. Gesundheitsamt*, Vol. XXXIII.

Cholera—*continued*

other hand, speak well of it, but as its alkalinity tends gradually to diminish they recommend the addition of 0·7 to 0·8 per cent. of a normal solution of soda or potash if the medium is to be used immediately, and of 1 to 1·(5) per cent. if it is to be employed after the lapse of 24 hours. Glaser and Hachla [1] have recently conducted a lengthy research in order to determine if this medium is elective for *V. cholerœ*. They find that this is not the case, for *B. fœcalis alkaligenes*, which is often found in normal stools, and may under certain conditions be pathogenic, also grows readily on it at incubator temperature, while *Proteus vulgaris* develops both at room and incubator temperature, and *Proteus piscicidus versicolor* at room temperature.

Crendiropoulo and Panayotatou,[2] of Ruffer's laboratory in Egypt, who naturally have great facilities for studying cholera, have devised a new medium which does not possess two inconveniences shown by Dieudonné's alkaline blood agar. With the latter one has to wait for 24 hours before seeding the medium, which is kept during this time in the incubator, and it does not inhibit the growth of *B. pyocyaneus*, whose colonies upon it resemble those of *V. cholerœ*. Their medium consists of peptone, and only the peptones of Witte or Chapoteau will serve. Five grammes of peptone are dissolved in 190 c.c. of tap water, and 10 c.c. of a 10 per cent. solution of caustic soda are added. The mixture is heated for from 3 to 5 minutes. On cooling it is filtered and sterilised at 100° C. for half-an-hour. If Witte's peptone is used 8 c.c. of the soda solution are sufficient. The proportions must be exact in order, after sterilisation to secure the proper degree of alkalinity, 0·28 per cent. to 0·4 per cent. calculated as sodium. When required for use 4 parts of the alkaline peptone are mixed with 6 parts of neutral agar peptone (3 grammes agar, 1 gramme peptone, 0·5 gramme common salt, and 100 c.c. water), and poured into plates. The mixture ought to be made aseptically, as subsequent sterilisation renders the medium not so suitable. The plates are inoculated in the usual way, the material being spread over their surface. They are then incubated. So far the authors have not tried their medium with cholera stools, but laboratory experiments have been highly successful.

The only other of these special media we need mention is that of Tuschinsky [3] :—

Take equal parts of normal solution of potassium hydroxide (KOH 56, water 1000) and ox blood, or blood from some other animal; the horse answers perfectly well. Sterilise the laked blood in streaming steam for half-an-hour, and mix it with nutrient agar-agar in the proportion of 3 to 7. It is said that the cholera spirillum multiplies readily on this medium, while with other bacteria little or no growth is obtained. If this medium is inoculated from a suspected stool the diagnosis usually can be made within 24 hours.

Our review of other papers dealing with the bacteriological aspect of cholera must be brief. A paper of very considerable importance and quite in line with recent work on other organisms is that by Ohno [4] on the changes undergone by *V. cholerœ* on culture media of different reactions. He finds that the cholera organism can assume four forms :—

(1) The bacillary form, which varies in length and thickness.

(2) The typical vibrio form, which shows variation in the degree of curving in length and in breadth.

(3) The " comma " form, with variation only in regard to length and thickness.

(4) The " coccus " form, which varies in its diameter, assuming sometimes an oval form and then again a spherical one.

In general, in acid media, it tends towards rod forms, and in strongly alkaline media towards the coccus type. He believes that in the routine technique for isolating the organism it is well to employ three peptone solutions of different reaction, and notes that the agglutinability of the vibrio appears to decrease the more acid or alkaline the medium is made.

Margouliès [5] describes certain allied spirilla met with as secondary infections in cholera cases. They are of two kinds—one stains faintly, has pointed ends, and is frequent in the stools (Russian cases); the other stains well, is larger, and is much less common. They appear to be non-pathogenic, and their precise significance is unknown. Of considerable importance

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[1] Glaser, E., and Hachla, J. (January 21, 1911), " Ist der Dieudonnésche Nährboden nur für Choleravibrionen elektiv ? " *Cent. f. Bakt.*, I. Orig., Vol. LVII., No. 4.

[2] Crendiropoulo, M., and Panayotatou, A. (July 9, 1910), " Sur un nouveau milieu pour le diagnostic du choléra." *Ibid*, Vol. LV., No. 3.

[3] Tuschinsky, M. (August, 1910), " Über den Dieudonnéschen Blutalkaliagar." *Ibid*, Vol. LIV., No. 1.

[4] Ohno, Y. K. (October, 1909), " The Reaction of Culture Media in Relation to the Morphology of the Cholera Organism." *Philippine Journal of Science*, B.

[5] Margouliès, M. N. (1909). " Contribution à l'étude du vibrion choléríforme." *Russk. Vrach.*, Vol. LII., quoted in *Bull. de l'Inst. Past.*, May 30, 1910.

would appear to be the researches of Van Loghem [1] in Sumatra, for in cases clinically resembling cholera he did not find the vibrio, but a slightly motile bacillus which in its cultural reactions rather resembled *B. coli communis*. He has named it *B. pseudocholeræ*, although it is true that he has not yet definitely proved it to be the cause of the choleraic condition. Cholera—*continued*

McLaughlin and Whitmore [2] investigated the cholera and cholera-like vibrios met with in the Philippines. The points they endeavoured to settle were :—

(1) Whether any "cholera-like" vibrios in the Philippines might agglutinate in a low dilution of a specific anticholera serum, and thus lead to error in the ordinary routine agglutination tests performed for the purpose of ascertaining the presence of cholera vibrios in the stools of cholera suspects or "carriers."

(2) Whether any cholera vibrios lose their morphology or agglutinability under any conditions, but especially in mixed cultures sent in from the provinces for diagnosis.

(3) Whether any vibrios of the *El Tor* type could be discovered in the Philippines. As the work progressed two other questions arose.

(4) Whether any of the "cholera-like" vibrios which do not agglutinate with a specific anticholera serum can under any conditions be made to acquire such agglutinability.

(5) Whether Dieudonné's medium is satisfactory for the isolation of cholera vibrios from the stools, and if so, whether it can be used to differentiate "cholera-like" vibrios from true cholera vibrios.

Finally, the question (6) as to whether the hog might act as a "cholera carrier" in the Philippines, was investigated.

They came to the following conclusions :—

We have not been able to add anything to what is already known to questions numbered (1) and (2). Every vibrio in our list which agglutinates in a 1 to 200 dilution of specific anticholera serum is a cholera vibrio, while none of the non-cholera vibrios agglutinated in a weaker dilution than 1 to 10. On the other hand, four of our cholera vibrios did not agglutinate equally with all of our cholera sera; with some they did not agglutinate in a weaker dilution than 1 to 200. It is noted that three of these vibrios had been in mixed cultures on agar for about seven days, in transit from the provinces, but whether this had anything to do with their lowered agglutinability we are not prepared to state.

None of our agglutinating strains were hæmolytic, so that we have not found any vibrios of the *El Tor* type in these Islands.

We have not been able to make "cholera-like" vibrios acquire agglutinability with cholera sera.

Dieudonné's medium is satisfactory for the isolation of cholera vibrios from the stools, but it does not assist in separating cholera vibrios from "cholera-like" vibrios.

We have not been able to show that the hog acts as a "cholera carrier" under as nearly natural conditions as possible.

If confirmed, a recent observation by Raybaud [3] is likely to prove important, for he has found that the cholera-red reaction is frequently given by cultures from stools which are not choleraic. He thinks it is due to the co-existence in the fæcal matter of *B. coli* and of *B. perfringens*. The great development of coli on the surface of the peptone-gelatine-salt medium of Metchnikoff favours the anærobic development of *B. perfringens* in the depth of the tubes. The latter reduces nitrates to nitrites, and the coli forms the indol.

Attention must be directed to the recent work of Horowitz [4] on the St. Petersburg epidemic of 1909–10. His summary is too lengthy to be fully quoted, but he emphasises the necessity in any cholera epidemic of regarding all cholera-like vibrios with the greatest suspicion. He also lays stress on the important part symbiosis plays in the biology of the cholera vibrio, citing especially in this connection its association with *Sarcina lutea* and the effect such symbiosis has on virulence and agglutinability.

In the same number of the *Centralblatt* occurs a paper by Zlatogoroff [5] on the length of time cholera vibrios can survive in the intestine after recovery from the attack. This has been found to be 55 days in some observations and 93 days in others. It has also been shown that the organisms can remain alive in excrement outside the body for from 7 to 9 months if access of air be prevented. Their date of disappearance from the intestine and the changes

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[1] Van Loghem (1910), "Over eene op cholera gelijkende ziekte in Deli." *Geneeskundig Tijdschr. v. Nederl. Indic.*, Vol. XLIX., No. 5.

[2] McLaughlin, A. J., and Whitmore, E. R. (October, 1910), "Cholera and Cholera-Like Vibrios Encountered in the Philippines." *Philippine Journal of Science*, B.

[3] Raybaud, A. (December, 1910), "La réaction indol-nitreuse dans les cultures de matières fécales en l'absence de vibrions cholériques." *C. R. Soc. Biol.*, Vol. LXIX.

[4] Horowitz, L. (March 6, 1911), "Zur Frage über die Diagnose der Choleravibrionen." *Cent. f. Bakt.*, I. Orig., Vol. LVIII., No. 1.

[5] Zlatogoroff, S. J. (March 6, 1911), "Über die Aufenthaltsdauer der Choleravibrionen im Darmkanal des Kranken und über die Veränderlichkeit ihrer biologischen Eigenschaften." *Ibid.*

Cholera—*continued*

they undergo depend largely on the accompanying intestinal flora. It must of course be remembered that these results, obtained in Russia, are not likely to hold good under tropical conditions.

The question of cholera carriers can now conveniently be considered. Forrest [1] demonstrated the presence of perfectly healthy carriers in Burma, and found that the vibrios could be excreted for at least six weeks after an attack.

Pfeiffer [2] notes that in the *entourage* of cholera cases there is always a certain but variable number of apparently healthy "carriers." Freidheim found 51 in connection with 241 cholera cases, and at another time 38 to 174 cases. Even so, however, the period during which these persons excrete vibrios is of no longer duration than in the cases of those who have been attacked. A sad but excellent example of the dangers of cholera carriers was exhibited by the outbreak among nurses of the Presidency General Hospital, Calcutta, in 1909. Food was contaminated through the medium of native servants (*masalchis*) in whose stools cholera vibrios were demonstrated by Haffkine. The report of this outbreak is by Macrae,[3] and is well worthy of study, giving as it does an excellent account of how an inquiry into any localised cholera outbreak should be studied.

Sacquépée,[4] in a general paper on carriers, considers those of cholera. He reviews all the recent work on the subject, citing especially the Russian observations. It is worthy of note that persons may excrete the vibrio for some days before being attacked by cholera.

In the Philippines there were found to be 7 to 8 per cent. of healthy carriers in the course of an epidemic. As a rule the number of vibrios excreted by a carrier is not numerous. He says the period of excretion is brief—from 1 to 18 days in cold or temperate climates—but notes that the organism can survive in the intestine for a much longer time. He is inclined to think that there are *healthy* carriers and *convalescent* carriers, citing in this connection the cases at El Tor.

The chronic cholera carrier had not been encountered at the time he wrote his paper.

Turning now to a few general papers we find McLaughlin [5] dealing with cholera in children in the Philippines. He says: "Cholera in children is often unrecognised and unreported as such, being reported as acute or chronic enteritis, gastro-enteritis, entero-colitis, dysentery, acute or simple meningitis, and probably also as infantile beri-beri, convulsions of children, and other diseases. The clinical picture in children is often atypical, and cerebral manifestations are very common." He suggests that during cholera outbreaks, all acute diseases of children should be notifiable, and that a bacteriological investigation of the intestinal contents should be made in every case. The same author [6] has a useful and practical paper on fighting cholera in Manila. There is nothing new in it, but the notes on disinfection and the use of lime are worth consulting.

Zouchello [7] has studied the types of vibrios found in the stools of Mecca pilgrims and in the water of pilgrim ships. As a result of his observations he believes the incubation period of cholera may be as much as sixteen days.

There are many other papers which might be mentioned, but it is perhaps well to discard them and take up the question of treatment. Mention was made in the first Review of the transfusion method of Rogers and Mackelvie. This has since been developed, and the former [8] has a paper on the indications for the use of hypertonic salt solution (1·25 per cent.), and the technique for transfusion. It is much too lengthy to be quoted here, and must be considered in the original, together with a subsequent paper [9] in which he points out that the blood changes, especially as regards its specific gravity, may be used as an indication for the employment of

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[1] Forrest, J. B. (November 2, 1908), "Cholera Carriers." *Journal Tropical Medicine and Hygiene.*

[2] Pfeiffer, R. (1908), "Die Verbreitung der Cholera durch sogenannte 'Dauerausscheider' und Bazillenträger." *Klin. Jahrb.*, Vol. XIX.

[3] Macrae, R. (October, 1909), "Report on the Recent Cholera Outbreak among the Nurses of the Presidency General Hospital, Calcutta." *Indian Medical Gazette.*

[4] Sacquépée, E. (June 30, 1910), "Les Porteurs de Germes." *Bull. de l'Inst. Past.*

[5] McLaughlin, A. J. (October, 1909), "Some Observations upon Cholera in Children." *Philippine Journal of Science*, B.

[6] *Idem* (February, 1909), "The Suppression of a Cholera Epidemic in Manila." *Ibid.*

[7] Zouchello, C. (1909), "I vibrioni isolati durante il pellegrinaggio mussulmano del 1907–1908 contaminato di cholera." *Ann. Ig. Sperim.*, Vol. XIX.

[8] Rogers, L. (November, 1909), "The Indications and Technique of Transfusion in Cholera, with a Note on Cholera in Europeans in Calcutta." *Indian Medical Gazette.*

[9] *Idem* (September 24, 1910), "A Simple Curative Treatment of Cholera." *British Medical Journal.*

the method. The hypertonic solution consists of 120 grains of sodium chloride, 6 grains of potassium chloride, and 4 grains of calcium chloride to one pint of sterile water. Tabloids and tablets of this formula can now be obtained. Four go to a pint, while three in a pint is a suitable strength for rectal injections. Rogers has invented a special stop-cock cannula and graduated transfusion bulb, described and figured in the article just quoted, and in marked collapse in an adult male with little or no pulse at the wrist he gives 3 or 4 pints intravenously at the rate of not more than 4 ounces per minute, this being slowed at once to 1 ounce per minute if any distress or severe headache is produced. The fluid should be at blood heat or at 100° F. In hyperpyrexia its temperature may be a little below blood heat. Rogers has now supplemented this method by the use of oxidising agents in the shape of the permanganates. We quote his note in full :— Cholera—*continued*

ADMINISTRATION AND DOSES OF PERMANGANATES

Although in cholera the bowels are so completely cleared out of their normal contents, and the watery stools contain very little albuminous matter, still, it is not to be expected that the usual small doses of 2 to 3 grains at long intervals, as given in amenorrhœa, could exert much influence in destroying toxins in the small intestine. On coming into contact with unstable animal albumens the oxygen is set free in a nascent form and manganese dioxide precipitated, which appears to be largely inert in the bowel. I have already given up to 50 grains within a day or two, without the slightest indication of any harm having resulted from it, and intend to push it still further in bad cases in the future.

The permanganates are given in two different ways. First, in solution, to drink *ad libitum* in the place of water. Beginning with ½ to 1 grain to the pint, on account of the unpleasant astringent taste, the strength is rapidly increased up to 4 to 6 grains in 1 pint, or even stronger if the patient will swallow it. Fortunately, in severe cases the thirst is so great that no difficulty is usually experienced in pushing the drug in this way. Vomiting may occur, but does no harm. On the contrary, it probably helps to remove some toxin. I have even known obstinate vomiting in cholera relieved by the permanganate drinks, doubtless by destroying some irritant substances in the stomach. Calcium permanganate is the best salt for this purpose, being somewhat less astringent than the potassium one, while as it is divalent it will exert a greater oxidising action. The calcium element may also possibly lessen the effusion through the bowel wall. The other method of administration is in pill form, for which purpose the potassium salt is more easily dispensed on account of the very hygroscopic properties of the calcium and sodium compounds. The simplest method is to mix two grains of potassium permanganate with a little kaolin powder and vaseline, and make as small a pill as possible. It is then coated with salol one part, in sandarach varnish five parts, or with keratin so as to only dissolve on reaching the alkaline small intestine, where its action is wanted. It is important to see that the pills readily dissolve, as they sometimes become hard and inefficient after being kept some time, and may then pass through the bowel unchanged. Two leading firms are investigating the best way of putting up the permanganates at my suggestion, so a thoroughly efficient preparation is sure to be available very shortly. I now give one pill every quarter of an hour for the first two hours, and then every half-hour until the stools become coloured green and less copious, which usually occurs in about twelve hours. In mild cases they need only be given during alternate four-hourly periods. Barley water may also be administered to maintain the strength, as it is not readily acted on by the permanganates. At the beginning of the second day eight more pills are given, and in severe cases this is repeated on the third day in order to avoid relapses which have occurred in three cases. They all promptly yielded to a renewal of the permanganate treatment, thus furnishing an additional reason for believing its action to be directly curative.

At a later date Stephens pointed out that preparations of calcium permanganate of the kind required already existed; one form in capsules mixed with paraffin, the other as palatinoids.

He does not claim these methods as infallible remedies for cholera, as he recognises there are certain specially virulent types which, if seen late at least, practically nothing can save, but he gives figures which prove its great value. Rutherford [1] has recently treated cases on these lines, and says, " The figures quoted are to my mind strong confirmatory evidence of the truth of Major Leonard Rogers' contention that hypertonic intravenous or, for certain cases, intraperitoneal saline infusion is *the* rational and hopeful method of treating cholera." He also says that the secret of success lies in the early performance of the operation, the sooner after the establishment of the diagnosis the better, and concludes :—

Even when the pulse is fairly good the infusion must aid in washing out toxins through the kidneys. To wait until the blood pressure has fallen and the specific gravity of the blood has risen seems to me to be about as rational as to wait for the development of an abscess to operate on a case of appendicitis or until the larynx is nearly blocked with membrane before giving anti-toxin in diphtheria.

Very good results have attended a somewhat similar line of treatment adopted by Lomelino in Madeira, and thus described by Stevens [2] :—

On admission the patient is given a large dose of castor oil, together with twenty drops of chlorodyne. This dose, if vomited, is repeated until retained. After this he applies a large linseed and mustard poultice to the abdomen, and gives intestinal antiseptics, such as solution of potassium permanganate, by the mouth, surrounding the patient with hot-water bottles meanwhile. For cramps, he rubs the limbs with linimentum opii, and gives stimulants by the mouth.

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[1] Rutherford, T. C. (December, 1910), "A Series of Cases of Cholera Treated by Major Leonard Rogers' Method of Infusion of Hypertonic Saline Solution, together with Remarks thereon." *Indian Medical Gazette.*

[2] Stevens, H. (January 21, 1911), " The Cholera in Madeira." *British Medical Journal.*

Cholera— *continued*

The reason that Dr. Lomelino's mortality statistics are so good is that he infuses with normal saline without hesitation the moment there are any indications of the approach of the algid and collapsed stage. If he cannot find a vein quickly he infuses under the skin of the axilla. I told him that my experience of subcutaneous infusion in cases of hæmorrhage was unfavourable as compared to the intravenous method, because of the very slow absorption when a patient is practically pulseless; but he replied that this objection did not hold good in cases of cholera, where the blood became so concentrated, owing to loss of fluid, that it greedily absorbed a subcutaneous infusion even when there was practically no circulation. He uses inhalations of oxygen in conjunction with this method.

Rogers is evidently not the only pioneer in, and advocate of, the transfusion method. Cox in China introduced a continuous method of intravenous saline transfusion, the technique of which has been described and its virtues extolled by Thomson.[1] The transfusion is started at once and kept up until the features are distinctly puffy unless there are symptoms of distress. No food is given for four days, an important point, as the vibrios as well as the patient are thereby starved. Water or weak tea without sugar or milk may be given as the patient desires.

Choksy[2] recommends rectal injections of one pint of normal saline solution made with boiling water, cooled to about 100° F., and given at intervals of four hours. This is best done by a gravitation douche, the hips being well raised. In order to keep up the circulation and restore the renal functions he has recourse to the following formula given in 20 minim doses in an ounce of water every two, three, or four hours, according to the state of the pulse.

Caffeine sodio-salicylate	grs. $2\frac{1}{2}$
Sparteine sulphate	gr. $\frac{1}{2}$
Liquor atropinæ (P. B.)	min. 1
Spiritus vini Gallici	ad min. 20

Friction, dry cupping, and poultices of digitalis leaves are also useful. Starvation is essential, but hot black coffee without milk or sugar should be given day and night as often as the patient requires a drink. After a few days an advance to arrowroot may be made. He advocates the use of cocaine hydrochlorate for persistent vomiting—one-eighth grain in a drachm of water or pepsin and bismuth. Bismuth or dermatol will control the after diarrhœa, while hypodermic injections of camphor (camphor 2, ether sulphuric 3, and olive oil 7), in 20 minim doses every 2 or 3 hours combats prostration. The discussion on this paper may be read with advantage. We have mentioned the vomiting. Menthol is said to be of value as an anti-emetic in cholera.

The question of a curative serum for cholera, which, be it noted, must needs be anti-toxic, not anti-bacterial, scarcely requires consideration here. Of recent papers on the subject that of Schurupow[3] may be consulted. He points out that the toxin is an endo-toxin, unlike that of the diphtheria bacillus. A paper by Hewlett[4] in the *Lancet* for October 22, 1910, may also be noted.

Quinine is said to be of value, and has been tried in China, 10 grains of the sulphate being given every hour until bile appeared in the motions. Basil[5] of Constantinople employs creolin, 4 to 6 drops on flour, which is then rolled into the form of a stick, swathed in cigarette paper and swallowed. He gives 4 to 6 doses of this bolus every second or third hour. The drug, he says, must be fresh.

A new line of treatment is the administration of nucleic acid in the form of injections of sodium nucleate, 5, 8 or 10 per cent. in normal saline solution, together with nucleic acid by the mouth in doses of 0·15 gramme ($2\frac{1}{2}$ grains). The injections were given once or twice daily, and the acid in cachets three or four times a day. Pissarev[6] records three deaths in grave cases treated in this way.

With the object of inducing vaso-constriction at the outset of the disease, Drake-Brockman[7]

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[1] Thomson, J. A. (May, 1910), "The Treatment of Cholera by Continuous Intravenous Saline Transfusion." *China Medical Journal.*

[2] Choksy, N. H. (1909), "On the Treatment of Cholera." *Transactions Bombay Medical Congress.*

[3] Schurupow, J. S. (1909), "Zur Frage der Gewinnung eines Heilserums gegen die Cholera." *Cent. f. Bakt.*, I. Orig., Vol. XLIX.

[4] Hewlett, R. T. (October 22, 1910), "The Treatment of Cholera Asiatica with an Anti-Endotoxic Serum." *Lancet.*

[5] Basil, M. M. (September 24, 1910), "Notes on Cholera." *British Medical Journal.*

[6] Pissarev, A. G., quoted in *Prescriber*, December, 1910.

[7] Drake-Brockman, H. E. (November, 1910), "The Value of Adrenalin and Pituitrin in the Treatment of Cholera." *Indian Medical Gazette.*

has tried and strongly urges the use of either adrenalin or pituitrin supplemented by saline infusions. The effects are apt to be transient, and the dose has to be repeated. The method would appear to merit a more extended trial. Cholera—*continued*

Additional Notes

A new method of isolating *V. cholerœ* from the fæces is that of Ottolenghi [1] :—

Fresh ox-gall is passed through filter paper, and to the filtrate are added 3 per cent. of a 10 per cent. solution of crystallised sodium carbonate, and 1 per cent. of sodium nitrate; the medium is then pipetted into tubes, and sterilised by heating in the autoclave for fifteen to twenty minutes. The author finds that this medium has a selective favourable influence on the growth of *B. cholerœ*, and has an inhibitory influence on the growth of other bacteria found in the fæces.

Pergola [2] also has a quick method. Examine stained and hanging drop preparations. Make a streak culture on blood-alkali-agar, and examine after ten to twelve hours incubation at 37° C. Make enrichment cultures in peptone-water, on peptone-water-gelatine, and on blood-alkali-gelatine. After six to eight hours incubation plate out the growths in blood-alkali-agar and incubate for ten to fourteen hours at 37° C. Test the colonies for agglutination. A reference is given to the paper describing Bandi's [3] method, which is said to be both simple and successful.

Kulescha [4] traces an analogy between *V. cholerœ* and *B. typhosus*, for he finds that the former, like the latter, tends to persist in the gall-bladder and the biliary passages. In the latter situation it remains longer than in the intestinal tract, an important fact as regards carrier cases. Emmerich [5] has advanced new proofs in support of his contention that the intoxication in cholera is due to nitrous acid :—

In the stomach after eating food rich in nitrates, the hydrochloric acid enters into combination with them, and free nitrous acid is produced, which is a strong poison.

In the small intestines a similar highly acid reaction is produced, because the cholera vibrios, under anærobical conditions, give rise to lactic acid and also to nitrous acid. This acid irritates and excoriates the mucous membrane of the intestine, and so it is possible that the poison may pass into the circulation and cause diarrhœa and vomiting. If this theory is true, nitrous acid must be found in the fæces, the vomit, the urine, and in the blood.

Proof that this is so has been obtained by Cappellani in Naples. It is worth noting that the presence of nitrous acid in the muscles of the trunk diminishes their contractility and vitality, but later excites it and causes spontaneous contraction.

It is known that nurslings are immune from the cholera, even if the choleraic mother suckles, whilst children fed on cow's milk are not immune. On the other hand, human milk does not contain nitrate, and, therefore, the author concludes that nitrous acid poisoning does not occur.

Gibbs [6] advances a plea for the extension of the quarantine period in cholera to ten days. This is a suggestion in the right direction, but with the thought of cholera carriers in one's mind, the question arises if even ten days is sufficient.

Climate. O'Connell [7] seeks to prove that exposure to the hot damp atmosphere found at certain seasons of the year in hot, and, to a less extent, in warm climates, can produce (1) pyrexia of an intermittent type; (2) increased hæmolysis or blood destruction; (3) the appearance in the blood of many abnormal forms of corpuscles; (4) increased production of pigment or melanæmia; (5) enlargement of the spleen. In support of his contention he quotes the observations of Frey and Heiligenthals on the temperature of a healthy man exposed for 25 minutes to a saturated atmosphere of 45° C. (113° F.), within a Russian vapour bath. The temperature was markedly raised, the pulse was quickened and the respirations increased; indeed a "paroxysm of pyrexia" was induced. This was not caused by the high temperature of the bath, but by the accompanying humidity. The action he believes to be due to (*a*) arresting evaporation of water—heat loss from the body, and (*b*) increasing the amount of

[1] Ottolenghi, D. (April 19, 1911), "Über eine neue Methode zur Isolierung der Choleravibrionen aus den Fäces." *Cent. f. Bakt.*, I. Orig., Vol. LVIII., No. 4.

[2] Pergola, M. (June 10, 1911), "Die rasche bakteriologische Choleradiagnose. Beobachtungen über das Dieudonnésche Blutalkaliagar." *Ibid.*, Vol. LIX., No. 1.

[3] Bandi, I. (1910), "Le Epidemie Coleriche delle Puglie e di Napoli." *Rivis. Crit. Clin. Med.*

[4] Kulescha, G. S. (1910), "Affektion der Gallenblase, der Gallengänge und der Leber und Veränderungen des Knochenmarkes bei der Cholera." *Klin. Jahrb.*, Vol. XXIV.

[5] Emmerich, R. (May 2, 1911), "Neue Beweise für die Verursachung der Cholera durch salpetrige Säure." *Münch. Med. Woch.*

[6] Gibbs, H. J. (April, 1911), "A Plea for the Extension of the Period of Quarantine for Cholera." *The Malaya Medical Journal.*

[7] O'Connell, M. D. (March 15, 1909), "Climate (Meteorological Environments) as a Possible Cause of Pyrexia." *Journal Tropical Medicine and Hygiene.*

Climate—*continued*

water in the blood and tissues, thereby increasing metabolism or heat production in the body. He points out that the ultimate source of heat production in the body is the metabolism which takes place during every act of vital energy. This is increased by physical and mental work, by food and by *water*. Heat loss on the other hand is due to evaporation of water from the skin and lungs, and to radiation, conduction and convection. The body temperature, therefore, he argues, must be intimately connected with the amount of water in, and the excretion of water from, the body. On a basis of these facts he founds his belief that meteorological environment in Nature, *i.e.* climate, can under certain conditions cause pyrexia. Such pyrexia, he thinks, caused by a warm or hot, damp, stagnant atmosphere must be of an *intermittent type*, for the hot, damp, stagnant atmosphere which causes it undergoes two well-marked changes in every period of twenty-four hours, as previously pointed out; that is, from early morning until the afternoon atmospheric temperature rises and atmospheric humidity falls. From the afternoon throughout the night until early morning the atmospheric temperature falls and atmospheric humidity increases. This periodical change in the environment which produces retention of water in the blood must produce a like periodicity, a sort of ebb and flow or tidal wave, in the water of the blood and tissues. Hence if meteorological environment produces pyrexia in the manner described, such pyrexia must obviously be of an intermittent type, with short paroxysms corresponding with the daily meteorological changes, *viz.*, under twelve hours, usually, in duration. The fact that the specific gravity of the blood falls during the day and rises during the night, in health, seems to indicate that a similar ebb and flow of water in the blood takes place to a limited extent in health.

He then goes on to consider the effect of excess of water on the red cells and of the increase of water in the blood, on the size of the spleen and of its pigments, and comes to the conclusions already stated which, as can be seen, may give a sound mechanical explanation for some of these curious febrile states in the Tropics whercin no parasitic agency can be found. Anderson's [1] views on the white man in the Tropics may be given. He says :—

(1) When a species is well adapted to the conditions which environ it, it flourishes; when imperfectly adapted, it decays; when ill-adapted, it becomes extinct.

(2) When a white man, native of a temperate zone, goes to the Tropics, there occurs a biological reaction of his system to the new environment, and a readjustment of co-ordination between his vital processes.

(3) In the Tropics the white man, individually, can exist; racially he cannot persist.

(4) Acclimatisation is not possible.

(5) No superior race can successfully govern an inferior race, superior in numbers, with equality before the law.

(6) Only by partial enslavement of the coloured natives, superior in numbers, can the white man rule and govern the Tropics, and it is only by relays of fresh representatives he can continue his sovereignty.

(7) No colony of northern origin has ever been able to lead a permanent and independent existence in the Tropics.

As the *Journal of Tropical Medicine and Hygiene* points out, these findings are at variance with the beliefs of those who assert that if the white man will only protect himself and his family from the prevalent diseases of the Tropics he and they will continue to thrive. Those who would study this subject more fully should consult Han's *Tropical Climatology*, and also a recent paper by Nocht [2] with the discussion thereon. In the course of the latter, Standel stated that it is recognised that in cases of prolonged residence in tropical highlands changes occur in the nervous systems of Europeans, if not in the first, certainly in the second and subsequent generations. Future observations alone will show if these become sufficiently prominent to imperil the well-being of European colonies.

The climate of Egypt and the Anglo-Egyptian Sudan forms the subject of a paper read by Lyons,[3] and noted in the *British Medical Journal*. He pointed out that the comparatively low relief of the country, combined with the effect of the north-easterly trade winds which swept over it, produced the hot and dry conditions characteristic of North-Eastern Africa. Modified somewhat in the north by the warm waters of the Mediterranean, and in the south by the rains of the monsoon in summer, the highest temperatures and most arid conditions were reached between Wadi Halfa and Dongola, where northerly winds, clear skies, and a great range of temperature prevailed throughout the year. The important rains were those falling in Uganda, on the southern plains of the Sudan, and on the table land of Abyssinia. Fed by the south-easterly air currents blowing in from the Indian Ocean, these monsoon rains supplied the equatorial lakes and the tributaries of the Nile. The Abyssinian table land,

[1] Anderson, C. L. G. (1908), "The White Man in the Tropics." *Journal American Medical Association*, Chicago.

[2] Nocht, B. (1910), "Der derzeitige Stand der Akklimatisationsfrage."

[3] Lyons, H. G. (March 26, 1910), "The Climate of Egypt and the Soudan." *British Medical Journal.*

with its heavy summer rainfall, was the most effective, since it furnished the whole of the Nile flood, and enabled the Nile to maintain itself through 1,500 miles of desert. As the sole source of the flood, the variation of these rains directly determined the abundance or deficiency of Egypt's supply. Hardly less important in these days of intensive cultivation of cotton was the study of the winter storms which occasionally broke in the Sudan and Abyssinia, raising the level of the rivers and increasing the supply of the Nile appreciably at a time when the normal supply was inadequate. The climate of the region not only influenced the water-supply, but the great range of temperature rapidly disintegrated the rocks, and the wind removed the finer portion of the material; in this way the deserts were being constantly modified, and vast ranges of sand dunes piled up. The distribution of vegetation was very markedly influenced both by the moisture and by the physical character of the country.

Climate—*continued*

A useful kind of paper is one by F. M. G. in the *Journal of Tropical Medicine and Hygiene*, which deals with winter health resorts for returned tropical residents. Amongst other things he notes that :—

> A great many believe they require a " bracing " climate, but in the majority of cases this is a delusion, which may result in their finding themselves braced into their coffins, especially in the case of the class we are specially considering, viz., the retired official who has left the Tropics for good; or it may be the reverse. Cases of pure heat neurasthenia, without serious malarial complications, are well-nigh the only ones likely to be bettered by a really bracing climate, and even with these it is essential that low temperature should be combined with plenty of sunlight, as such cases are usually particularly sensitive to the depressing effects of gloomy weather.
>
> In chronic malaria, cold and damp will often provoke a paroxysm, and for the dysenteric sharp cold is almost as harmful as extreme heat.

The climate of Pau is considered the best in the more easily accessible parts of Europe, as it enjoys a singularly mild and uniform temperature with a large amount of sunshine and an almost entire immunity from strong winds. The prevalence of rain is, however, a drawback. A table is given of its meteorological constants for the colder months of the year based on the averages of eight years. At the same time, with the possible exception of Sicily and the South of Spain, the writer cannot point out an ideal winter climate for the purpose in Europe, and indicates Africa, the Canaries or the West Indies, with a recommendation of Northern India for the retired Anglo-Indian.

Clothing. At the period when the first Review was penned, and indeed for some time thereafter, red or black undergarments were being "boomed" for tropical wear. Thus we find a note in the *Journal of Tropical Medicine and Hygiene* for September 15, 1908, praising the red aertex cellular garments. It states that the body certainly, and perhaps the limbs, should always be covered by a double layer of clothing, and points out the value of the red colour in protecting from the blue or actinic rays said to be the immediate cause of sunstroke. It is even said that the red flannel so long used in rheumatism probably owes its virtue to its colour. The first swing of the pendulum in the other direction is perhaps seen in a preliminary paper by Phalen and Nichols,[1] who say :—

> The whole subject is in a somewhat hypothetical state. Neither the effects of light nor the remedies proposed are on any such firm ground as the need for sterilised water or mosquito nets and light clothing in the Tropics. Enthusiasts who have, perhaps, more fondness for ethnology and analogy than actual experience make it seem quite plain. Others, perhaps equally biassed, hold that the ills of tropical life are all included in the results of infection, heat and moisture. Take for instance a sunstroke as an example of the unsettled state of opinion. Duncan's article is entitled " The Actinic Theory of Sunstroke," and he says there can be no doubt that this actinic theory of sunstroke is the correct one. Manson, however, says that in his opinion Sambon's hypothesis of the infectious nature of Siriasis has more in its favour than any of the many theories that have been based on a purely thermic etiology. On the other hand, Rogers has shown, quite conclusively it seems to us, that sunstroke is correlated with a high temperature and a certain degree of moisture in the air.

The good sense of this statement is borne out by the final results of the very extensive series of experiments made. These are quoted in the *Indian Medical Gazette* for November, 1910, as follows :—

> From the results of the whole test and the experiments the conclusion was reached that the physiological effects of the climate in the Philippines can be and probably are produced by moist heat without the aid of the sun's actinic rays, and no evidence was found that the sun's rays alone could or did produce these effects. On the contrary, the test underclothing added materially to the burden of heat which the system was compelled to endure, and which is probably the chief cause of tropical deterioration. Even if the actinic rays have any influence whatever on the system, it is believed that they are sufficiently excluded by the khaki uniform and the campaign hat.

It must, of course, be remembered that these results refer to soldiers in the Philippines,

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[1] Phalen, J. M., and Nichols, H. J. (1909), " Outline of an Experiment to determine the Value of Coloured Underclothing for United States Soldiers serving in the Philippines." *Transactions Bombay Medical Congress.*

Clothing—*continued*

but that they may have a wider application is shown by Schmidt's [1] work and the more recent experiments of Mouchet.[2]

The former concluded that :—

(1) For thick clothing white stuffs are in all cases the best.

(2) For thin clothing white stuffs are the best if the clothing fits tightly to the body. If it is loose a dark colour is best because the heat absorbed by the stuff does not warm the body by contact.

(3) The best clothing is one of loose, thin stuff, with large sleeves and easy at the neck.

(4) When the sun is very strong the exterior of the clothing should be light, as yellowish-white or pale grey, and the interior dark, brown, blue or black.

(5) "Solaro" clothing (*see* First Review) is not a specific against sunstroke, but marks an advance from the point of view of ventilation. The German "Assolar" fabrics allow the light to pass a little more, but are more porous—hence better than "Solaro."

The latter (Mouchet) confirms these results in so far as he finds white the best colour for heavy clothes and khaki for thin ones. He notes, however, that thick reps and drills are superior to thin materials. Solaro, though slightly superior to khaki and nearly equal to a yellowish rep, proved inferior to thick white rep and drill. He concludes that these latter ought still to remain the basis of colonial tropical clothing, and speaks in favour of the thick rather than the thin clothing, provided it be efficiently ventilated. Somewhat the same views are advanced in a sensible paper by Fink,[3] which is too lengthy for quotation, but which deals with children's clothing in the Tropics, and warns against the use of cotton because the weather is hot and oppressive. Cantlie [4] considers the weight of clothing in relation to health, and states that he has never found a young man, who wears neither undervest nor drawers, whether in winter or summer, to be physically fit for work in the Tropics. He is considering rather the question of persons in the British Isles when he remarks that "a man who has not sense to keep clothes on his back is neither mentally nor physically of much use in this world," but he more or less asks if this dictum is not applicable also to the Tropics.

Additional Notes

A detailed account of an experiment with orange-red underwear carried out on a large scale on American troops in the Philippines is given by Phalen.[5] He concludes by saying :—

A final judgment then is that the test underclothing has added materially to the burden of heat upon the system, a burden which undoubtedly is the great cause of Tropical deterioration. To balance this, it is protective against the chemical ray, the influence of which is regarded as of little moment, and which is sufficiently excluded by khaki clothing and the campaign hat worn at present. Certainly no beneficial effect whatever was observed from the use of this clothing. This experiment suggests that any efforts toward increasing the physical well-being and efficiency of the soldier shall be directed toward protecting him from the debilitating effects of heat and humidity. One effect quite aside from these factors is that upon the eyes. We see here the result of the sunlight in many distressing symptoms, but these are probably due to the light rather than to the chemical rays. Any protection afforded the eyes from the glare of the tropical sun deserves to be heartily welcomed.

Dengue. A lengthy paper by Megaw [6] seeks to show that the term dengue can be properly applied to the "Three-Day Fever," and the "Seven-Day Fever" of India. The arguments advanced are very potent, and in addition the author suggests that in most parts of the plains of India, and perhaps in many parts of the Tropics generally, dengue exists as an endemic fever, assuming a great variety of forms. In proof of this theory he cites the fact that many of the inhabitants of the plains of India have a marked degree of immunity towards dengue.

A table of signs and symptoms comparing the Indian, Philippine and Australian types of dengue with seven-day fever is given, and the paper is illustrated by numerous temperature charts. There is also a table contrasting the main features of "Seven-Day Fever" with those of dengue, and there can be no doubt as to their very close resemblance. The "Three-Day Fever," as described by Fooks, also strongly suggests dengue. In the light of recent work,

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[1] Schmidt, P. (1909), "Zur Bestimmung der Luftdurchlässigkeit von Kleidungsstoffen." *Arch. f. Hygiene.*

[2] Mouchet, R. (1911), "Note sur la valeur hygiénique des différentes étoffes employées pour les vêtements coloniaux." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XV., No. 2.

[3] Fink, G. H. (November 1, 1909), "Clothing in the Tropics." *Journal Tropical Medicine and Hygiene.*

[4] Cantlie, J. (December 15, 1910), "The Weight of Clothing worn an important factor in the Maintenance of Health." *Ibid.*

[5] Phalen, J. M. (December, 1910), "An Experiment with Orange-Red Underwear." *Philippine Journal of Science.*

[6] Megaw, J. W. D. (January, 1909), "Are 'Seven-Day Fever' and 'Three-Day Fever,' Forms of Dengue?" *Indian Medical Gazette.*

Megaw gives a new description of dengue. We quote what he says regarding its various types. Dengue—*continued*

The great majority of the cases will fall into one of the following classes :—

(1) *The Evanescent Type.*—Here the rise in temperature is so slight in degree and so short in duration that it is usually overlooked. This form will naturally be incapable of definite diagnosis till a vital test of the disease has been discovered, but during the period of prevalence of dengue a good many cases of "febricula" are often seen, in which the occurrence of headache, with slight pain in the loins lasting for one or two days, could most reasonably be accounted for as modified attacks of dengue occurring in persons who had become almost immune by previous attacks; in these cases it is probable that the temperature always rises slightly if only for a few hours, but it is possible that some of the attacks may be absolutely afebrile, as suggested in my previous paper. Evidently Ashburn and Craig are alive to the possible occurrence of this type of the disease, for they say "there is no one symptom that can be said to be pathognomonic, or even constant, if we except fever. We do not state positively that even fever is constant."

(2) *The Short Fever Type.*—This type, as in the instance of the three-day fever of Chitral, may be the prevailing form of the disease in some epidemics, but it may also be common in outbreaks where the prevailing type is of six or seven days' duration. It lasts from thirty-six hours to eighty-four hours, and as in the great majority of cases fever is present on three consecutive days, it might fairly be called the "three-day fever type of dengue."

(3) *The Interrupted Fever Type.*—This is simply the short fever type with the addition of a further rise of temperature of one or two days' duration coming on the fifth or sixth day from the onset.

(4) *The Saddle-Back Type.*—This form is due to the prolongation of the primary fever, so that the secondary rise in temperature is superimposed on the end of the primary fever. The term was first used by Major Rogers to describe the characteristic curve in many cases of the fever in Calcutta.

(5) *The Continued Fever Type.*—This is a rare form in which the primary fever is continued without any definite diminution, so that if a secondary fever does occur, it is merged into the end of the primary fever in such a way as to be indistinguishable.

The last three forms are almost invariably of six or seven days' duration, and they are probably, strictly speaking, relapsing forms, the relapse occurring with considerable regularity on the fifth or sixth day. There are thus really two main types of the fever, the simple or short type and the relapsing or long type, but the latter may show a variety of forms according to whether the primary fever has or has not subsided before the occurrence of the relapse. For practical purposes the types which should be borne in mind are the short type, the interrupted type, and the saddle-back type, as the vast majority of actual cases will fall into one of these classes.

Exceptional features of temperature are the prolongation of the fever to as much as ten days, or even a fortnight, and the occurrence of hyperpyrexia, which may be fatal, especially in children.

Later on he deals with the blood changes, noting especially the diminution in the polymorphs which occurs after the second or third day of the fever, and which he thinks is likely to prove of diagnostic value in doubtful cases. Dengue is to be diagnosed from malaria by the microscopic blood examination. If this cannot be performed, then treat the case as malaria, says Megaw. It is certainly safer to do so. The absence of marked respiratory symptoms, and its occurrence in the hot weather, serve as a rule to distinguish it from influenza. It may, however, be impossible to distinguish it from yellow fever of a mild type. If one waits for seven days before making a diagnosis early typhoid can be differentiated from dengue, as in the latter the temperature nearly always falls after this date. From measles, rubella and scarlatina, the history, character of rash, symptoms and leucocyte count, help to separate dengue, while rheumatic fever is excluded owing to the absence of marked redness or swelling of the joints. As regards treatment, aspirin is said to relieve the pain best. Quinine is harmful when given in large doses. Massage and belladonna liniment relieve the joint pains.

It is only since this paper appeared that the more complete researches on phlebotomus fever have been made public, and these undoubtedly modify our ideas regarding some of these dengue-like fevers, as will indeed be seen.

A paper which tends to prove that Megaw is correct in his contention that "Three-Day Fever" is identical with dengue, is that by Allan [1] on an outbreak at Christmas Island. Infection was derived from a vessel, hailing from Bombay, on which there were cases of fever. The fever on the island was of the three-day type, and a second precisely similar but more limited outbreak followed the visit of a second ship from Bombay, on board which there were typical cases of dengue. Clayton [2] believes seven-day fever to be in a reality a sporadic form of dengue, its epidemic extension being promoted by certain unrecognised factors. *Culex fatigans* is probably the vector of the virus.

Craig [3] has pointed out the close similarity existing between the virus of yellow fever,

[1] Allan, J. C. D. (October 15, 1909), "Dengue, or Three-Day Fever." *Journal Tropical Medicine and Hygiene.*

[2] Clayton, F. H. A. (December 18, 1909), Under Proceedings United Service Medical Society. *Lancet.*

[3] Craig, C. F. (February 25, 1911), "The Nature of the Virus of Yellow Fever, Dengue, and Papataci Fever." *New York Medical Journal.*

Dengue—*continued*

dengue and phlebotomus fever. All have a sudden onset, run a rapid course and terminate by crisis rather than lysis. In all three the cause is present in the blood, but only during certain periods. In dengue, so far as is known, this is during the third and fourth days of the attack. In all, the injection of both filtered and unfiltered blood produces the disease, while all are transmitted by insects, two by mosquitoes, the other by a phlebotomus. In dengue the average incubation period approximates to that of the other two fevers, being four days, eighteen hours, and in all the causative agent is ultra-microscopic. Moreover, none of the three diseases is of a contagious nature. Craig therefore thinks, probably correctly, that all three fevers are due to allied species of an unknown protozoal organism.

In this connection a paper by Legendre [1] is of interest. His observations during an extensive epidemic at Hanoi go to show that *Stegomyia* (species not stated, but presumably *fasciata*) is the transmitter of the virus. He bases his view on the following facts :—

(1) The resemblance of the epidemiology of the outbreak of dengue to that of yellow fever.

(2) The great increase of *Stegomyia* during the epidemic period.

(3) The rarity of other mosquitoes at this time.

(4) The arrest of the epidemic with the onset of the cold season, with an accompanying diminution in the numbers of *Stegomyia* and a great increase in the number of other mosquitoes.

(5) The absence of other biting insects which could serve as vectors.

Ardati [2] describes a so-called parasite of the red cells in dengue like that seen by Graham of Beirut. The following is his description :—

(1) Fresh specimens examined carefully with the dark-field illuminator showed, in many erythrocytes, small, brilliant, light-reflecting bodies, which changed their shape, at one time appearing round, and at another fusiform, and moved freely in the blood corpuscles.

(2) In specimens stained according to Giemsa-Romanowsky, I was able to find in the erythrocytes small, usually round, but sometimes elongated fine, granulated, from purple to blue coloured bodies, of the size of one-fifth to one-third of a normal erythrocyte, occupying the margin, but also at times the centre of the blood corpuscles. In some specimens these bodies seemed to be half-way outside the corpuscles and in others to have completely left the erythrocytes; these latter, however, are sometimes difficult to differentiate from the blood platelets. For the blood examination, special care was taken to select patients who never had had malaria.

The parasites were present in the blood of each case, showing clinically the symptoms of dengue, and they seem to be very similar to, if not identical with, those described by Professor Graham.

The life-history of the parasite is not easy to follow. At an early stage of the disease it appears in the erythrocyte as a speck, which enlarges and eats away the hæmoglobin around it; and inside of twenty-four to thirty-six hours the speck reaches the size of about one-fifth a normal erythrocyte and fine granules appear in it.

About sixty hours after the beginning of the attack the parasite seems to reach its maximum size and begins to migrate out of the erythrocytes, usually by rupturing the latter. From this time on we find many parasites that are extra-corpuscular and others intra-corpuscular, as it were another crop beginning its cycle.

The extra-corpuscular parasites look like a group of fine granules arranged more or less in circles, sometimes two or three of them lying side by side, each of them resembling a group of blood platelets. In the leucocytes are often found small granules which seem to show that the parasites were taken up by the white corpuscles.

Microscopically there are some points of differentiation between the dengue parasite and that of malaria.

	Dengue	*Malaria*
1.	Smaller.	Larger.
2.	Usually round.	Different shapes.
3.	Slightly pigmented.	More pigmented.
4.	Finer granules.	Larger granules.
5.	Less stainable.	More stainable.

It is possible that in unstained films the author has mistaken Maraglianos or Cropper's bodies for parasites, but I must say his account of the life history strongly suggests a condition similar to the intra-corpuscular stage (schizogony cycle) of the Sudan spirochæte of fowls. Personally I would not be surprised to hear that dengue and possibly also yellow fever and phlebotomus fever had been proved to be spirochætal diseases. Indeed, Stimson already favours this view so far as yellow fever is concerned (*vide page* 414).

Diarrhœa. Questions of etiology first claim attention. A number of new organisms have been described as associated with epidemic diarrhœa. Of these we may mention the Liverpool F. bacillus, Morgan's bacillus, and a bacillus identical with *Bacillus suipestifer*. Until, however, something absolutely definite is known regarding the precise rôle these

[1] Legendre, J. (January 11, 1911), "Dengue et Stégomyia." *Bull. Soc. Path. Exot.*

[2] Ardati, N. (September 3, 1910), "Observation on Dengue." *Medical Record.*

organisms play in epidemic diarrhœa, it hardly seems worth while reviewing the papers relating to them, while those likely to be specially interested in the question can readily gain access to the articles in the *Lancet* (F. bacillus), and *Proceedings of the Royal Society of Medicine* (Morgan's bacillus). Diarrhœa —*continued*

In addition to so-called specific organisms we find streptococci blamed, their source being probably infected milk, while *B. pyocyaneus* has been claimed as a cause, and recently Metchnikoff in infantile diarrhœa has incriminated *B. proteus*. The type of case due to the blue pus bacillus is described by Baginsky,[1] and deserves consideration, as it probably occurs amongst children in the Tropics. The enteritis is very sudden and violent; a muco-sanguinolent diarrhœa sets in, accompanied with infiltrations of the skin, which may necrose. Cystitis or pyelo-nephritis may be present and a sub-normal temperature. Metchnikoff's [2] work is very suggestive. He found *B. proteus* very commonly in the stools of children suffering from diarrhœa, and young rabbits and chimpanzees proved very susceptible to infection with this organism.

B. proteus was rarely found in cow's milk—only once in ten samples bought in different Paris creameries—and, moreover, diarrhœa occurred in a number of breast-fed infants. The cause was, therefore, not in the cow's milk; the infection was communicated by the persons who cared for the infants. M. Metchnikoff found the *B. proteus* frequently in the stools of healthy adults during August, September, and October, although the stools of the same persons had been previously examined during the cold weather with negative results. *B. proteus* was found in large quantities in the fæcal matter of many animals—cow, horse, dog, and cat—on the surface of the meat, and on the outside of cheeses: Camembert, Brie, and Pont l'Evêque; but especially on vegetable foods, more particularly on salads, radishes, and on grapes. M. Metchnikoff considered that during the hot weather flies transported the microbes from the dejecta of animals on to the food they prefer, especially cheese and grapes, which, being consumed without disinfection, introduced the microbes in quantity into the intestines of persons who, being in constant contact with the infants, contaminated them. To prevent infection of infants, the hands and breast of the parent should be well washed with soap, and adults should dip their grapes and vegetables for a few seconds in boiling water, and pass a flame over the cheese, as *B. proteus* is easily destroyed, since it does not form spores. The cleaning of streets and destruction of flies would also be valuable prophylactic measures.

On the other hand an organism like *B. dysenteriæ* (Shiga), which Hewlett considered as probably playing an important part, is now declared by Grulee [3] to account only for a small proportion of cases. Lucas, Fitzgerald and Schorer,[4] however, found it in 38 out of 45 cases of "infectious diarrhœa" in infants. It is quite evident that at present the bacteriological aspect of the question is far from being settled, and it is probable there are several varieties of diarrhœa each due to a different organism which itself may only play a somewhat subordinate part in the etiology, at least in the infantile forms. Some support is given to this view by La Fétra,[5] who finds that, in infants, certain foodstuffs can produce diarrhœa. Thus excess of carbohydrates results in the formation of lactic and other acids, and these are capable of giving rise to loose, acrid and frothy stools. Maltose, besides producing diarrhœa, favours it by stimulating peristalsis.

Pearse [6] describes a curious condition called Sutika, which is a diarrhœa of puerperal women in Bengal. It commences within 2 or 3 weeks after delivery, or may appear later. The stools contain neither blood nor mucus, and their passage is not accompanied by pain. They vary from 5 to 15 a day, and are watery or frothy. The disease is fatal in from 5 to 8 months, and its cause is, so far, unknown.

Another form of Indian diarrhœa, that of the Hills, has been dealt with by Newell.[7] He does not think mica particles in the water have anything to do with the disease, in which the diarrhœa is frequently painless and the stools white and free from blood. Hill diarrhœa appears to be due to chill in those predisposed by residence in the plains, and not sufficiently

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[1] Baginsky, A. (1908), "Zur B. pyocyaneus-Infektion im kindlichen Alter." *Cent. f. Bakt.*, I. Orig., Vol. XLVII.

[2] Metchnikoff, E. (December 4, 1909), quoted in *British Medical Journal*, under "Paris."

[3] Grulee, C. G. (August 14, 1909), "The Etiology and Treatment of the so-called Summer Diarrhœa in Infants." *Journal American Medical Association.*

[4] Lucas, W. P., Fitzgerald, J. G., and Schorer, E. H. (February 5, 1910), "Methods of Serum diagnosis in Bacillary Dysentery (infectious diarrhœa) in Infants." *Ibid.*

[5] La Fétra, L. E. (November 27, 1909). *New York Medical Journal.*

[6] Pearse, F. (November 7, 1908), "Sutika, the Puerperal Diarrhœa of Bengal." *Lancet.*

[7] Newell, A. G. (1909), "Hill Diarrhœa." *Transactions Bombay Medical Congress.*

Diarrhœa —*continued*

careful as to their clothing. It is a catarrh of the chylopoietic viscera, and is in no way related to sprue. Newell regards a combination of Liquor hydrarg perchlor, Acid hydrochlor dil, Acid sulph dil, Vin pepsinæ, with chloroform water as a specific. The good effect of the mercury is probably due to its action as a cholagogue. At the Bombay Medical Congress, Macy [1] read a very useful general paper on tropical diarrhœas. He classes them provisionally as follows :—

(1) Diarrhœa due to causes exclusively within the gastro-intestinal tract.

a. Benign, or non-specific in origin.
b. Malignant, or specific in origin.
(i) Those due to vegetable parasites.
(ii) Those due to animal parasites.

(2) Diarrhœa due to causes outside the gastro-intestinal tract.

These latter include cases resulting from disturbances in other organs; from toxins eliminated elsewhere in the body, solar, climatic and thermic influences, parasites, malaria organisms, nervous disturbances, hepatic derangements, abscess, cancer of other parts, etc. Some portions of the paper are well worth quoting *in extenso*. He says :—

In the benign or non-specific diarrhœas the dejecta are practically always liquid and numerous. They do not differ essentially from similar attacks outside the Tropics, and are all characterised by relative shortness of duration, and ready response to appropriate treatment. If the cause be removed there is no permanent anatomic, functional or constitutional change. To this division belongs the ordinary acute catarrhal enteritis, due to the ingestion of improper or unaccustomed food; such as unripe fruit on the one hand, and fresh meat after a long period of deprivation on the other. Or the attack may be provoked by some mechanical irritant, such as dust swallowed in unusual amounts during a march, or inorganic matter introduced with the drinking water. Often these attacks are not strictly catarrhal in nature, but are induced more especially by increased peristalsis as a result of the irritation produced by the foreign substance. The discharge, under these circumstances, is watery or serous, rather than catarrhal or mucous.

Any portion of the digestive tract may be affected, from the stomach and duodenum to the rectum; but inasmuch as the entire canal is more or less involved, it is seldom possible to differentiate the part chiefly concerned; nor, for the matter of that, is it of prime importance to do so, in many cases, so far as treatment goes.

But the next class, the specific diarrhœas, deserve more careful attention. They are more strictly tropical in distribution, are always attended by more or less permanent anatomic and constitutional changes, and tend to become chronic in spite of treatment. They are, as a group, always due to parasites of some kind, either animal or vegetable.

And right here we are forced to admit that we know comparatively little about either variety of infection. The field is becoming larger each day, our knowledge is increasing, and we are on the eve of undreamed of things. But at present we see too often some strong man brought low and invalided for the rest of his life, and the only explanation we can offer is that he had diarrhœa. No amœbæ of any kind were ever found, nor any other sort of parasite. His blood did not agglutinate Shiga's bacillus. In short, no specific cause was ever discovered. He was given everything from bismuth to ipecac. He was lavaged with this and with that, and finally he was sent home, a human derelict. It is a common picture, common to all alien races whose destiny compels them to inhabit the Tropics. It is for us to recognise causes, and to ascertain means to destroy them.

In the first place, the fact has apparently been overlooked that the *bacillus dysenteriæ* is not the only kind of vegetable parasite that is capable of producing diarrhœa, even of a fatal sort, that is found in the human intestine. There are over twenty others that are potentially pathogenic. Under predisposing conditions many of the ordinary putrefactive bacteria may excite violent symptoms: such as the proteus group; certain micrococci; some of which have received names and some not; and others resembling the subtilis group. Besides these, there must be considered the *bacillus enteritidis*, the *bacillus lactis œrogenes*, the *bacillus mucosus capsulatus*, the ray fungus, and others. Given a case in which the presence of animal parasites and the so-called bacilli of dysentery can be excluded, we are scientifically not justified in resigning it to the unknown until a biologic test has been made with every organism that can possibly be a cause.

He deals with Sprue (*vide page* 344), and then continues :—

There is another class of vegetable organism which is unquestionably an etiologic factor in many cases of chronic tropical diarrhœa, as well as certain acute cases. I refer to yeasts, and coincidently to moulds. There seems to be no literature on the subject of a comprehensive nature, and what there is is limited chiefly to a description of the varieties that are most frequent contaminations in the laboratory. Blastomycosis is being described, but not of the intestine. As to the moulds, they, too, have received no consideration in works on intestinal diseases, except the occasionally encountered comment that the aspergillus may cause fatal symptoms. A brief reference is sometimes made to the *oidium lactis*. Yeasts and moulds in other conditions than intestinal are often described. But no importance has apparently been attached to their presence in the digestive tract. Yet a careful examination of the fæces will demonstrate in many cases fungi of this sort which are constantly present in the same patient. Their spores can be unmistakably identified in the fæces, sometimes scattered here and there, sometimes in masses. It is less common to find mycelia. Not every one of these is pathogenic, of course; and we can find them in normal fæces to an almost equal extent. For instance, the *penicillium glaucum* is present in every case in the hospital under my charge, and in 82 per cent. of the normal specimens examined by me. It would be folly to assign any pathologic significance to it in these instances under the circumstances. But in one case I isolated a penicillium which grew best at body temperature and but slightly at room temperature. The patient with chronic diarrhœa from whom I obtained it may not have been diseased with this mould, but

[1] Macy, F. S. (1909), "Notes on Tropical Diarrhœas." *Transactions Bombay Medical Congress.*

Diarrhœa —*continued*

the point demonstrated was that some common and innocuous fungus may assume unusual features at times and under conditions now unknown to us; and when so altered in nature there is a possibility that it is harmful. I mention this only to suggest that we investigate this subject more fully and with more attention than it has hitherto received. Again I have four yeasts which I have isolated constantly in the patients so infected, 75 per cent. of whom have gastro-enteritis of undetermined causation, and all of whom are profoundly neurasthenic. This fact suggests the possibility that certain yeasts may elaborate substances which have a special affinity for the nervous system resulting in derangement of function or even in structural changes. Incidentally one yeast is from a sprue patient, but all such cases do not exhibit it. I have not as yet established any causal relationship to an intestinal disorder, in any instance, at least to my own satisfaction; but the possibilities suggested by such findings deserve mention. We must bear in mind, however, that baking does not entirely sterilise bread or toast, and we must, therefore, compare yeasts isolated from patients with those in all articles of food given them which are likely to contain these organisms.

Although I cannot at present give any further results of investigation in this matter of yeasts and moulds as factors in producing diarrhœas, yet I shall soon be able to quote the results of animal experimentation with at least a few varieties, all obtained from diarrhœas of obscure origin and chronic duration.

Proceeding, he gives a list of the parasites within and outside the intestine which he believes can cause diarrhœa. Here is his extra-mural list: *Schistosomum japonicum*, *Sch. hæmatobium*, *Leishmania donovani*, the malaria parasites, and *Tænia echinococcus*.

He has some very useful notes regarding diagnosis; and points out that it is as important to examine the second as the first stool after a saline purge has been given. Here is his procedure:—

While still warm, the specimen is examined for ova under the low power of the microscope, and every field in the preparation rigidly searched. In spite of the oft-repeated statement that the ova of uncinaria, of ascarides and of other parasites are present in great numbers in such infections, and usually in almost every field, it is not unusual to find only one ovum in an entire spread, or even only after several slides have been examined. The search for amœbæ, yeasts, moulds, or other minute abnormal organisms, or the study of details, is then conducted with the higher powers. During these procedures a gross estimate of the digestive activities and deficiencies can be made from the débris, crystals, fibres, etc., observed. It is not amiss also to ascertain the reaction of the dejecta.

Not only one but several slides should be prepared from the same specimen, even though the findings in the first are sufficient to account for the symptoms. All the abnormalities may not be demonstrable in the one slide, and what is found last may be the most important of all. Careful notes are made of all the findings, with remarks on any unusual morphological phenomena that may be seen, especially in the case of amœbæ, so much discussed at present. The specimen is now carefully covered and put away at room temperature. This is because larval forms or flagellata occasionally develop in the course of twenty-four hours, of which the material showed no sign at first. It is necessary, of course, to rule out accidental contamination in such an event.

Not only should several smears of the same fæces be examined, but specimens should be obtained at frequent intervals, as, for example, when the patient complains of a new symptom, or one which he has not hitherto exhibited; when he is worse, and, on the other hand, when he says he is better.

If it is desired to study any fungi that may be present or suspected, it is well to sow a loopful of the fæces in sterile bread paste. For a time the bacteria, or certain of them, will develop, as well as the other fungi; but they are so overgrown by the latter that a series of plates of saccharine media made at the end of a week or more will show colonies of yeasts and moulds, if present, almost exclusively.

Separate plates should be made to isolate the bacteria, and the media selected should all be plated in long series if it is desired to make the isolation comprehensive. Even then there will remain some organisms which cannot be recovered.

Finally, both the solid and the fluid portions of the specimen should be examined separately. Ova are most numerous in the formed material; larvæ, flagellata and amœbæ in the liquid or mucous part. These examinations can often be advantageously supplemented by a chemical one.

The necessity for examining the blood is insisted upon, and he concludes with the following valuable list of principles upon which cases of diarrhœa should be treated:—

(1) Removal of the cause, whether it be organic or inorganic. In the non-specific cases a purge should be given unless there is good reason to believe that the offending material has been removed by nature. An intestinal sedative or astringent should then suffice. In the specific cases the removing agent must be some special measure which is known to destroy the specific origin, in addition to the purge.

(2) Minimising the digestive labour. This is regulated by the diet, which should be selected with a view to assist in meeting the next indication, which is—

(3) Improvement of the general or constitutional deficiencies, such as anæmia, exhaustion, neurasthenia, malarial cachexia, and faulty hepatic action, which are the defects most commonly encountered.

(4) Checking of too profuse evacuations. Diarrhœas are so often an effort on the part of nature to remove deleterious chemicals or parasites, that we should be well satisfied with our knowledge of the case before we adopt too stringent measures. Yet nature sometimes acts not wisely but too well, and we should then attempt to govern, but not to control her. The mere fact that the bowels are too active is not the first consideration.

(5) The relief of pain and other special symptoms, such as sleeplessness, tympanites, thirst, and craving for special kinds of food. These desires are not seldom an expression of the needs of nature and a guide to the kind of medication that will be most efficacious. The commonest request, perhaps, is for something acid, as pickles. Of course the patient cannot have pickles, but dilute sulphuric acid will sometimes satisfy him and relieve his symptoms. What he desires is not necessarily the particular article of food, but is sometimes a substance unknown to him, which is translated into terms of food, the distinguishing quality of which he instinctively recognises as most nearly resembling that of the substance wanted by his system. While too much stress must not be laid upon these cravings, they should not be wholly ignored.

Diarrhœa —*continued*

In principle, a single drug is better than a combination if it will meet as many indications. When a combination is given, it should consist of as few remedies as will answer the requirements, remembering the capabilities of a carefully selected diet, of massage, etc., and the individual peculiarities of the case. Probably more patients are hindered by over-drugging than by under-drugging.

On the other hand, we are apt to underfeed our patients. The endeavour should be to give them the maximum of nourishment with the minimum of digestive labour; including in our calculations, to some extent, the portion of the bowel affected, as well as the degree of ulceration that may be present. In this connection I wish to emphasise the point that milk must be considered a solid food, and not as easily digested as was formerly supposed. Sometimes the ill effects attributed to over-eating in these diseases are the result of errors in selections, not in quantity.

The drugs chosen for the case must, of course, be selected with reference to the special action desired. Ipecac. does signal good in bacillary infections. It is not a specific, however, as some have claimed. In the Philippines we have seen much benefit derived from it in amœbic infections also. The first course of the drug seems to confer the maximum of benefit. Subsequent courses are of progressively less value. I have so rarely seen the disagreeable effects ascribed to the large doses directed that I believe this feature of the ipecac. treatment has been exaggerated.

A decoction of simaruba and pomegranate is a most unpleasant remedy, but a very efficient one. It sometimes effects an apparent cure when all else has failed. Lactic acid bacilli are valuable.

Rectal irrigations of very dilute sulphuric acid are sometimes successful in removing flagellata. As to the high flushings, I believe that they are of benefit in a small portion of cases who can endure them. As a routine procedure they are to be condemned.

A paper of almost equal value and of a somewhat similar type, though limited rather to a consideration of the infantile form of diarrhœa, is that by Maynard.[1] The object of the paper is to show :—

(1) The need for simplification in nomenclature and more uniform methods of registration.

(2) The importance of the age factor.

(3) That specific infection of food as a cause of these diseases has probably been overrated.

(4) That lowering of the body resistance due to improper feeding, climatic changes, insanitary conditions, etc., is of prime importance in the etiology of these diseases.

And the conclusions reached are as follows :—

(1) That in children under five years the diarrhœal diseases cannot be distinguished clinically or bacteriologically. No useful purpose, therefore, is served by continuing the use of the present complicated nomenclature.

(2) That there is urgent need for uniformity in the registration of the diarrhœal group of diseases both as regards nomenclature and age grouping.

(3) That the incidence of these diseases at various ages is a function of the age, a fact which cannot reasonably be explained by assuming that certain age periods are free from liability to infection.

(4) That the organisms which have been claimed as the infective agents in the diarrhœal diseases of infants are normal inhabitants of the intestinal tract.

(5) That if infected milk is a common cause of these diseases, it is curious so few epidemics have been traced to this source.

(6) That the case against flies as the cause of epidemic diarrhœa still lacks scientific proof.

(7) That the foods most prone to bacterial infection are not those associated with the highest diarrhœal mortality.

(8) That there is some evidence to show that the addition of farinaceous food to either cow's or condensed milk diets, lowers the death-rate from diarrhœal diseases.

(9) That one of the most important factors in the etiology of infantile diarrhœa is a lowered resistance, caused by improper feeding, climatic changes being the determining cause of the appearance of the disease in epidemic form.

The vexed question as to the rôle of flies has been mentioned, so we may now look into this matter along with other important points in connection with epidemic diarrhœa. Glover [2] is a strong believer in the house-fly as a vector. He goes so far as to say that the infant who sleeps with its mouth open is on this account more likely to contract diarrhœa than one who sleeps with his mouth shut, and he recommends a fine muslin mesh being kept over the sleeping infant's face. Amongst other ways of getting rid of flies he mentions pouring a little turpentine over some dying cinders on a shovel. One has not seen this method mentioned elsewhere. Powell [3] is another supporter of the fly theory, and is an advocate of clean streets and the immediate removal of soiled napkins from the room where the infants live. One might multiply references galore, but there are three papers which claim special attention. The first

[1] Maynard, G. D. (September, 1910), "Aestival Diarrhœas of South Africa." *Transvaal Medical Journal.*

[2] Glover, V. J. (September 5, 1908), "Epidemic Infantile Diarrhœa." *Lancet.*

[3] Powell, H. R. (August, 1908), "Treatment of Gastro-enteritis in Infancy." *American Journal Clinical Medicine.*

Diarrhœa —*continued*

is that by Niven,[1] who is an upholder of the fly hypothesis, in order to establish which, he says, the following conditions must be fulfilled :—

(1) A fairly close correspondence must exist between the number of house-flies in circulation and the number of deaths from fatal diarrhœa.

(2) Flies must be present in considerable numbers before the rise of the diarrhœa curve.

(3) Any deviation from the correspondence must be explicable in terms of the natural history of the flies and diarrhœa.

(4) Flies must have been generally present in numbers sufficient to cause infection of food or of infants' mouths.

(5) There must be no such correspondence with any other possible cause of diarrhœa capable of explaining its course.

(6) House-flies must be shown to be capable of acting as transmitting agents.

Some of these, he points out, have already been proved. In the discussion which followed several expressed themselves as opposed to the theory. The second paper embodies the very important and extensive research work undertaken by Peters [2] of Mansfield. It deals not only with flies, but with every possible source of infection, and one pregnant statement made is that "the fly-carrier" theory is, at present, the one best able to stand alone as a complete and all-sufficient explanation of the facts at present available. The paper, which is a lengthy one, may be read as a whole, but the "Statement of Known Facts" may be quoted here with advantage :—

(1) There *is* a constantly controlling and facultatively inhibitive force, exercised by temperature.

(2) There *is* exhaustion of epidemic potential, apart from the decline of fly prevalence.

(3) There *is* undoubtedly a good deal of acquired immunity in the population; and this will account for some part of the phenomenon of epidemic decline.

(4) There *is* undoubtedly a good deal of transmission of infection from person to person.

(5) There *is* widespread infection to be found from the very beginning of the season, that is, at least from the end of the pre-epidemic period.

(6) There *is* also a definite pre-epidemic period of favourable temperatures, during which diarrhœa appears to undergo practically no increase—at least at all comparable to the rate found at the time of the main rise.

To these facts of positive import may be added a few of a negative character.

(7) We have *no* knowledge, at present, of such occurrences as that of a direct effect of temperature upon infectivity during transmission from case to case.

(8) There are, at present, few facts to support a theory as to exhaustion of infectivity, during repeated passage of organisms from person to person throughout the season.

(9) No evidence was found in this paper adverse to the fly carrier theory. On the other hand a great deal of indirect evidence was obtained in its favour. The extent of correlation of the prevalence curves of flies and diarrhœa appeared to be quite compatible with the fly theory.

The general summary is very suggestive, but is too long to be here detailed. The concluding paragraphs on prevention and treatment, however, besides being useful in themselves, give an indication of the views expressed, and are accordingly given :—

Treatment. Much might be expected from a remedy such as an effective antitoxin or antibacterial serum.

Prevention. There is good reason for believing that a great deal can be accomplished by the following preventive measures :—

(*a*) *Notification of diarrhœa sickness :* notification, of a partial kind, is shown to be practicable, and useful.

(*b*) *Isolation of attacked persons :* generally practicable to some slight extent.

(*c*) *Cleanliness in the household :* particularly with regard to avoidance, or cleanly removal, of fæcal diarrhœal pollution.

(*d*) *Education of the Public* as to the specific nature, and infectiousness, of the disease; as to infection through stools, etc.

(*e*) *Breast feeding*, wherever possible, *and proper care of food :* failing the breast a wet nurse should be procured, or a cow or goat obtained; or again in default, only milk newly drawn, and given unboiled. No reliance to be placed on boiling stale milk, *i.e.* milk which has lost its first freshness : *such milk is better not given at all.*

(*f*) *General sanitary measures* should be attended to : but however complete their provision, diarrhœa may rage with undiminished violence where their beneficial influence is neutralised by :—

(i.) Dirty and careless habits of living; including carelessness with food.

(ii.) Want of care in isolation of attacked persons, and in the handling and exposure of their stools.

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[1] Niven, J. (September 3, 1910), "The Etiology and Prevention of Summer Diarrhœa." *British Medical Journal.*

[2] Peters, O. H. (December, 1910), "Observations upon the Natural History of Epidemic Diarrhœa." *Journal of Hygiene.*

Diarrhœa —*continued*

It is not sufficient to merely establish good water-closets, drains, etc.: in dirty districts supervision as to their cleanly working is absolutely necessary.

A demonstration of fly carriage would call for destruction of fly-breeding grounds, and for precautions against exposure of infective discharges, as well as of food.

The third paper is a recent one by Tibbles.[1] He gives a useful classification as regards the causes of infantile diarrhœa. Autogenetic: (1) gastro-enteric catarrh—(*a*) acute, (*b*) chronic; (2) intestinal fermentation; (3) toxæmia. Heterogenetic: (4) mechanical irritation; (5) nervous influences; (6) drugs; (7) improper feeding; (8) bacterial infection. Another kind of classification is that given by Meirelles [2] of Rio de Janeiro. It is based on the colour and reaction of the stools. These are either green or not green, and in each case they may be either acid or non-acid. If non-acid they are neutral or alkaline in reaction. The test is made with litmus paper. He thinks that every kind of infantile diarrhœa can be relegated to one or other of these classes, *i.e.*:—

(A) Green stools { (1) acid / (2) non-acid (B) Non-green stools { (1) acid / (2) non-acid

A 1 is nearly always bilious. The liver is always more or less enlarged. This type is more common during the first year of life. It is usually benign, but may be accompanied by fever and vomiting. Its cause is overloading of the alimentary tract. As the author gives the treatment under each heading it will be convenient to follow his plan, though the main question of treatment comes later. For this type he reduces the food, or suppresses it altogether, for 12 to 24 hours, giving only boiled water. As drugs he uses purgatives and alkalis. Amongst the former he uses castor oil, also a powder of calomel, scammony and lactose. Amongst the latter Vichy water, or fluid magnesia and bicarbonate of soda combined.

A 2. This is due to a toxic infection from the intestinal contents. There may be a simple enteritis or a true septicæmia. It may mark the commencement of infantile cholera or precede a broncho-pneumonia. Its causes are to be found in bad quality or infective nature of the milk or other foodstuffs. The treatment consists in remedying the cause, semi-starvation, and the use of lactic acid; the formula for which is sterilised water, 100; lactic acid, 2, given in a spoonful of coffee every 15 to 30 minutes until the stools become acid. Bismuth and benzo-naphthol may be given alternately with the lactic acid.

B 1. This is a disease of dentition, and is due to a toxic infection associated with digestion. There is sometimes acidity of the saliva. It is usually benign, but has a tendency to become chronic. There may be fever, headache, and vomiting. In treating it any faults in the dietary have to be corrected. If the saliva is acid, give Vichy water with the milk. Other foods may have to be substituted for milk. The drugs to be used are bismuth and neutral or alkaline powders. Fluid magnesia may also be given.

B 2. This may be a very simple affair, or may produce infantile cholera. It is, therefore, well to be on one's guard. It is caused by over-feeding, by infected food or food of bad quality, and may also be associated with verminous infections of the bowel. In this case there may be fever and convulsions. Here again lactic acid is the drug, and along with salicylate of bismuth and benzo-naphthol may be exhibited with advantage. The author has had twenty-five years of experience, apparently for the most part in the Tropics, and claims that these methods of diagnosis and treatment, while simple and rational, have given excellent results.

Naish [3] thinks too much stress has been laid on milk as a cause. The discussion on his paper is worth reading and favours this view. Buchan [4] notes the evils of feeding with patent foods, and as a preventive measure strongly urges isolation of the patient. The paper by Sandilands [5] and the discussion thereon are important. Some of his conclusions may be noted. He says:—

Two formidable difficulties have to be faced by every one who sets out to consider the epidemiology of diarrhœa. The first, which is common to all apparently communicable diseases, is the difficulty of determining the relative parts which have been played by the three factors—common environment, contact, and coincidence—in the production of any given group of phenomena observed. The second arises from our inability to distinguish from one another the disease we are considering and the disorders which it simulates.

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[1] Tibbles, W. (March 4, 1911), "Infantile Diarrhœa." *Lancet.*

[2] Meirelles, F. (January 12, 1910), "Diarrhées des enfants." *Bull. Soc. Path. Exot.*

[3] Naish, A. E. (February, 1910), "Summer Diarrhœa." *Public Health.*

[4] Buchan, J. J. (February, 1910), "Reduction of the Infantile Mortality from the Diarrhœal Group of Diseases: Administrative Measures." *Journal Royal Institute of Public Health.*

[5] Sandilands, J. E. (1910), "The Communication of Diarrhœa from the Sick to the Healthy." *Proceedings Royal Society of Medicine*, Vol. III., No. 5.

Diarrhœa —*continued*

There is evidence in this paper, amounting to proof, that certain fatal forms of summer diarrhœa are communicable, and Dr. Low has brought forward conclusive evidence to the same effect. Nevertheless, communicability is by no means a conspicuous feature of epidemic diarrhœa in every case.

In five hospitals there is no evidence of the spread of diarrhœa from patient to patient, and the sum of the evidence suggests that diarrhœa is not more infectious than typhoid fever, and is not conveyed except by the same channels. There is, however, this difference between the two diseases—namely, that typhoid fever spares young children, whereas diarrhœa selects them for its victims. Obviously, young children suffering from diarrhœa cannot avoid contaminating their surroundings with fæcal excrement to a much greater extent than adult persons, and for this reason, in districts with a water-carriage system of sewerage, diarrhœa will be more likely to spread from the sick to the healthy than typhoid fever.

Abstract considerations such as these can, with the aid of the house fly, be made to fit the theory that every case of summer diarrhœa is derived from the fæcal excrement of a previous case; but practical experience of single attacks in persons living far removed from other patients and of groups, the members of which show some proximity on a map, though actually separated from one another by considerable distances of space and time, suggests that the manifestations of diarrhœa observed in water-closet towns neither disprove the existence of impersonal sources of infection in many fatal cases nor demand the rule of universal human origin which they can be forced to support.

In privy towns, whilst heterogeneous filth and sewage-polluted soil may exert the influence attributed to them by Ballard, the phenomena observed can, without any undue strain, be fully explained on the assumption that the effective cause of fatal summer diarrhœa is conveyed to the healthy in the freshly-passed excrement of the sick, and is not acquired from any other source.

Vincent [1] believes in food, and especially milk, being fouled from an unclean soil, and thereby giving rise to the disease, but the special point in his paper is the danger of boiling milk, and thereby depriving the infant of the virtues of the raw product. His watchword is, "procure pure raw milk, protect it from infection, and administer it fresh and unboiled."

Moore [2] has a short paper on the value of notification of the disease, and describes the measures in force after receipt of a notification, in Huddersfield. These are :—

Forthwith an inspector proceeds to the dwelling, and sees to it that every accumulation of refuse of an objectionable character is removed without any delay; the walls, ceilings, and floors of the outbuildings, including closets and ashes-place, are sprayed thoroughly with an efficient chemical disinfectant. Any likely breeding-place for flies is dealt with along the same lines. The drains are flushed, and any sanitary defects therein noted and made good as early as possible. The disease not being directly infectious, as in the case of measles, whooping-cough, and scarlet fever, but only indirectly, isolation of the patient is not attempted, but efforts are directed to instruct the mother, or other responsible person, as to the nature of the infection and the precautions to be taken to guard against it.

Craig [3] believes that possibly *Paramœba hominis* may be a cause of a form of chronic diarrhœa occurring in the Tropics, characterised by exacerbations of acute diarrhœa alternating with periods of constipation. Irrigation of the bowel caused a disappearance both of the parasites and the diarrhœa.

Schmidt [4] deals with the pathogenesis and treatment of forms of chronic diarrhœa with watery stools. He has found that the fluid is not water, but an albuminous liquid very liable to decomposition, hence the offensiveness of the stools in these conditions. It is this fluid, a secretion, a transudate or an exudate, which causes the increased peristalsis. It is evident that disinfection of the bowel is indicated in such a condition, and the author finds hydrogen peroxide best for this purpose. It is best given in combination with pure agar-agar, which takes up from 10 to 12 per cent. of it, and only gradually is the oxygen given up. This medication is effectual in diarrhœas originating high up in the intestinal tract, but fails in cases of intestinal tuberculosis and affections of the large intestine.

Something has already been said about treatment, but a few additional notes may not be out of place. Le Dantec [5] treats chronic diarrhœa of warm countries by insisting on an exclusive diet of albuminoids. After about a dozen days of this regimen, when the Gram-positive bacilli previously present in the acid stools have well-nigh wholly disappeared, he gives lactic acid bacilli. Success was rapid even in obdurate cases.

Houssay [6] has found that washing out the lower bowel of affected infants with red wine

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[1] Vincent, R. (May 2, 1910), "The Etiology of Zymotic Enteritis (Epidemic Diarrhœa)." *Journal Tropical Medicine and Hygiene.*

[2] Moore, S. G. (June, 1910), "The Notification of Summer Diarrhœa." *Journal Royal Institute of Public Health.*

[3] Craig, C. F. (July 15, 1910), "Further Observations on *Paramœba hominis*, an Intestinal Parasite of Man." *Archives of Internal Medicine.*

[4] Schmidt, A. (March 28, 1909), "Über Durchfall." *Med. Klin. Berl.*

[5] Le Dantec, A. (September 15, 1908), "Nouveau traitement des diarrhées chroniques des pays chauds." *Bull. de l'Inst. Past.*

[6] Houssay, F. (1908), "Les lavages intestinaux au vin rouge dans le traitement des diarrhées infantiles." *Anjou Méd.*, Angers.

Diarrhœa —*continued*

gives excellent results. A double cannula should be used. Old wine, rich in alcohol, is not suitable.

Other methods of treatment will be found under some of the papers already mentioned. Thus Powell (*loc. cit.*) sponges the skin with vinegar water and washes out the mouth with glycothymoline or listerine. He gives copper arsenite in doses of $\frac{1}{3000}$ to $\frac{1}{250}$ grain in solution every hour or two hours in infantile diarrhœa, or nuclein in doses of 2 to 10 drops of the solution three or four times daily. Where there is much collapse he gives sulphate of atropine $\frac{1}{500}$ grain every hour hypodermically until there is a reaction, after which he gives it by the mouth at longer intervals. The very multiplicity of drugs used shows how unsatisfactory the treatment often is. Here, above all things, prevention is better than cure. Foods and decoctions to take the place of milk will be found given in the *Medical Annual* for 1910, while in that for 1911 La Fétra's (*loc. cit.*) treatment will be found detailed. Here, also, the use of banana flour and plantain meal is mentioned, and a short account of the most recent medicinal measures is appended.

One has dealt thus fully with the question of diarrhœa, because, even in the infantile form, it is quite as important in the Tropics as in the slums of great cities in temperate countries, perhaps even more so. As to this, however, little can be said, for the disease in infants in the Tropics requires investigation, though, so far as I know, it answers closely to the well-known types. It is significant that out of 426 persons interred during the last ten years in the small Christian cemetery at Khartoum, 154 were children. If statistics were available I am inclined to think that a goodly number of these would have been found to have perished from some form of diarrhœa.

In warm climates, perhaps more than in temperate ones, the taking of a strong purge may result in a severe attack of diarrhœa which it may be difficult to check. In such cases either of the two prescriptions given here will be found useful. One can speak from experience of the great value of the second in such a condition. They are recommended by Hare.

R.	Tinct. kino	℥ i.
	Tinct. catechu	℥ i.
	Mist. cretæ	℥ iii.
	Aquam. cinnamomi	ad ℥ ii.
	M. Sig. ℥s. every three hours.	
R.	Acid sulph. aromat.	℥s.
	Ol. cajuputi	M xl.
	Ext. hæmatoxyli	℥ ii.
	Spir. chloroform	℥ i.
	Syrup. zingiberis	ad ℥ iii.
	Sig. ℥ i. in water every two or three hours.	

Additional Note

Simonin [1] describes a case of chronic enterocolitis in Cochin-China cured by the use of the photothermic radiator. The paper must be consulted for details.

Diphtheria. The bacteriology of this disease, the question of carriers, and that of prophylaxis, are all so intimately associated that it does not seem advisable to divide the papers dealing with these three subjects into definitely separate groups. They will therefore be considered more or less together, and then articles on the clinical aspects of diphtheria and on treatment will be briefly discussed. Questions of variability in the morphology or cultural characteristics of the Klebs-Lœffler bacillus are important, and have recently attracted some attention. Goodman [2] discusses this subject, giving a lengthy bibliography, and concludes as follows :—

Separation of the members of the diphtheria group into two or more species on the basis of morphology, staining properties, character of growth, or pathogenicity is not justifiable because of inconstancy. The same applies to immunity reactions, which have the additional objection that their significance as species reactions is as yet unknown. The only character which experience has not shown to be untrustworthy is that of difference in behaviour toward carbohydrates. It is unnecessary to discuss here the propriety of establishing species on the basis of but a single differential character, but the foregoing experiments demonstrate that even these fermentation properties are not species characters since (*a*) almost every intermediate grade of development can

[1] Simonin, J. (March 8, 1911), "Un cas de diarrhée de Cochinchine guéri par le radiateur photothermique de Miramond de la Roquette." *Bull. Soc. Path. Exot.*

[2] Goodman, H. M. (October 20, 1908), "Variability in the Diphtheria Group of Bacilli." *Journal Infectious Diseases.*

Diphtheria —*continued*

be found by proper methods in different members of the group as they exist in nature, and (*b*) the extent to which the zymogenic power is exhibited can be readily and markedly altered at will by artificial selection. On the strength of those facts, then, I venture to suggest that the division of the diphtheria group of bacilli into several distinct species is probably based upon a misconception, and that all the forms which have been described under so many different names are but variants of a single species, *B. diphtheriæ*, which constitutes the entire group.

This, be it noted, refers to *B. pseudodiphthericus* and *B. xerosis*. Schultz [1] of Cleveland, Ohio, has of late years observed a change in the type of *B. diphtheriæ* found in swabs sent for examination. Barred forms have almost entirely disappeared, and granular forms have taken their place. The latter, he notes, have to be carefully distinguished from a non-pathogenic bacillus which in 12–24 hour cultures closely resemble them. Prior to the date of this paper the best book of reference is, of course, that by Nuttall and Graham-Smith,[2] of which only mention need be made, as it is the standard text-book in English on the subject. Trautmann and Dale [3] found curious coccoid or spherical forms of virulent *B. diphtheriæ* in agar cultures made during an epidemic at Hamburg. On serum, huge metachromatic granules developed, which caused the bacilli to assume curious swollen shapes. Balfour [4] has found the same or a similar condition in the Sudan. Indeed he describes coccoid forms, not only in cultures but in smears, made direct from the throat swabs. Hence the presence of diphtheria is very apt to be overlooked. These changes probably depend on the reaction of the medium, be it human tissue or of laboratory manufacture. Dale [5] returns to the subject in a more recent paper.

Cappellani,[6] in two cases of diphtheria, found in the exudate ramifying, filamentous forms accompanied in one case by the true Klebs-Lœffler bacillus, in the other case not so accompanied. These forms could be cultivated readily on blood serum, glycerine agar-agar, and in broth, and yielded classical forms of *B. diphtheriæ*. They also produced a true diphtheritic toxin. The author thinks that the ancestral form of the diphtheria bacillus is a streptothrix which takes on a bacillary form in its passages through the organism and acquires a greater virulence. Here, also, mistakes in diagnosis might easily be made.

A somewhat allied subject is that of the relation of the so-called pseudo forms to the true *B. diphtheriæ* and the methods employed for differentiating the latter. Amongst other papers on this subject we note one by Mandelbaum and Heinemann [7] who, as a distinguishing medium, employ glycerine agar in Petri plates. On its surface some drops of sterile human blood are placed and spread, and then this surface layer is inoculated with the culture to be tested. Diphtheria bacilli appear as white or yellowish-white colonies, while the pseudo forms appear as red and wrinkled colonies. The contrast is very striking, as one can affirm, having tested this method. A coloured plate shows the appearances both in young and more advanced colonies. Job [8] uses Neisser's new process as a means of distinction. The mixtures are :—

A.	Methylene blue	1
	Alcohol	20
	Distilled water	1000
	Glacial acetic acid	50
B.	Crystal violet (Hochst)	1
	Alcohol	10
	Distilled water	300

Two parts of A are mixed with one of B. The film is stained with this for fifteen seconds, washed and counterstained with a 1 in 300 watery solution of chrysoidin.

Job is of opinion that if polar staining be visible in a culture not older than twenty-four

[1] Schultz, O. J. (November 26, 1909), "The Proportion of Granular and Barred Forms of *Bacillus diphtheriæ* in Throat Cultures." *Journal Infectious Diseases.*

[2] Nuttall, G. H. F., and Graham-Smith, C. S. (1908), "The Bacteriology of Diphtheria." *Cambridge University Press.*

[3] Trautmann, and Dale, J. (October 4, 1910), "Beitrag zum Formenkreis des Diphtheriebazillus." *Cent. f. Bakt. Beilage*, zu Abt. I., Ref. Volume XLVII.

[4] Balfour, A. (1911), "Diphtheria in the Tropics." *Fourth Report, Wellcome Tropical Research Laboratories*, Volume A.

[5] Dale, J. (December 7, 1910), "Über eine ungewöhnliche Form des Diphtheriebazillus." *Cent. f. Bakt.* I. *Orig.*, Vol. LVI., Nos. 5 and 6.

[6] Cappellani, S. (1910), "Sulle ramificazioni del bacillo di Lœffler." *Ann. Ig. Sperim.*, Vol. XX., No. 3.

[7] Mandelbaum, M., and Heinemann, H. (1910), "Beitrag zur Differenzierung von Diphtherie-und Pseudo-Diphtheriebazillen." *Cent. f. Bakt.*, I. Orig., Vol. LIII., Part 3.

[8] Job, M. E. (March, 1910), "Bacilles diphtériques vrais et bacilles pseudo-diphtériques." *Journ. Phys. et Path. Gén.*, quoted in *Journal Royal Army Medical Corps*, November, 1910.

Diphtheria —*continued*

hours, then the bacillus is that of diphtheria. Should the examination be negative, he attaches importance to the size of the bacilli—(pseudo are shorter than diphtheria bacilli, and are not arranged in Chinese letters)—and to their number in comparison with other bacteria present.

It would then be necessary to study the sugar reactions. Rothe's medium gives the most satisfactory results. Rothe adds one part of sugar-free neutral broth to four of ox-serum. With ninety parts of this he mixes ten of Kahlbaum's litmus solution, in which 10 per cent. dextrose or levulose has been dissolved. This litmus fluid is sterilised by heating to 100° C. for two minutes on three successive days. Plates are made by heating till coagulation takes place. Diphtheria bacilli redden the levulose and dextrose media. Pseudo-diphtheria growths do not change the dextrose plates but sometimes attack the levulose.

Job regards the pseudo-diphtheria bacillus as a harmless saprophyte.

Clark[1] reviews the whole subject, and gives an account of his own research work in connection with the true *B. diphtheriæ* to Hofmann's bacillus. He came to conclusions very different from those of Goodman (*loc. cit.*). They are :—

(1) Solid-staining types are not more prevalent at the end than at the beginning of a case of diphtheria.

(2) Successive passages of *B. hofmanni* through guinea-pigs, chickens, pigeons, or canaries produce no effect either on the animals or on the organisms inoculated.

(3) Doses as large as 7 per cent. of the body weight of half-grown or young guinea-pigs do not kill the animals nor change the type of *B. hofmanni*.

(4) Guinea-pigs inoculated with cultures of *B. hofmanni* sensitised with homologous serum show no unusual effects.

(5) *B. hofmanni* grown in an increased supply of oxygen shows no biochemical or morphological change.

(6) By using celloidin sacs it was found that long-continued growth in the body cavity of guinea-pigs either alone or together with *B. diphtheriæ* or *Micrococcus aureus* does not change *B. hofmanni*.

(7) *B. hofmanni* inoculated into animals in combination with toxin, either directly or in celloidin sacs, exhibits no change in the cultures recovered.

(8) Artificial selection on the basis of morphology does not change the form of *B. hofmanni*.

(9) Solid-staining forms are common to both *B. hofmanni and B. diphtheriæ* during the first eight to twelve hours of growth. Occasionally, however, these types are retained by the *B. diphtheriæ* for much longer periods, and some strains of *B. hofmanni* may show barred types on long incubation.

(10) The frequency curves of acid production of *B. hofmanni and B. diphtheriæ* show marked differences.

(11) We would suggest that the term pseudo-diphtheria bacillus be discarded for the less perplexing one of *B. hofmanni*, and that the symbol D be restricted to those organisms of the correct morphology which produce acid and diphtheria toxin.

(12) From a careful study of the literature, and from the experiments described in this paper, we are forced to take the position that the pseudo-diphtheria bacillus or *B. hofmanni* belongs to a different species from the true Klebs-Lœffler bacillus. Doubtless both organisms do belong to the same group and came from common ancestors, but the differences seem to be sufficiently constant to place them in separate species.

The relationship of avian to human diphtheria has long been a subject of dispute, and Sambon's views were quoted in our last Review. Since then Dean[2] has investigated an outbreak of diphtheria in wood-pigeons, where the cause was apparently a filter-passer, and in no way related to the Klebs-Lœffler organism. Rappin and Vanney,[3] on the contrary, believe the human and avian bacillus of diphtheria identical. It would seem that several different conditions are described as avian diphtheria. Certainly in a roup-like disease of turkeys in Khartoum I have found a bacillus which morphologically and in staining reactions is very like *B. diphtheriæ*. Its cultural characteristics and toxicity have not been determined.

A paper by Dudgeon[4] discusses the literature, and states that there can be no doubt that diphtheria bacilli can retain their virulence for prolonged periods in the throats of infected persons (in Williams' case, 157 days). In some instances they may lose their virulence to some extent, but the majority have been found to retain it in full up to the time of their final disappearance. In the monthly *Bulletin, New York State Department of Health* for October, 1909, an account is given of a persistent diphtheria infection which appeared to be due to the practice of releasing patients from hospital without any bacteriological examination of their throats. In one case living and virulent diphtheria bacilli were found in the throat

[1] Clark, P. F. (May 20, 1910), "The Relation of the Pseudo-diphtheria and the Diphtheria Bacillus." *Journal Infectious Diseases.*

[2] Dean, G. (1909), "Observations indicating that the Recent Outbreak of Diphtheria in the Wood-Pigeon (*Columba palumbus*) is caused by a 'Filter-Passer.'" *Journal Pathology and Bacteriology*, Vol. XIII.

[3] Rappin and Vanney, A. (February 10, 1911), "Sur l'identité des diphtéries avaires et humaines." *C. R. Soc. Biol.*

[4] Dudgeon, L. S. (December 5, 1908), "Latent Persistence and the Reactivation of Pathogenic Bacteria in the Body." *Lancet.*

Diphtheria —*continued*

of a person five weeks after discharge from hospital, the "carrier" being all this time apparently in perfect health. Mathieson [1] draws attention to the phenomena described by Sevestre and Martin which are apt to supervene in diphtheria cases about the twelfth or thirteenth day of attack, and which are believed to be of streptococcic origin. Indeed antitoxin is supposed to lower the resistance to this secondary infection. The author cites some cases in favour of these contentions, the phenomena being (1) a cutaneous eruption, (2) joint pains, (3) otorrhœa, (4) albuminuria, (5) general constitutional disturbance. Burnet [2] has carried out experimental work with the chimpanzee which, though not refractory, is resistant to infection. This resistance he is inclined to attribute to the bacterial flora of the animal's mouth. Bonhoff [3] has recently signalised the presence of virulent diphtheria bacilli in the blood and cerebro-spinal fluid of patients. It was not merely a post mortem infection. These results may, of course, have a far-reaching significance, but require confirmation. Millard [4] has pointed out that very often although diphtheria bacilli cannot be detected in culture within 24 hours, they may be found in them after 48 hours, a point of practical importance.

Strain [5] records a case where a servant remained a carrier for nine months with bacilli intermittently present in the nasal passages, a fact which suggested a lodgment in one of the sinuses whence they were discharged at intervals. He points out how necessary it is to swab both throat and nose. Petruschky,[6] in his efforts to destroy the bacilli in the throats of carriers, found that they exist not only on the surface but in the depth of the tonsillar tissue and in the bronchial tubes. He succeeded in getting rid of them by a method of active immunisation. Briefly, autogenous bacilli were taken, cultivated, killed by chloroform vapour, suspended in normal saline and injected into guinea-pigs. If the latter were unaffected the persons were treated with their own bacilli by subcutaneous injection of the fluid containing them. An important paper and discussion on latent infections will be found in the *British Medical Journal* for August 28, 1909. It is too lengthy for consideration here, and in any case some of the views there expressed are not in accordance with more recent utterances, *i.e.* there is now a tendency, at least so far as school cases are concerned, more or less to ignore the healthy carrier and to look upon systematic swabbing of contacts as an unnecessary counsel of perfection. We find this view expressed by Edwards [7] in a most interesting and suggestive paper. He points out that it is now recognised that the Klebs-Lœffler bacillus may exist in a carrier who is daily and intimately in contact with children without infecting these children. "Moreover," he says, "evidence is increasing that a bacillus indistinguishable morphologically and to be distinguished culturally only with an uncertain degree of accuracy from the Klebs-Lœffler, and therefore to be regarded as the diphtheria bacillus, is to be found in a much higher degree of frequency than was formerly anticipated. By morphologically indistinguishable is meant that the bacillus shows both the polar staining and the palisade arrangement, and the pseudo-diphtheria bacilli are not included in this description." He also states that return cases to fever hospitals were not common even in the days before bacteriological examinations were made, that *B. diphtheriæ* is more widespread in skin lesions than was thought to be the case, and is common, but very doubtfully virulent, in cases of otorrhœa. It is evident, therefore, as he indicates, that we have not yet got to the root of this matter of *B. diphtheriæ*, and of latent infections and carrier cases. As Edwards says :—

> It is reasonable to expect, therefore, that the bacilli which we now class as Klebs-Lœffler bacilli will in the future be found to an extent which will make the isolation of their carriers impracticable. We may look with hope to the microscopists—to men whom Bernard Shaw would call super-microscopists—to differentiate the present morphologically correct Klebs-Lœffler bacilli into classes, enabling us to pass over the carriers of some classes as being not harmful to the public health, inasmuch as their bacilli are not diphtheria-producing bacilli; and we may hope that it will become possible to differentiate between the diphtheria-producing bacilli and the possibly non-diphtheritic bacilli appearing and being ever more widely recognised in otorrhœal rhinorrhœa, and skin diseases. If these hopes are realised, then the public health methods of attacking diphtheria will be simplified; instead of distributing our forces and attempting the supervision of carriers of all kinds of the morphologically correct Klebs-Lœffler bacilli, we shall be able to concentrate our efforts on the particular bacilli which we will know to be potent to cause diphtheria.

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[1] Mathieson, D. M. (November 20, 1909), "Streptococcal Infection in Diphtheria. Observations in Eighty Consecutive Cases." *Lancet.*

[2] Burnet, C. (February 25, 1910), "Diphtérie expérimentale chez le Chimpanzé." *Ann. de l'Inst. Past.*

[3] Bonhoff, F. (December 31, 1910), "Über das Vorkommen von virulenten Diphtheriebazillen im Blut und in der Zerebrospinalflüssigkeit des Menschen." *Zeit. f. Hyg. u. Infekt.*

[4] Millard, R. J. (1909), quoted in *Report Government Bureau of Microbiology, New South Wales.*

[5] Strain, T. (October 17, 1909), "A Diphtheria 'Carrier': Persistence of the Klebs-Lœffler Bacillus Nine Months after Attack." *Lancet.*

[6] Petruschky, Dr. (1908), quoted in *Journal Royal Institute of Public Health,* February, 1909.

[7] Edwards, A. D. (August, 1910), "The Increasing Difficulty of the Diphtheria Carrier." *Practitioner.*

Diphtheria —*continued*

A paper of the same type specially dealing with school infections is that by Garrett,[1] who gives some interesting statistics, and points out how hopeless it may be and also how unnecessary to swab the throats of all contacts in the case of school outbreaks. Both these papers are worth reading, as is one by Arkwright [2] on the more purely bacteriological aspect of the subject. He says :—

With the greatest care and experience bacilli resembling virulent *B. diphtheriæ* are sometimes found in the fauces or nose which are non-virulent for guinea-pigs and produce no toxin capable of killing a guinea-pig. (These bacilli are at the time, therefore, probably non-pathogenic for man.) What is the nature of these bacilli, and can those who harbour them pass on diphtheria ?

These bacilli, which resemble *B. diphtheriæ* morphologically, are not all of the same kind, and should be classified in accordance with the scheme of Park and Beebe, advocated by Graham-Smith, namely :—

(1) Bacilli which do not ferment glucose.

(2) Bacilli which do produce acid from glucose, which are non-virulent for guinea-pigs, but resemble virulent *B. diphtheriæ* in every other respect.

(3) Bacilli which ferment glucose and are virulent for guinea-pigs.

(1) Rarely a bacillus of the Hofmann type resembles a virulent *B. diphtheriæ* morphologically. When isolated, such a bacillus is easily distinguishable by the fact that it does not ferment glucose.

(2) Certain other bacilli occur which closely resemble *B. diphtheriæ* morphologically, but have different characters when grown on solid media. I have come across several such in supposed carriers, which when isolated are easily distinguishable from *B. diphtheriæ* by the opacity of the growth on agar, and by the fact that they ferment cane sugar as well as glucose.

(3) Besides the above, strains are met with which resemble the true *B. diphtheriæ* in every respect, but which are quite non-pathogenic for guinea-pigs in ordinary doses, and produce none, or only very small quantities, of specific diphtheria toxin.

Graham-Smith has very carefully discussed the question of the nature of these non-virulent *B. diphtheriæ*, and he points out that they occur, when a large number of observations are collected, in from 1 to 2 per cent. of all healthy persons not in contact with diphtheria. Graham-Smith's and Cobbett's figures for the occurrence of these non-virulent *B. diphtheriæ* among "contacts" do not exceed this proportion of 1 to 2 per cent. Graham-Smith therefore suggests that the non-virulent *B. diphtheriæ* is a distinct bacillus, and bears no relation to diphtheria.

One has many other references to the carrier question, but those given must suffice, especially as the matter is in a transition stage. It may well be that the important determining factor is to be found in the organism and not in the bacillus. It may be a question of symbiosis, of tissue reaction, of loss of tone, quite apart from any special species of *B. diphtheriæ*. Time will show, but in a town like Khartoum where we operate on a small scale our rule is to deal with what may be called the "intimate contacts," *i.e.* to swab these and isolate them if they show bacilli morphologically and culturally like the Klebs-Lœffler rods.

So far such a method seems to have worked well, but, as Garrett says, it is easy to claim that one has checked an epidemic, but quite another thing to prove it. In this connection reference may be made to one other paper, that of Buchanan,[3] who says that infected contacts rarely develop the disease themselves, although the virulence of the bacilli which they harbour is only slightly lessened.

This writer also gives a method which in practice is said readily to distinguish the true *B. diphtheriæ* from the troublesome *B. xerosis* and *B. hofmanni*. Coagulate some ox-serum in an equal quantity of water, and filter. To one-half 1 per cent. glucose, and to the other 1 per cent. saccharin are added. These two media are coloured with neutral red as an indicator and placed in tubes. "In 24 hours a marked acid reaction is produced in the glucose tube by *B. diphtheriæ*, in both the glucose and saccharin tubes by *B. xerosis*, while no change is produced in either tube by the bacillus of Hofmann.

As, for the most part, treatment spells antitoxin, the question of the conservation of antitoxin under tropical conditions is of primary importance. Anderson's [4] paper yields some useful information in this connection. He gives an account of previous work, of his technique and the experiments made, the latter being illustrated by charts. His conclusions are that :—

The average yearly loss in potency of diphtheria antitoxin at room temperature is about 20 per cent.; at 15° C., about 10 per cent.; at 5° C., about 6 per cent., although in some instances these percentages may be much increased.

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[1] Garrett, J. H. (December, 1910), "Propositions of To-Day in Connection with the Prevention of Diphtheria." *Public Health.*

[2] Arkwright, J. A. (November 12, 1910), "Diphtheria Carriers." *British Medical Journal.*

[3] Buchanan, R. M. (February, 1910), "Discussion on the Latent Infections by the Diphtheria Bacillus and Administrative Measures required for dealing with Contacts." *Journal of Laryngology.*

[4] Anderson, J. F. (May 20, 1910), "The Influence of Age and Temperature upon the Potency of Anti-diphtheritic Serum and Antitoxic Globulin Solution." *Journal Infectious Diseases.*

Diphtheria —*continued*

As a result of this work there appears to be but little difference in the keeping qualities of untreated sera, and sera concentrated by the Gibson process.

Diphtheria antitoxin to be placed upon the market and there kept under unknown conditions as regards temperature should not be labelled with a return date longer than two years, and should contain an excess of at least 33 per cent. to allow for decrease in potency; in addition, when the serum is sold in syringes with an absorbable piston, an excess should be added for this loss.

Dried diphtheria antitoxin kept in the dark, at 5° C., retains its potency practically unimpaired for at least five and a half years.

The lack of confidence in the therapeutic properties of old sera is without basis, as such sera, unit for unit, are as potent as new sera.

The protective value of diphtheria antitoxin is in exact accord with its unit value, and is independent of the volume of the serum or other properties in the serum.

Another paper is that by Banzhaf [1] on the deterioration of the antitoxin, also American work. His results may be quoted in full. So far as one knows there are no statistics from the Tropics where, as a rule, serum is kept stored in ice chests. It would be well if figures were forthcoming both from hot dry countries and from hot humid climates, though it appears to be the temperature and the length of storage which are the determining factors.

Banzhaf says :—

Lots in duplicate of native antitoxic sera, antitoxic citrated plasma, and concentrated antitoxin globulin solution were taken. One lot of each was kept at ice-box temperature, varying from 4° to 7° C. The remaining lots at room temperature (22° to 26° C.).

On starting this work it was my intention to retest these lots every two months, but, after several retests, I found it was too expensive an undertaking. I therefore lengthened the retest time to six months, and later to once a year. The unit value of these lots of sera was determined very carefully with a toxin that was standardised every two months against a standard test serum furnished by the Hygienic Laboratory of the Public Health and Marine-Hospital Service. The deterioration of these various lots was as follows :—

For the native antitoxic sera kept in ice-box, the average deterioration for one year was 14 per cent.; for two years the average was 22 per cent.; for three years, 24 per cent.

For the antitoxic citrated plasma, kept in ice-box, the deterioration was extremely low. The average for one year was 6 per cent.; for two years, 8 per cent.; for three years, 9 per cent.

The deterioration of potency with the concentrated antitoxic globulin solution, kept in ice-box for one year, was 13 per cent.; for two years, 17 per cent.; for three years, 20 per cent.

The average deterioration of potency with the native antitoxic sera kept at room temperature for one year was 18 per cent.; for two years, 24 per cent.; for three years, 26 per cent.

For the antitoxic citrated plasma kept at room temperature the average deterioration for one year was 8 per cent.; for two years, 10 per cent.; for three years, 12 per cent.

For the antitoxic globulin solution kept at room temperature the average deterioration for one year was 16 per cent.; for two years, 20 per cent.; for three years, 23 per cent.

The questions of diagnosis and treatment now claim attention. A new staining method has been described by Rush [2] :—

The following are the materials required. Grübler's methylene blue; Grübler's eosin, "W. G.," or "rein"; tartaric acid; alcohol, 96 per cent.; and distilled water. The solution should be prepared as follows :—(*a*) Saturated aqueous solution of methylene blue, filtered, 10 c.c.; tartaric acid, 10 per cent. aqueous solution, 10 c.c.; distilled water, 80 c.c. (*b*) Tartaric acid, 10 per cent. aqueous solution, 10 c.c.; alcohol, 96 per cent., 50 c.c.; distilled water, 40 c.c.; (*c*) Eosin, saturated aqueous solution, filtered, 1 c.c.; distilled water, 199 c.c. Stain thin films—on a cover-glass or slide, fixed by a flame in the usual way—ten seconds in (*a*); wash ten seconds in (*b*); stain ten seconds in (*c*); blot and dry. Drying or washing between the different steps in water is unnecessary. The polar bodies will be stained deep violet blue; the remainder of the bacillus is of an intense pink colour, as are most other organisms that may be present.

The toluidin blue method is useful and simple. The formula is given by Ker,[3] whose chapter on diphtheria is excellent. The mixture is toluidin blue 0·05 gramme, absolute alcohol 1 c.c., glacial acetic acid 2·5 c.c., distilled water 50 c.c. The dried film is stained from 25 to 30 seconds and the stain blotted off, or the preparation very lightly and quickly washed. Great care must be taken not to overstain.

Appiani [4] believes the local treatment to be as essential as the general treatment by antitoxin. It may be carried out by irrigation, nebulisation, or painting. His best results were obtained by occasional swabbing with oxygen solution (1 volume peridrol Merck, in 10

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[1] Banzhaf, E. J. (1908–9), "On the Deterioration of Diphtheria Antitoxin." *Collected Studies, Research Laboratory Department of Health, City of New York*, Vol. IV.

[2] Rush, W. H. (December, 1908), "A New Method of Staining the Diphtheria Bacillus." *American Journal Medical Science*, quoted in *Medical Annual*, 1910.

[3] Ker, C. B. (1909), *Infectious Diseases.*

[4] Appiani, G. (September 13, 1908), *Gaz. degli Osped.*, quoted in Epitome, *British Medical Journal*, 1908.

Diphtheria —*continued*

of water), followed by swabbing with Bandi's bivalent serum for local use. The value of this method was tested by watching how soon the membrane separated, how long the bacilli could be detected, and what local effects were observed. The throat was first carefully swabbed with the oxygen solution. This usually caused a good deal of white froth to accumulate, and induced a cough, which often caused the expulsion of shreds of membrane. After an hour the same swabbing was again practised, and again, until the membrane was nearly all cleared. As soon as this occurred, the parts were painted or sprayed with Bandi's serum diluted with 100 c.c. of water. It is well to confine the oxygen solution to the parts covered with membrane, as it may set up undue irritation in the healthy parts. As a result of this method of local treatment the average stay of the patients was 23·7 days (54 maximum and 13 the minimum). In the application it gave less trouble and caused less discomfort to the patient than the other more generally used disinfectants. In the rhinitis cases the results were particularly good. The Bandi serum is non-toxic, non-coagulating, and non-caustic, and causes the diphtheria bacillus to disappear more quickly than any other application. Probably the reason for its success lies in its very strong opsonic power.

Pyocyanase, which is an enzyme obtained from the concentrated filtrate of fluid cultures of *B. pyocyaneus*, and then specially treated, has been recommended for the treatment of diphtheria by Tucker [1] and others. It is used in watery solution for spraying or swabbing from two to fourteen times a day, or even oftener. It is powerfully bacteriolytic, and should be used along with antitoxin.

Of great importance is the question of the value of antitoxin as a preventive. A good many papers could be cited testifying to benefit derived from its use. Thus Fayrer [2] records a school outbreak in which it was used in the case of a large number of contacts, and where, along with the detection and prompt isolation of carrier cases, it appeared to be effective in checking the spread of the disease. One has already, however, considered the fallacies in such reasoning. Goodall,[3] a leading authority on this question, has never placed much reliance on antitoxin used as a prophylactic, and has recently advanced some cogent arguments against its use in this way. In the first place he points out that such protection as the injection affords only lasts about three weeks, but he admits the value of even such a short period of immunity. He does not, however, advocate its routine employment, because it is not a harmless drug. It may cause erythematous rash, fever and arthritis, the condition resembling a mild attack of rheumatic fever. A more serious condition, however, is the serum sickness, which is specially apt to attack those subject to asthma and prove fatal. Cyanosis, rapid respiration, rigors and collapse are the leading symptoms. The condition is one of hyper-sensitiveness or anaphylaxis, and may also occur in those who at some previous time have had a dose or doses of antitoxin. Therefore, as Goodall points out, one runs a risk in giving a contact case antitoxin. Later on he may develop diphtheria and then urgently require it, when it can only be given with some danger of anaphylaxis occurring. Another point with which the author deals is the question as to whether it is advisable to give antitoxin to persons who are only suspected to be suffering from diphtheria. This is partly a matter of probabilities, and partly one of the patient's age. As a rule, doubtful cases are not severe, and in persons over 10 years of age a little delay will clear up things and do no harm. In patients under 10 the only doubtful and dangerous class of case is the laryngeal, especially when the disease begins in the larynx and the fauces are clear. In such, if measles, retro-pharyngeal abscess, etc., can be excluded, it is not only justifiable but imperative to give the serum. The general notes on serum treatment are also valuable. The drug differs from others in that the dose is not regulated by the age of the patient.

Hardwicke,[4] while admitting the force of Goodall's arguments, remains in favour of cautious prophylactic treatment with serum. He thinks 500 units is a safe and effective dose, and urges that in all records of untoward results following injection the following points should be stated,—source and age of serum, amount injected, method of standardisation, conditions of storage, patient's general medical history, number of bacteriological examinations made from throat swabs. Evidently he inclines to think the serum rather than the patient

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[1] Tucker, K. (January, 1909), "Die Pyocyanose-Behandlung bei Erkrankungen der Tonsillen, etc. mit besonderer Berücksichtigung der Diphtherie." *Berl. Klinik.*

[2] Fayrer, J. (September, 1909), "An Account of a threatened outbreak of Diphtheria in the Duke of York's Royal Medical School, and the measures adopted to stamp out the Disease and prevent it assuming an Epidemic Form." *Journal Royal Army Medical Corps.*

[3] Goodall, E. W. (January, 1911), "The Antitoxin Treatment and Prophylaxis of Diphtheria." *Public Health. See* also *British Medical Journal,* February 11, 1911.

[4] Hardwicke, G. (March 4 and 11, 1911), "Points Connected with the Serum Treatment of Diphtheria," etc. *British Medical Journal.*

Diphtheria —*continued*

may be at fault. According to Hodgson [1] the conclusions generally accepted at the present time are :—

(1) That the phenomena are not due to any substance in the antitoxic elements of the serum, but to a protein body inherent in the serum itself.

(2) That serum rash and serum sickness or disease may follow one injection only, but will follow more rapidly when a second injection is made, coming on earlier as a rule, the more recent the first injection ; and

(3) That anaphylaxis usually only becomes a possibility when a second injection is made from ten to twelve days and onwards, after the primary one.

As a means of obviating ill effects he gives thyroid gland tablets simultaneously with, and for some days following, the administration of antitoxin, as thyroid gland substance appears to have some modifying influence. A case is recorded in which the administration of morphine apparently effected a cure in a very serious case of serum sickness, while adrenalin has been suggested in the asthmatic cases. Doubtless further work will clear up much that is at present obscure.

Hall [2] records a case in which antitoxin was successfully given by the mouth, and commends this method under certain conditions; 2000 units was the dose given. Waldron [3] puts in a plea for big doses, at least in South Africa, where the disease is usually virulent. He believes in 6000 units as the very smallest initial dose however mild the case may be, and however early it may be seen. He gives another 6000 in six or eight hours if the membrane is not quickly loosening and clearing. In severe cases with extensive membrane 10,000 to 12,000 units is the dose suggested, while if the case is not seen till the third or fourth days and the membrane is widespread, 20,000 is recommended for an initial dose.

Amidst much that is confusing, and perhaps a little disheartening, it is a relief to read in the *Lancet* of December 17, 1910, an account of the fight being waged on a large scale against this dread disease in Chicago, the methods employed and the excellent results obtained.

Additional Notes

Sörensen,[4] in a paper on return cases of diphtheria, states that—

he has never seen a fatal return case of true diphtheria, and adds that of 7,037 cases of diphtheria observed in 1898–1909, only 82, or 1·16 per cent., were return cases. The greatest number of these occurred from four to twelve days after discharge of the patients (source of infection). Of the 82 cases, 8 showed diphtheria bacilli on discharge, 73 none (1 was not examined); that is, 90 per cent. were free from bacilli. Sörensen accounts for these results by assuming that the "supposed" cases may not be the true sources of infection, and that many of the cases in which the bacilli were not discovered might still be sources of infection, as, owing to the inaccessibility of parts of the naso-pharyngeal cavity, the bacilli might have escaped detection. An examination of the figures, therefore, shows that the bacilli were present in 10 per cent., that is 700 out of 7,037 of the discharged patients, but only 8, or 1·14 per cent., infected their families or were return cases.

It seems, therefore, that the presence of bacilli in the throat does not necessarily indicate an imminent danger for the family of the released patient, nor does the absence of the bacilli from the throat give an absolute guarantee of the innocuity of the released person. The author concludes by suggesting that other means of detecting the infectivity of diphtheria convalescents ought to be looked for. He points out that amongst other probabilities a negative result as to diphtheria bacilli of a throat examination may be caused by the particular character of the pharyngeal flora—an opinion which certainly should be taken into serious consideration and experimentally tested.

In this connection one must refer to the spraying and swabbing of the throats of contacts with a pure culture of *Staphylococcus pyogenes aureus*. This method, described by Page,[5] would appear to have a future before it. It is harmless, and destroys Klebs-Lœffler bacilli in the throat in from two to three days. It should be adopted, he says, for all carriers, and immediately after convalescence from an acute attack.

Terrien [6] considers the three chief forms of unrecognised diphtheria in childhood are (1) nasal, (2) bronchial, (3) adenitis. The first form may only appear at first to be a slight cold which gradually gets worse, and may

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[1] Hodgson, A. E. (February 11, 1911), "The Administration (*sic*) of Thyroid Gland Substance upon Serum Rash and Serum Sickness in Diphtheria." *Lancet.*

[2] Hall, D. (March 4, 1911), "Diphtheria Antitoxin by the Mouth." *British Medical Journal.*

[3] Waldron, F. T. (January, 1911), "A Note on the Dosage of Diphtheria Antitoxin." *Transvaal Medical Journal.*

[4] Sörensen (March 28, 1911), "Über Retourfälle (return cases) bei Diphtherie." *Münch. Med. Woch.*, No. 13.

[5] Page, H. (January 15, 1911), "Diphtheria Bacillus Carriers." *Archives of Internal Medicine.*

[6] Terrien (March, 1911), "Les Diphtéries méconnues de l'enfance." *Ann. de Méd. et Chir. Infant.* Quoted in Epitome, *British Medical Journal*, April 1, 1911.

Diphtheria *—continued*

have disseminated the disease for some time before its true nature is discovered. In any child with coryza which persists for some time, diphtheria should be thought of even in the absence of false membrane. The bronchial form is frequently unrecognised until the false membrane is ejected. Some signs should raise a suspicion, such as polypnœa without dyspnœa or spasm, *a bruit de drapeau* perceived on auscultation, and feebleness of the vesicular murmur in one part of the chest. Adenitis, primary and localised to the glands, is the most serious form. It is associated with an ordinary adenitis coupled with the signs of a severe intoxication, such as great depression without fever, rapid pulse, and extreme pallor. Such a condition ought to raise suspicions, and bacteriological examination will often reveal the bacillus of Lœffler.

Fox [1] has a paper on the incidence of diphtheria in India. He thinks that it is much more common than is supposed. In children, nasal diphtheria appearing only as a rhinitis may easily be overlooked.

An important paper from the bacteriological standpoint is that by Weston and Kolmer [2] on the best method of carrying out the guinea-pig test of the virulence of diphtheria bacilli. It cannot be considered in detail here, but the reference is given.

Disinfection. We do not propose to consider papers dealing with the standardisation of disinfectants, as this is purely a laboratory question, and such articles cannot be reviewed in a limited space. Only a few practical papers will receive attention here. Reference may be made to two articles [3 & 4] on disinfecting measures in India. Neither contains much that is new, but the concluding paragraphs of Cornwall's paper give prominence to two points: (1) "The desirability of teaching all persons employed in disinfection work the nature of the disease they are engaged to limit, of explaining the object of the measures they are required to take, and, in addition, of imparting to them a working knowledge of the properties of the disinfectants to be employed. (2) The want of experimental data concerning the action of potassium permanganate in wells and reservoirs contaminated with cholera." The last part of the first proposition will be found partly answered by a paper in the *British Medical Journal* of July 24, 1909, which quotes the results of Laubenheimer's investigations. Here one can only give a few of these in tabular form.

Substance tested	Strength of solution	Time of contact required to kill *S. pyogenes aureus*
	Per cent.	
Pure carbolic acid	1·0	90 minutes
Lysol	2·0	5 ,,
Liquor cresoli saponatus (containing 50 per cent. cresol)	2·0	4 ,,
Corrosive sublimate	0·1	30 ,,

The second is, perhaps, also answered in some measure by Bousfield [5] in his paper on the permanganates. He points out that they

have many qualities which, given a reasonable disinfectant power, entitle them to consideration. Their very great power as generators of nascent oxygen, their non-poisonous character, their cheapness, and lastly their distinctive colour, are all features of value, whilst they alone possess the power of destroying the odour of putrescent matter and of thus affording, in the absence of odour, a very evident, if somewhat rough and ready, criterion of the amount of disinfection that has been effected. Finally they have the advantage of leaving the substance to which they have been applied, whether solid or liquid, in a condition in which it is incapable of giving rise to disease either by the bacteria contained in it or by their products.

This author experimented with crude sewage, and found potassium permanganate more efficient than either Jeyes' fluid or izal. The work, however, would require confirmation. Some instructions as regards the use of cyllin may be quoted. They were issued by Philip [6] in Ceylon.

To prepare Cyllin Solution.

(*a*) *Ordinary Strength Solution.*—Fill an ordinary 3-gallon bucket to within 2 in. of the top with water, add 1½ oz. (a small wineglassful) of cyllin, and mix.

[1] Fox, C. J. (May, 1911), "The Incidence of Diphtheria in India." *Indian Medical Gazette.*

[2] Weston, P. G., and Kolmer, J. A. (April 12, 1911), "Guinea-pig Test of the Virulence of Diphtheria Bacilli." *Journal Infectious Diseases.*

[3] Cornwall, J. W. (1909), "The Disinfection of Native Habitations." *Transactions Bombay Medical Congress.*

[4] Hormusjee, S. C. (1909), "Disinfection of Indian Houses." *Ibid.*

[5] Bousfield, E. C. (October 10, 1908), "An Attempt to Rehabilitate the Permanganates." *Lancet.*

[6] Philip, W. M., quoted in *Journal Tropical Medicine and Hygiene*, September 15, 1908.

(*b*) *Double Strength Solution.*—Add 3 oz. (two small wineglassfuls) of cyllin to the bucket of water and mix. *To Disinfect.* **Disinfection—** *continued*

Use ordinary strength solution for all ordinary purposes, such as disinfecting walls, ceilings, cement floors, furniture, clothing, flushing drains, etc. In the case of clothing put them in the solution and see that they are completely covered by it, stir occasionally to ensure thorough soaking, keep them in the solution for not less than one hour. Use ordinary strength solution also for disinfecting the hands.

Use the double strength for disinfecting earth or cowdung floors and for cement floors, which have been fouled with discharges, such as vomit, fæces, sputum, etc. Use the double strength solution also for privies, cesspits, dust-bins, or wherever the disinfectant is mixed with solid or liquid matter.

In studying this question the reader cannot do better than refer to Hewlett's [1] excellent Milroy Lectures. We insert a few extracts from them. He states that the requirements necessary for an ideal chemical disinfectant are :—

(1) The substance must be cheap. (2) It should be relatively non-poisonous. (3) It should have no corrosive or other action on the ordinary metals, and it should not stain linen, etc. (4) It should not separate into layers on standing, and should run freely from the containing vessel at all times. (5) It should possess high germicidal power. (6) It should be miscible with ordinary tap water in all proportions to form a stable solution or homogeneous emulsion which should not separate appreciably into layers on standing. (7) It may with advantage have a solvent power for grease, for greasy surfaces have often to be disinfected. (8) Its germicidal power should not be markedly reduced in the presence of organic matter. (9) Heating to a moderate temperature should not affect it, so that it may be used hot if desired.

Again he says :—

The far greater *resistance of spores* as compared with the vegetative bacterial cells without spores has been known since the early "eighties" of the last century, but we owe to Boer and to Sternberg in particular the appreciation of the fact that different *non*-sporing species show a very *variable resistance* to disinfecting agents. Thus with the anthrax, diphtheria, glanders, typhoid, and cholera organisms, Boer found that the strength of the disinfectant which killed these organisms with an exposure of two hours to its action for carbolic acid varied from 1 in 200 to 1 in 400, for hydrochloric acid from 1 in 200 to 1 in 1,350, for nitrate of silver from 1 in 4000 to 1 in 20,000, and for the double chloride of gold and sodium from 1 in 400 to 1 in 8000. Moreover, an organism which is very susceptible to the action of one disinfecting agent may not be so susceptible to the action of another which is equally potent with the first on some other organism. That is to say, if two germicides X and Y in concentrations C_1 and C_2 have an equal germicidal effect on some particular organism, it by no means follows that the same relation will exist when they are tested on some other organism.

He deals fully with the methods of testing disinfectants, and concludes with some remarks on their sale and the laws relating to them. These matters are beyond the scope of this Review, but it may be noted that he insists on the necessity for any disinfectant being used only in large excess, *i.e.* a quantity greatly in excess of what laboratory experiments have proved will just do the work required. This is the "margin or factor of safety" recommended by Defries. As one has mentioned the standardisation of disinfectants, a single reference to the most recent and possibly the best work on the subject may be given for the convenience of laboratory workers. It is the paper by Anderson and McClintic.[2]

An illustrated review of a work entitled *Disinfection and Disinfectors*, issued by the Thresh Disinfector Co., Ltd., will be found in *Public Health* for August, 1909.

A very useful kind of paper is that by Barlow.[3] Put very briefly, the facts he brings to light are that much money is wasted in the purchase of disinfectants, that many of the uses to which they are put are farcical, that the practice is of limited value, and that in some respects the universal use of disinfectants is a positive danger, *i.e.* by engendering a false feeling of security and preventing the employment of more efficacious, but perhaps less simple, methods. The other side of the question, at least from the tropical standpoint, is put forward by Lindsay [4] who, writing from Paraguay, states that for the prevention of typhoid, dysentery, ankylostomiasis, plague, tuberculosis and leprosy, he finds the free use of chemical disinfectants invaluable. His remarks on the disinfection of earth closets are useful and, I think, sound :—

However well an earth closet in the Tropics may be attended to, it is very difficult to keep flies away; earth may be heaped in, but one soon finds it moving with maggots. The flies that result do not leave the closet altogether free from contamination, seeing that they generally remain near where they were hatched for some little time. From there they may fly to the nearest kitchen or dining-room! "The bacterial action of the earth" does not keep down flies, so one must use some other means. If one knew the breeding grounds of and could destroy the larvæ of all the different kinds of flies that are known or supposed to convey diseases, a great advance

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[1] Hewlett, R. T. (March 13, 20, and 27, 1909), "Disinfection and Disinfectants." *Lancet.*

[2] Anderson, J. F., and McClintic, T. B. (January 3, 1911), "A Method for the Bacteriological Standardisation of Disinfectants." *Journal Infectious Diseases.*

[3] Barlow, T. W. N. (April, 1910), "Disinfectants: their Scientific Uses, their Quack Uses, and their Dangers." *Public Health.*

[4] Lindsay, J. W. (August 13, 1910), "Disinfectants in the Tropics." *British Medical Journal.*

Disinfection—*continued*

would be made in preventive medicine. For the prevention of typhoid fever, dysentery, ankylostomiasis, and a host of other tropical diseases, I recommend as one measure the destruction of all larvæ in closets. How is it to be done ?

In typhoid and dysentery I prescribe a strong solution of creolin for continual use in the bedpans. I point out that there lies the danger, and that creolin will help to prevent the propagation of the disease. Keep a solution in the bedpan and let the patient evacuate into it. If you attempt to disinfect the stools afterwards, you will find that you have been forestalled by the flies, and at your next meal you will be ingesting what the flies have contributed to your table.

For the destruction of larvæ of flies in earth closets I have used and recommended various methods—throwing in a spadeful of lime occasionally, pouring in a strong solution of creolin, lysol, or carbolic. These latter do not always destroy the larvæ, and for this the cheapest way, where one uses a pail or other small receptacle, is to pour boiling water on the wriggling mass.

I find that in the Tropics one is often asked questions about the use of bleaching powder as a disinfectant. A note in the *British Medical Journal* for December 24, 1910, on some recent work on this subject by Taylor, may therefore be cited with advantage, especially as it somewhat modifies existing views.

Taylor claims to have shown that the action of carbon dioxide in the air on bleaching powder is to liberate chlorine only, with no hypochlorous acid, the carbon dioxide acting just like any other acid, and decomposing both the hypochlorite and any chloride contained in the bleaching powder. His researches further show that ordinary moist air liberates, even at first, a large amount of free chlorine and only a very small amount of hypochlorous acid, while after a time nothing but free chlorine is produced. And if ordinary air is passed through a solution of bleaching powder, a mixture of chlorine and hypochlorous acid is swept out, at first in about equal amounts, but later the free chlorine is increased to about 90 per cent. Taylor concludes that in the ordinary processes of bleaching the active agent is probably free chlorine, any hypochlorous acid playing only a very minor part, and the same would seem to apply when calx chlorinata is used without a mineral acid for disinfecting purposes.

For reviews of a large number of recent papers on disinfectants reference may be made to the *Centralblatt, für Bakteriologie* Referate, for October 25, 1910. In the first Review Supplement one mentioned the formalin and permanganate method. Here is the process detailed by Barrat [1] in a recent paper :—

The place to be disinfected is prepared in the usual way, *i.e.* all the openings, except the exit, are hermetically stopped by means of pieces of paper gummed over the apertures. The capacity of the room is next obtained. The following are the quantities of substances to be used for each cubic metre—

Formalin	20 c.c.
Potassium Permanganate	8 grammes.

The only utensil that is required is one of relatively large dimensions, because of the chemical reaction which takes place, and is accompanied by a brisk effervescence, and the liquid will overflow if the utensil is too small As soon as the mixture is made the reaction commences immediately. It is then necessary to leave the room and shut the door, sticking paper over the cracks. The time taken for disinfection is four hours, after which the room is well aerated.

We conclude by considering some of the applications of disinfecting measures. A very important one both in the Tropics and elsewhere is that having cattle trucks as its object. Schnürer [2] has investigated this subject. He gives a long list of the conditions which a method of disinfecting these vehicles must fulfil. He then considers gaseous and liquid disinfectants, decides in favour of the latter, and recommends formalin as the only efficient substance at the present time. As regards liquid disinfection he says :—

The greatest advantage of this method is that the disinfection can be controlled and varied as necessity arises. The fluid must be effective in a solution as dilute as 5 per cent., and anthrax spores with at least thirty seconds' steam resistance must be certainly killed in four to five hours; for the disinfection is more certain when a large quantity of liquid is used, and cost of the material is then not so great. The effectiveness of the method may be absolutely increased by a repetition of the treatment. The fluid must be directed against the surfaces to be disinfected under a pressure of three to four atmospheres, so that the forcible entry of the liquid into cracks and crevices is assured. The fire hose which must be provided at each station will serve this purpose. A fine spray, such as is given by whitewashing apparatus, is to be absolutely avoided, as the pressure exerted is very slight, with the result that there is no mechanical effect and the liquid does not penetrate to any depth. On the same grounds it is not advisable to use brushes for the application of the fluid, apart from the labour and care entailed by the method.

In addition to the properties already mentioned, the fluid or the material used for the preparation of the watery solution must be a definite chemical substance, constant in composition, very stable, neither explosive nor poisonous, and soluble in water in the required concentration without the necessity of any other procedure, such as filtration.

The disinfection of ships has now reached a high degree of efficiency. Chantemesse and Borel have devised a simple and non-patented apparatus for the use of sulphur dioxide. It consists of a stove for burning the sulphur, of a force-pump to liquefy the gas, a reservoir, a

[1] Barrat, H., quoted in *Journal Royal Institute of Public Health*, February, 1911.

[2] Schnürer, J. (April 23, 1910), "Die Desinfektion von Eisenbahn-Viehwaggons." *Deutsche Tierärztl. Woch.*

gas-holder and a fan. It is easily fitted up, and can disinfect a large ship in two or three hours (*see* note under "Paris" in *Lancet*, February 27, 1909). A record of a discussion on the subject at the Sixteenth International Medical Congress will be found in the *Lancet* for September 18, 1909. Opinions differed as regards the relative values of carbon monoxide and sulphur dioxide. The former is odourless, and therefore rats do not try to escape from it and are killed, but it has no effect on mosquitoes or bacteria. Clemow believed the ideal gas for a loaded ship has not yet been found, but that at present the Clayton apparatus gave the best results. Tauffer pointed out that the Nocht apparatus was much more costly, but might be used at wealthy ports. Further information on this subject will be found under the heading "Vermin." Disinfection—*continued*

Salmon [1] considers the measures at one time in force for disinfecting letters coming from countries infected with cholera, plague, or yellow fever. He points out that such precautions are no longer necessary. In this connection, however, it is interesting to note that infection in a case of scarlet fever in a remote Himalayan station was recently conclusively traced to the reception of an infected letter from England. It would seem that the formalin methods for book disinfection mentioned in the last Review are practically useless, as shown by the recent experiments of Renney. Hence any one interested in this question is referred to an account of Gærtner's [2] special apparatus designed for the use of the mixed vapours of alcohol and water. A translation of the original article occurs in *Public Health* for March, 1910. Owing to recent discoveries as regards carrier cases in typhoid fever, efforts at the disinfection of bile and urine by the internal administration of disinfectants are worthy of note. Stern [3] records experiments with menthol and salicin for the bile, and new urotropine, helmitol and hippol (formaldehyde preparations) for the urine. Menthol in 0·5 gramme doses, 3 to 5 times daily for three days, gave good results in one case. One point brought out was that the simultaneous use of alkaline water weakened the favourable action of urotropine.

Additional Note

An interesting extract of a paper by Salvado on "Clayton" gas as a destroyer of rats and insects will be found in the *Journal of Tropical Medicine and Hygiene*, for April 15, 1911. One notes specially that it is effectual in destroying bed-bugs on board ship, and also that it prevents the deteriorations of foodstuffs by insects. It is also specially good for getting rid of ants.

Dropsy (Epidemic). The dispute still proceeds as to whether this disease is or is not identical with beri-beri. Pearse is an upholder of the former view, which is combated by Chatterjee and others. It is pointed out that in epidemic dropsy there is anæmia with a low hæmoglobin value, a symptom absent in beri-beri. Tenderness of the calf and loss of knee jerk are absent in epidemic dropsy, but then again the knee jerk may persist in beri-beri. A brief account of the discussion from which these notes are taken will be found in the *Lancet* for October 10, 1908. Naturally the subject attracted attention at the recent Bombay Medical Congress. Macleod [4] mentioned the three views held—(1) that the disease is beri-beri; (2) that it is epidemic dropsy and not beri-beri; (3) that beri-beri and epidemic dropsy are the same disease, presenting in different cases and outbreaks variations of type, more especially as regards the prominence of nervous and dropsical phenomena. He presented a lengthy table, compiled from several sources, which certainly tended to prove that the diseases are distinct. Megaw [5] has described cases the symptoms of which strongly tended to prove the reverse, and what is more, the cause appeared to be a rice dietary just as in beri-beri. As a special research has been instituted in Calcutta, it is likely that ere long this vexed question will be cleared up.

Dust. This must ever be an important subject in the desert regions of North Africa. There can, I think, be no doubt that the prevalence of dust in the atmosphere of the Sudan accounts for the frequency of nasal and pharyngeal catarrh, the presence of cases of asthma,

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[1] Salmon, P. (June 9, 1909), "Présentations de lettres provenant de pays contaminés et soumises à la désinfection." *Bull. Soc. Path. Exot.*

[2] Gärtner, A. (1909), "Über Bücherdesinfektion im grossen." *Zeit. f. Hyg. u. Infektion*, Vol. LXII.

[3] Stern, R. (1908), "Über antiseptische Beeinflussung von Galle und Harn durch innere Anwendung von Desinfizienten." *Zeit. f. Hyg. u. Infektion.*

[4] Macleod, K. (1909), "Beri-Beri and Epidemic Dropsy." *Transactions Bombay Medical Congress.*

[5] Megaw, J. W. D. (April, 1910), "Note on Cases of the 'Epidemic Dropsy' type of Beri-Beri at the Presidency General Hospital, Calcutta." *Indian Medical Gazette.*

Dust— *continued*

and possibly also renders the native more liable to the onset of pulmonary tuberculosis. It is Wegmann who says :—

> Scarcely any one who continuously breathes a dusty atmosphere escapes an acute catarrh set up by the irritation. In some cases, subsequent continued exposure to the same influences will not produce other serious effects. In others, however, the dust penetrates into the bronchial tubes and sets up chronic mischief. In the sputum the characteristic cells lining their walls may be seen. Many who survive this stage do not suffer further. But in certain cases the dust fills at first single air cells, and then groups of them, destroying the walls and rendering them useless for breathing purposes.

True he is speaking of dusty occupations and factory life, but in a lesser degree the statement may, I believe, be fitly applied to out-of-door conditions in the Sudan and elsewhere at certain seasons of the year. A good deal has been heard of Dustolio, a special preparation for laying dust on floors, etc., but it is probable that it is more suited to conditions in temperate climates than those obtaining where there are regular sand storms and dust devils.

Sheard [1] of Toronto has described his experiences in the application of oil to streets for the purpose of laying dust. He used crude petroleum there with such satisfactory results that he extended its use to the macadamised roads throughout the city generally. The oil is applied in several relays at intervals of a few days. The number of applications required varies according to the character of the road. If the road is good and free from ruts and not subject to heavy traffic, three applications, which are regarded as one oiling, should last from one to three months. But if the road is bad and traversed by heavy drays and wagons, the oiling will probably not last longer than one month. The better the road the smaller the dose required. If the road has a high gradient, and is much exposed to the sun, the oil will dry up sooner than if the road is more or less shaded by trees. The oil is lightly sprinkled from a watering cart driven at a fairly rapid rate, so that the drops will be, to a great extent, separate, and puddles of oil will not be left in depressions. Should these occur they should be swept away with a broom, so that they will not be splashed by the traffic on the clothes of pedestrians. After three or four days a second application is made, and, after a week, a third. It is an advantage to prepare the road beforehand by cleaning out channels and filling up ruts, but this may not be practicable and is not necessary. Rain does not affect disadvantageously an oiled road ; such a road dries more rapidly after a shower. The surface water runs speedily into the channels and the road is improved rather than injured. When the sun comes out the last traces of water are removed and the surface of the road is oily again. Dr. Sheard finds that 1,500 gallons of petroleum per mile is sufficient for one oiling (three applications) of an ordinary road ; 2000 gallons may be required for a road in bad repair. At 4 cents a gallon for the oil and from 10 to 15 dollars for its application the cost is from 70 to 75 dollars per mile, and in Toronto this is 20 per cent. less than the cost of watering. Oiling has many advantages over water. A watered road dries quickly, and in three hours is as bad as ever. Moreover, after traffic it is more damaged, and its general appearance is inferior to that of an oiled road. The objection may be raised that the oil has an odour. Dr. Sheard finds that this is little complained of, and that it generally passes off in three or four hours.

Forbes [2] has carried out experiments from the bacteriological standpoint with dustless oils as a dressing for schoolroom floors, and finds :—

> (1) That the relative number of bacteria is approximately the same in the air of the class-room whether the floor be treated or not, provided the scholars do not move about.
>
> (2) That the relative number of bacteria in the air of a room where drill is being carried on, and where the floor has not been treated, is three times as high as in a room the floor of which has been treated.

The advantages are as follows :—

> (1) Economy of labour in cleaning the room.
>
> (2) Prevention of the rising of dust once deposited ; hence a healthier atmosphere for breathing.

Dysentery. This subject, of course, falls naturally into two main divisions : (1) Amœbic ; (2) Bacillary. As regards the first, little need be said owing to the recent publication of Carnegie Brown's [3] excellent volume on the subject. Some recent papers, however, require notice. A translation by Sutherland of Werner's [4] paper on the pathogenic amœbæ will be found in the *Indian Medical Gazette* for July, 1909. He describes and figures *E. histolytica* and *E. tetragena*, the latter being Hartmann's *E. africana*. He also mentions the possibility

[1] Sheard, C. (November, 1909), *Canadian Journal of Medicine and Surgery*, quoted in *Lancet* for January 22, 1910.

[2] Forbes, D., quoted in *Public Health*, September, 1910.

[3] Brown, W. C. (1910), *Amœbic or Tropical Dysentery.*

[4] Werner, H. (1908), "Studien über pathogene Amöben." *Beihefte z. Arch. f. Schiffs-u. Tropen-Hyg.*

Dysentery —*continued*

of mistaking *Amœba limax* for these pathogenic forms, especially in culture media. So far as they went the author's experiments yielded no proof of the spread of dysenteric material by the intestinal tracts of flies. Vincent [1] records cases of what appear to be amœba carriers. These may show no sign of illness, or may have some slight dysenteric symptoms persisting. Certain exciting causes may bring about fresh acute dysenteric attacks in these "carriers." Musgrave draws attention to the occurrence of intestinal amœbiasis without diarrhœa, and contributes a study of fifty fatal cases of this condition. The infection was in the colon, most commonly the cæcum and ascending portion, and in some of the cases symptoms were entirely absent, though characteristic amœbic lesions were found post mortem. Musgrave describes the symptoms as follows :—

Abdominal aching, usually more or less general, worse at night and early in the morning, and often accompanied by flatulence and occasionally by constipation, is one of the most frequent of the symptoms, but unfortunately this is extremely common among a large class of patients with mild forms of indigestion who are not suffering from amœbic infection. Distension of the abdomen and the discomforts of flatulence are of frequent occurrence. Constipation is a particularly common complaint. In this class of patients the lack of result from ordinary doses of the usual cathartics may be brought to the attention of the physician, or in other instances the action of these drugs may be unusually severe and prolonged. Loss of weight occasionally becomes a noticeable symptom, but in many instances the nutrition remains good and the patients may even increase in weight. Interference with the appetite is usually first shown by lack of desire for breakfast, and this may be accompanied by morning nausea and the accumulation of considerable mucus in the mouth and throat during the night. Active indigestion or dyspepsia are not very common symptoms, but do occur in a certain percentage of the cases.

Excessive perspiration, particularly of the palmar and plantar surfaces, is very frequent, and in many instances the physician is first consulted because of this complaint. The whole chain of symptoms of so-called "Philippinitis" or tropical neurasthenia, characterised by dullness, headache, loss of memory, weakness, desire for sleep, etc., is a rather common condition encountered in these infections, but it is also particularly prevalent in the absence of such parasitic invasion.

The only method of diagnosis is the recognition of amœba in the stools, though the sygmoidoscope is of service in certain cases and at certain stages of the disease.

Koidzumi [2] has described a new parasitic amœba found in the intestines of Japanese, and named *E. nipponica*, while Elmassian [3] has discovered a new human species now called *E. minuta*. The first paper in English is merely an illustrated preliminary note, the second points out that *E. minuta* is near *E. tetragena*, and is associated with latent or chronic dysentery. It was found in the excreta along with *E. coli* in a case from Paraguay, South America, and the author appears to have satisfactorily differentiated it from other species. In this connection the reader should be referred to Hartmann's [4] special work on the parasitic amœbæ, probably the most important record on the subject which has yet appeared. Another paper by this author,[5] well illustrated and supplying a good deal of general information about the *Entamœbæ*, is that on *E. testudinis*, a new species in the European tortoise.

Bacillary dysentery is quite as important as the amœbic form, and the recent literature upon it is larger, especially from the purely bacteriological standpoint. We must, however, be content with a limited number of references. Galli-Valerio, dealing with the etiology and prophylaxis of bacillary dysentery at the Sixteenth International Medical Congress in 1909, pointed out that the disease is due to many bacilli belonging to the Shiga group, and condemned the terms para-dysentery and pseudo-dysentery as tending to cause a neglect of prophylactic measures. He cited the following chief means of spread :—

(1) By personal contagion either from sick persons or from healthy "carriers" of the bacilli, and either directly or through fomites.

(2) By water, which plays a most important rôle in the spread of the disease.

(3) By means of flies, as proved by experiments.

(4) By milk, which may be infected by flies, or by the addition of infected water, or the washing of vessels with such water.

(5) By vegetables, for similar reasons.

(6) By the soil and dust.

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[1] Vincent, H. (February 10, 1909), "Note sur la latence prolongée de l'Amibe dysentérique dans l'intestin humain. Les 'porteurs d'amibes.'" *Bull. Soc. Path. Exot.*

[2] Koidzumi, M. (October 9, 1909), "On a new parasitic Amœba, *Entamœba nipponica*, found in the intestines of Japanese." *Cent. f. Bakt.*, I. Orig., Vol. LI.

[3] Elmassian, M. (1909), "Sur une nouvelle espèce amibienne chez l'homme, *Entamœba minuta* n. sp. 1er mémoire. Morphologie. Évolution. Pathogénie." *Ibid*, Vol. LII.

[4] Hartmann, M. (1909), "Untersuchungen über parasitische Amöben." *Arch. f. Protist.*, Vol. XVIII. *et seq.*

[5] *Idem* (April, 1910), "Über eine neue Darmamoeba, *Entamoeba testudinis* (n. sp.)." *Mem. Inst. Oswald. Cruz.*, Vol. II., No. 1.

Dysentery —*continued*

Ruffer and Willmore,[1] in an important paper on the bacteriological aspect of cases of dysentery amongst pilgrims at El Tor, divide the micro-organisms found into two provisional groups :—

GROUP A—AMŒBIC DYSENTERY

(*a*) Cases in which the *E. histolytica* is found in the stools. (Typica symptoms, etc. Common form.)

(*b*) Cases in which the *E. histolytica* is present, together with the *Bacillus dysenteriæ*, El Tor, No. 1.

GROUP B—BACILLARY DYSENTERY

(*a*) Cases in which the Shiga-Kruse bacillus is found in the stools. Comparatively rare.

(*b*) Cases in which the *Bacillus pseudo-dysentericus*, D (Kruse) is found.

(*c*) Cases in which the *Bacillus dysentericus* (Flexner) is present. One case only noted.

(*d*) Cases in which the *Bacillus dysentericus*, El Tor, No. 1, is found.

(*e*) Cases in which other similar, but not identical, micro-organisms are found. Two varieties at least exist.

In the paper they deal with the characters of Group B. (*d*), this *B. dysentericus*, El Tor, No. 1, being the most important of the lot. Its cultural characteristics, serum reactions, etc., are fully considered and illustrated by means of comparative tables. These must be consulted in the original, but the outcome of the work is to be found in their remarks, which we append :—

As has been stated already in the beginning of this paper, there are, during the Mussulman pilgrimage, at least seven different causative agents of dysentery, the most important one being the one we have just described under the name of *B. dysentericus*, El Tor, No. 1. This multiplicity of causative agents renders the treatment of dysentery extremely difficult, for, whereas it is comparatively easy to recognise, by examination of the stools, the cases which are due to amœbæ, it is impossible to diagnose in this way, or by the physical signs, to what class of dysenteric bacilli the other cases are due. And yet this diagnosis is most important, for we have found that whereas the serum prepared by injection of the Shiga-Kruse bacillus, has a most remarkable curative action on the cases in which the disease is clearly due to this bacillus ; the severe cases caused by the *B. dysentericus*, El Tor, No. 1, are not at all affected by this serum. On the other hand, the few severe cases which we have treated with the serum of a horse, repeatedly injected by *B. dysentericus*, El Tor, No. 1, were not only benefited, but quickly cured. Unfortunately, it is not practicable to establish the bacteriological diagnosis before using the serum. The minimum period necessary for such a diagnosis is thirty-six hours, and this valuable time must not be lost, as most of these patients arrive in an almost hopeless condition. The treatment, therefore, must be commenced at once, and our only hope is to prepare a polyvalent serum, as Shiga has already done in Japan. Thanks to a grant from the Egyptian Government, we hope to have such serums ready for the next pilgrimage season.

In a later paper these authors [2] report on the preparation and successful use of this polyvalent serum. They consider that it should be used as a routine measure or, in lieu of it, multiple injections of different monovalent serums. The dosage was 40 to 60 c.c. in mild cases, 80 c.c. in severe cases, and 100 to 120 c.c. in desperate cases, these doses being repeated as required, as much as 320 c.c. being given in the 24 hours. In some cases 80 c.c. of the polyvalent serum were given, followed as soon as the diagnosis was made in cases of single infection by 80 c.c. of the specific serum. The results were remarkable, and there were no serious untoward effects. This paper certainly constitutes a very important addition to the literature of bacillary dysentery.

Wise [3] has drawn attention to a peculiar condition occurring in British Guiana, and affecting the small intestine only. It is described as follows :—

A short length (6 to 8 in.) appears deep purple, acutely congested, and the mucous membrane is covered by a muco-fibrinous deposit. No strangulation has taken place, and there is no associated peritonitis. Ten to twelve loose, watery, and mucoid stools are passed daily, free from amœbæ. Microscopically, the inflammation is limited to the mucous and sub-mucous layers. Bacteriologically, there is present a very short bacillus, ·0003 mm. long, which has well-marked and distinctive characters. It is extremely dangerous and highly virulent, killing a guinea-pig in from four to fourteen hours after intraperitoneal injection.

From the above account I should not be surprised if this is a condition similar to that which I mentioned on *page* 52 of our first Review as occurring in Khartoum. Certainly it is very like it, and I believe that there are certain acute and often fatal inflammatory conditions

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[1] Ruffer, M. A., and Willmore, J. G. (September 25, 1909), "On the Etiology of Dysentery." *British Medical Journal.*

[2] *Idem* (November 12, 1910), "The Serum Treatment of Dysentery." *Ibid.*

[3] Wise, R. S. (1909), quoted in *Journal Tropical Medicine and Hygiene*, September 15, 1909.

Dysentery —*continued*

of the small intestine which occur under tropical conditions and about which we know very little. They can, however, be classed as forms of bacillary dysentery.

Pottevin [1] points out that bacilli of the Flexner type ferment mannite, while those of the Shiga type are supposed not to do so, and in a preliminary note gives some results which upset this view, for he found that *B. Shiga* does ferment mannite, and that the action is more marked the more peptone there is in the liquid medium. Lunz [2] has recently applied the deviation of complement test for the differentiation of dysentery bacilli. His paper must be consulted for details.

Whatever may be the case as regards amœbic dysentery there seems little doubt but that flies can act as vectors in the bacillary form. This is brought out by Galli-Valerio,[3] who quotes several papers favouring this view in a recent interesting review. The question of carriers now claims brief attention. In a review of a paper by Vincent, the *British Medical Journal* of December 25, 1909, quotes him as placing dysentery carriers on much the same footing as enteric carriers. The bacillus of dysentery may persist for three or four weeks in the intestine of persons cured of the disease, and it may also occur in healthy persons who have not shown the slightest sign of dysentery. The dysentery bacillus does not, however, persist in the gall bladder, bile being unfavourable to its growth. The *E. histolytica* may persist for six months, a year, or even several years as above, and healthy people who have never had dysentery may be " carriers " and harbour virulent amœbæ.

One may note here Vincent's method of destroying such amœbæ, *i.e.*, lavage with a solution of sodium hypochlorite (10 or 12 in 1000), a litre being given at one time and retained for an hour. The addition of laudanum aids retention. Two or three injections suffice. The original papers [4] will be found in the *Bulletin de la Société de Pathologie Exotique*. An important paper on the subject is that by Sacquépée,[5] who brings out much the same facts, dividing the carriers in bacillary dysentery into healthy convalescents and chronic. The first-named are rare. A paper founded on investigations on a large scale is that by Simon [6] who made successive examinations of the fæces in the cases of dysentery carriers (84), and soldiers (70) who had suffered from dysentery due to Hiss's bacillus of dysentery. His investigations lead to one practical conclusion, viz., that each soldier who has been suffering from dysentery, or has been found to be a carrier, should have his fæces examined at least once monthly during the whole subsequent period of his military service. I confess this sounds like a counsel of impossible perfection. Macalister [7] also has a paper on the subject, and his three conclusions may well be quoted :—

(1) Healthy carriers are very rare, and of no importance.

(2) The actual carriers are to be found among the incomplete convalescents, which form a high proportion of the cases.

(3) In combating an epidemic it is necessary to reduce as far as possible the number of such cases, and to isolate very strictly those which are of this type.

Passing now to prevention and treatment we need not again allude to Vincent's method (*loc. cit.*) of treating chronic amœbic forms. Simon [8] has used ipecacuanha for two years, is now a firm believer in its efficacy, and believes that its want of success in other hands is due to incorrect methods of use. Absolute rest in bed with restricted diet is particularly essential. Castor oil is given as an initial purgative, and then each evening after a three hours' fast, 40 to 60 grains of ipecacuanha in pill form coated with salol. The dose is then reduced 5 gr. each evening until 10 gr. is reached. The 10 gr. are then continued each day for two weeks. Irrigation with saline solution may be used at the same time when the dose of ipecacuanha is reduced to 10 gr. Before using ipecacuanha, irrigation was found inefficacious. Forster's

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[1] Pottevin, H. (January 12, 1910), " Relation des différents bacilles dysentériques sur la fermentation de la mannite." *Bull. Soc. Path. Exot.*

[2] Lunz, R. (March 22, 1911), " Zur Differenzierung der Dysenteriebazillen mittels der Komplementablenkungsmethode." *Cent. f. Bakt.*, I. Orig., Vol. LVIII., No. 2.

[3] Galli-Valerio, B. (1910), " L'état actuel de nos connaissances sur le rôle des mouches dans la dissémination des maladies parasitaires," etc. *Ibid*, Vol. LIV., No. 3.

[4] Vincent, H. (February 10, 1909), " Note sur la latence prolongée de l'Amibe dysentérique dans l'intestin humain. Les ' porteurs d'amibes.' " Also " Emploi de l'hypochlorite de soude pour le traitement de la dysenterie amibienne chronique." *Bull. Soc. Path. Exot.*

[5] Sacquépée, E. (June 30, 1909), " Les Porteurs de Germes." *Bull. de l'Inst. Past.*

[6] Simon, G. (November 12, 1910), " Über Nachuntersuchungen bei ehemaligen Ruhrkranken und Ruhrbazillenträgern." *Cent. f. Bakt.*, I. Orig., Vol. LVI., Nos. 3–4.

[7] Macalister, G. H. K. (November 12, 1910), " Dysentery Carriers." *British Medical Journal.*

[8] Simon, S. K. (November 6, 1909), " Amœbic Dysentery." *Journal American Medical Association.*

Dysentery —*continued* anti-dysenteric vaccine was favourably mentioned in our first Review. Since then Newman [1] has recorded two severe chronic cases where it proved of the greatest benefit. A paper by Cantlie [2] deals with the surgical treatment of chronic recurrent dysentery and stenosis of the sigmo-rectal pylorus, and lies outside the scope of this Review. The reference, however, may be useful. Macy [3] in his admirable paper, already largely quoted from under "Diarrhœa," says that in chronic amœbic dysentery there is no treatment so valuable as appendicostomy. The meso-appendix should be left intact to ensure a good blood supply. The bowel is irrigated through the appendix.

An account of the operations required, of cases treated, and a statement as regards its great advantages over colostomy, are given by Tucker.[4] Buchanan [5] deals with dysentery in jails, a most important subject in the Tropics. What he says is very practical, and some of it may be quoted. After pointing out the necessity for good cooking and well-prepared clean food, the danger of soiled clothing and blankets, and the necessity for general cleanliness, he says :—

> Once we get hold of the view that it is the convalescing or sick dysentery patient that is the danger, and that for several weeks after apparent recovery he may be, and probably is still shedding the bacilli in his stools, it is not difficult to suggest means for prevention. The latrine, for example, may become an important factor in the spread of dysentery, and the use of the left hand by natives of India for ablution is also an obvious source of infection and re-infection. The free use of dry earth by each prisoner is one safeguard, the burning of sulphur or cow-dung to keep off flies is another precaution, as also is the use of kerosene in the lime-wash in latrines. The proximity of cowsheds and cattle to a latrine is clearly undesirable, as it is very difficult to keep a byre free from flies. The use of a *lota* or other vessel for ablution as well as for drinking is obviously objectionable, and it is not difficult in latrines to supply special ablution vessels, kept only for these purposes and washed by the sweeper-gang after the latrine parade is over. Here I may also mention the importance of not hurrying over the latrine parades. In Bengal we have a sufficient number of latrine seats to permit of every man being allowed five minutes, and the whole parade is over in half-an-hour (*i.e.* one latrine seat for every six prisoners). Objection has been taken by laymen to a "latrine parade," but in the first place prisoners are certainly not forbidden to use them at other times; and secondly, it is sound physiology to accustom the prisoners to regularly evacuate their bowels at fixed times. The practice of taking notice of all prisoners who use the latrine at night is a useful one, if carefully used, as it enables the hospital assistant to catch many cases in the very earliest stage.

The author is a believer in the sulphate of soda treatment, and as a dietary for native patients recommends strained rice-pulp mixed with curdled milk. A more elaborate paper on the same subject, and one of great value, is that by Forster.[6] It should be studied by every one who has to do with jail sanitation in the Tropics, even though all his Indian conclusions may not be applicable to jails in other countries. Thus he does not find the water-supply often at fault, while in the form of well water it has certainly been to blame for sporadic cases in the Khartoum Central Prison. He points out that repeated attacks of dysentery in the same individual are common in jails where the bacillary form is due to Shiga's bacillus, though Flexner's bacillus and the Y-bacillus of Hiss may also be operative. The last can cause a very severe and even fatal form of dysentery. As regards the diagnosis of the bacillary forms, he remarks :—

> The best method is to isolate the bacilli from the stools, but as this method will rarely be available reliance must be placed on the following points :—
>
> (*a*) *The Character of the Stools.*—In the acute stage of bacillary dysentery the stools are devoid of fæcal matter. Microscopically the mucus shows the leucocytic exudate I have already spoken of. Except in cases of mixed infection there are no amœbæ in the stools. If, however, magnesium sulphate be given beforehand the stools will generally be found to contain amœbæ. I would therefore strongly advise you not to give magnesium sulphate before examining the stools.
>
> (*b*) *Pyrexia.*—Pyrexia in the early stages is a common feature of Shiga infections. It also occurs with other types of dysentery bacilli.
>
> (*c*) *The Agglutination Test.*—This test is not of much value. In the first place there are several kinds of dysentery bacilli, and each case ought to be tested against each type. In my investigations I made observations on the value of this test for two organisms only, viz., Shiga's bacillus and Flexner's bacillus. I found that the agglutinins rarely show any marked increase before the fifth day, and that in the case of Shiga infections the agglutinins seldom show any very great increase. Briefly my views with regard to this test are as follows. The test should be performed twice, once on the fifth day and again on the twelfth day. The test is only of value when a positive indication is obtained.

Dysentery due to the tubercle bacillus and the leprosy bacillus must not be forgotten.

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[1] Newman, E. A. R. (May, 1909), "Note on Two Cases of Chronic Dysentery, treated by Forster's Anti-Dysenteric Vaccine." *Indian Medical Gazette.*

[2] Cantlie, J., quoted in *Journal Tropical Medicine and Hygiene*, August 16, 1909.

[3] Macy, F. S. (1909), "Notes on Tropical Diarrhœas." *Transactions Bombay Medical Congress.*

[4] Tucker, E. F. G. (1909), "The Use of Appendicostomy in the Treatment of Intractable Ulceration of the Colon." *Ibid.*

[5] Buchanan, W. J. (1909), "The Prevention and Treatment of Dysentery in Jails." *Ibid.*

[6] Forster, W. H. C. (1909), "The Nature, Prophylaxis and Treatment of Dysentery in Indian Prisons." *Ibid.*

The amœbic form is rare in jails in India, and if uncomplicated is not accompanied by pyrexia. Like Buchanan, he believes the spread is due to the human host, and from certain experiments concludes :—

(*a*) Under natural conditions the extra-corporeal existence of dysentery bacilli is very short.

(*b*) A high air temperature combined with a low degree of humidity is unfavourable to the extra-corporeal existence of dysentery bacilli, but a moderate air temperature combined with a high degree of humidity is favourable to their extra-corporeal existence.

(*c*) Dysentery bacilli do not carry on a saprophytic existence outside the human host.

As regards prophylaxis he lays great stress on the detention of patients in hospital until they have been absolutely cured, and advocates the following routine :—

Patients were only discharged from hospital after they had eaten ordinary food and passed normal motions for fifteen days. Further, no patient was discharged from hospital, however satisfactory his motions might be, if there was any evidence of unhealed lesions on palpation of the large intestine.

There should also be a post-dysentery gang, *i.e.* a segregation of convalescents, the chief value of which, however, is that it helps one to detect an incompletely recovered case. He speaks highly of the value of vaccine-therapy in treatment, both of the acute and chronic forms. In the latter, it may be combined with mercury in the form of a perchloride solution.

In a discussion on this paper Heard spoke to the value of a good oral hygiene amongst the prisoners. A few lines on the preparation of Dopter's [1] immunising vaccine may not be out of place. He uses sensitised bacilli, and proceeds as follows :—

Five mg. of culture of Shiga's dysentery bacillus are weighed out, killed by exposure to 60° C. for an hour and dried *in vacuo ;* they are then made into a uniform emulsion with a few drops of sterile physiological salt solution ; to this, unheated antidysenteric serum of high agglutinating power is added, so as to make the total quantity of the material up to 2 c.cm. The whole is mixed and allowed to stand at laboratory temperature for about twelve hours. At the end of this time the agglutinated and sensitised bacilli have collected at the bottom of the tube, and the supernatant serum is clear. The liquid is decanted, the deposit is washed twice by centrifugalisation with normal saline, and after the last liquid is poured off the deposit is emulsified with 2 c.cm. of salt solution. This liquid emulsion constitutes the vaccine.

In experimental animals he states that it confers an immunity of much longer duration than is obtained by any other method, and consequently suggests its prophylactic use in human beings, especially in troops ordered to a region where dysentery is epidemic.

South African practitioners will find a short account of the two species of monsonia, *ovata* and *biflora*, in the *Prescriber* for January, 1910. The latter as a tincture, 1 in 8, is said to be excellent in dysentery. It tends to constipate, but the active principle, *Entericin*, isolated by Maberly, while acting beneficially, has not this drawback. A new line of treatment is the injection of normal serum recently advocated by Piotrowsky.[2] It is given subcutaneously, 10 c.c. in the case of children, 20 c.c. for adults. Two daily injections are given, and it is said to effect a rapid cure.

Begg [3] speaks highly of yellow santonin in dysentery as well as in sprue. It is best given in olive or almond oil, a 5-grain dose night and morning. It must be yellow, not merely lemon coloured, for it is the substance formed from santonin by the action of sunlight that possesses the real value. It should be used as early in the disease as possible, and its virtues are supposed to be due to its strong germicidal action.

Hewes [4] advocates the use of a 5 per cent. solution of nitrate of silver. A dose of magnesium sulphate is first given. After the motion a rectal tube is inserted for eight or twelve inches, and a pint or more of solution is injected. The injection should be retained for half-an-hour. Defæcation is then permitted, and after this, irrigation with saline solution is carried out. Another silver injection is given in about two days. The average duration of the cases under this treatment was ten days ; while Shiga gives the duration of cases under vaccine treatment as twenty-five days.

The treatment of amœbic dysentery forms the subject of a recent paper by Deeks and

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[1] Dopter, C. (September, 1909), "Vaccination préventive contre la Dysenterie bacillaire (ses bases expérimentales)." *Ann. de l'Inst. Past.*

[2] Piotrowsky, V. V. (November 23, 1910), "Traitement de la Dysentcrie par le sérum sanguin." *Semaine Médicale.*

[3] Begg, C. (December 15, 1910), "Yellow Santonin in Sprue and Dysentery." *Journal Tropical Medicine and Hygiene.*

[4] Hewes, H. F. (April 21, 1910), "The Treatment of acute Dysentery by Intestinal Irrigation, with a 5 per cent. solution of nitrate of silver." *Boston Medical and Surgical Journal,* quoted in *Medical Annual,* 1911.

Dysentery —*continued*

Shaw.[1] They term it the "rest-supportive" treatment, and it consists of absolute rest, an absolute milk diet in abundance, saline or water irrigations, and bismuth subnitrate in heroic doses. As they say, "It is because milk is the least prone to bacterial fermentation, and that it is practically all absorbed before it reaches the large intestine, that it is the ideal diet in amœbic dysentery." Eggs for these reasons are contra-indicated. The bismuth is given in doses of a drachm or a drachm and a half by measurement (three drachms by weight), stirred in a glass of water, every three hours till there is a general improvement, which is from three to ten, or at most fifteen days. The drug acts both as a mechanical sedative and astringent and as a powerful intestinal antiseptic. They record very good results by this method. Ruffer and Willmore (*loc. cit.*) state that the "enema kartulis" night and morning is of value in early amœbic cases. It consists essentially of an emulsion of iodoform and tannic acid.

Space does not permit a review of other forms of dysentery, but references are given to the papers of Bowman [2] and of Bel and Couret [3] on *Balantidium coli* infections. The latter is specially worthy of study. Another paper which may be consulted is one by Martini [4] describing an amœba-like ciliate producing dysentery in man. An illustration of the parasite is given.

Additional Notes

A bacteriological paper by Morgan [5] deals chiefly with strains obtained in England, and he finds that :—

(1) A large number of dysentery-like strains isolated from sources not obviously connected with clinical dysentery in this country have been thoroughly tested, and a certain proportion of them has been found to be entitled to membership of the mannite-fermenting dysentery group.

(2) Bacillary dysentery must be more widely distributed in this country than has hitherto been believed, and thorough bacteriological investigation may throw light on the etiology of dysenteric forms of diarrhœa which at present are not clinically recognised as such.

(3) Like certain foreign strains recently isolated from definite dysenteric sources, these home strains cannot be identified completely with any of the well-known types of the group, on application of extensive fermentation and absorption tests.

(4) When a sufficiently extended series of carbohydrate media is tested the fermentation properties of the mannite-fermenting group afford an indication of differences between the members of the group which are not brought to light by agglutination and absorption tests.

Another lengthy paper which we can only mention, and which deals with the bacilli found in connection with a dysentery epidemic in Mid-Germany is that by Schroeter and Gutjahr.[6] Mayer [7] deals with the epidemiology and bacteriology of pseudo-dysentery, but the mere reference must suffice.

Jail dysentery in India again receives attention at the hands of Gillitt.[8] He testifies to the value of the prophylactic inoculation of new arrivals.

Brem and Zeiler [9] state that the bismuth treatment of Deeks and Shaw (*loc. cit.*) cannot be relied upon. They are in favour of ipecacuanha, and state that—

the drug is best administered in salol-coated pills, the thickness of the coat being carefully regulated so as to prevent vomiting on the one hand and on the other the passage of intact pills through the intestines, one-sixteenth in. being a suitable thickness. It is best to begin the treatment by giving 60 to 80 grains at bedtime, decreasing the dose by 5 grains daily until a dose of 10 grains is reached, by which time it is usually advisable to discontinue treatment, lest the further administration of small doses should keep up the catarrhal condition of the bowel which

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[1] Deeks, W. E., and Shaw, W. F. (1909), "The Treatment of Amœbic Dysentery." *Proceedings Canal Zone Medical Association.*

[2] Bowman, F. B. (December, 1909), "Two Cases of *Balantidium coli* Infection, with Autopsy." *Philippine Journal of Science*, B.

[3] Bel, G. S., and Couret, M. (October 25, 1910), "*Balantidium coli* Infection in Man." *Journal Infectious Diseases.*

[4] Martini, (December 31, 1910), "Über einen bei amöbenruhrähnlichen Dysenterien vorkommenden Ciliaten." *Zeit. f. Hyg. u. Infekt.*, Vol. LXVII., No. 3.

[5] Morgan, H. de R. (March, 1911), "The Differentiation of the Mannite-fermenting Group of *B. dysenteriæ*, with Special Reference to Strains Isolated from Various Sources in this Country." *Journal of Hygiene.*

[6] Schroeter and Gutjahr (May 27, 1911), "Vergleichende Studien der Typhus-Coli-Dysenteriebakterien im Anschluss an eine kleine Ruhrepidemie in Mitteldeutschland." *Cent. f. Bakt.*, I. Orig., Vol. LVIII., No. 7.

[7] Mayer, O. (1910), "Zur Epidemiologie und Bakteriologie der Pseudodysenterie." *Klin. Jahr.*

[8] Gillitt, W. (April, 1911), "More Notes on Jail Dysentery." *Indian Medical Gazette.*

[9] Brem, W. V., and Zeiler, A. H. (1910), "Ipecac in the Treatment of Intestinal Amœbiasis." *Collected Papers, American Society of Tropical Medicine.*

Dysentery —*continued*

the larger doses have already excited. Rapid cures may sometimes be effected by giving 40 grains three times during twenty-four hours. During treatment the patient should be kept in bed and upon a liquid diet, and since solid food and milk curds may delay the pills in the stomach, nothing of this kind should be given for at least six hours before the ipecacuanha, and no food of any kind for three hours before. The pills should be given about 8 or 9 p.m., after which the patient should be kept lying on the right side for some time, the colon having been flushed out with normal salt solution during the preceding afternoon. No opiate is needed, and experience shows that a large proportion of amœbic infections can be eradicated by this method, which has proved itself to be far superior to any other line of treatment, and deserving of a thorough trial before any surgical treatment is attempted.

Vedder [1] has recently published an important paper in which the efficacy of ipecacuanha in protozoal dysentery is strongly upheld. Experiments *in vitro* were conducted, and the following conclusions reached :—

(1) That 2 per cent. fluid extract of ipecacuanha inhibits the growth of dysentery bacilli.

(2) That this is not a specific action, since ipecacuanha also inhibits the growth of other bacteria, while other drugs such as hydrastis and digitalis are quite as powerful as the former in inhibiting dysentery bacilli.

(3) That the *B. dysenteriæ* of the Shiga type that he worked with appears to be more susceptible to the action of ipecacuanha and other drugs than the Flexner strain.

(4) That the treatment of bacillary dysentery by ipecacuanha is not recommended, because it has not been shown that this drug possesses any greater activity against dysentery bacilli than many other drugs, and because it would probably be difficult, on account of dilution with intestinal contents, to give sufficient of it to make a solution in the intestine as strong as a 2 per cent. solution of the fluid extract which was the strength used in these experiments. However, since it has been shown to inhibit the growth of dysentery bacilli to some extent, it has probably done patients with bacillary dysentery no harm, and on the other hand, may possibly have accomplished some good, particularly if the dysentery was caused by the Shiga type of *B. dysenteriæ*.

He sums up by saying that—

the ipecacuanha treatment of dysentery caused by protozoa should not on light grounds be set aside in favour of any other, but that in using this treatment great care should be taken to make sure that the dysentery is truly caused by protozoa, and is not bacillary, and also to obtain an ipecacuanha that is shown by actual analysis to contain its proper amount of emetin, and when this is not possible to insist upon obtaining the Brazil root.

It is curious how opinions differ, for we find Manaud,[2] who believes the antidysenteric action of the drug is due to ipecacuanhic acid, lauding the preparation without emetin, and reporting good results from its use. It may be that the special powder prepared by Dausse which he employed explains the discrepancy.

Elephantiasis. Although too lengthy for review here, Daniels' [3] paper and those following it on the discussion of lymphatic diseases in the Tropics are worthy of note. There were the usual arguments for and against Manson's view that filariæ are the cause. Daniels, who favours it, points out that we need not assume that all cases of elephantiasis are produced in the same manner by filariæ, and draws attention to subsequent bacterial invasion which may cause acute lymphangitis, and may even cause the death of the worm. Manson's view that the eggs are really at fault is rejected by Havelock Charles, but it is scarcely necessary to enter here into all the points of the discussion, which can only be profitably studied *in toto*. In the light of one of Daniels' hypotheses, a paper by Dufougere [4] is of interest. He, like Le Dantec, found not only fragments of the dead bodies of filariæ in the blood, but also a cocco-bacillus, the lymphococcus of Le Dantec, which it is believed kills the filaria. It is the dead bodies of the embryos which, according to Le Dantec, block the lymphatic vessels and give rise to the symptoms of elephantiasis. The lymphococcus alone cannot produce lymphangitis. Handley [5] has also recorded a case of lymphangitis of the thigh and scrotum in a man who had never been out of England, and in whose blood a diplococcus was found. From this a vaccine was prepared, the administration of which rendered the blood sterile, and possibly contributed to the good results obtained by lymphangioplasty.

Foulerton and Whittingham [6] discuss the significance of coccal infections associated with elephantiasis, and cite the above case in which they proved the diplococcus to be the *Micrococcus pyogenes albus*. Discussing Dufougere's work (*loc. cit.*), they think his lympho-coccus

[1] Vedder, E. B. (May 15, 1911), "A Preliminary Account of some Experiments undertaken to Test the Efficacy of the Ipecacuanha Treatment of Dysentery." Quoted in *Journal Tropical Medicine and Hygiene.*

[2] Manaud, A. (May 10, 1911), "Traitement de la Dysenterie Amibienne par la poudre d'ipéca désémétinisé." *Bull. Soc. Path. Exot.*

[3] Daniels, C. W. (October 31, 1908), "Lymphatic Diseases in the Tropics." *British Medical Journal.*

[4] Dufougere, W. (October 14, 1908), "L'éléphantiasis, ses rapports avec la lymphangite endémique des pays chauds." *Bull. Soc. Path. Exot.*

[5] Handley, S. (December 12, 1908), "The Relief of Elephantiasis." *British Medical Journal.*

[6] Foulerton, A. G. R., and Whittingham, H. K. (March 18, 1909), "On the Significance of Coccal Infections associated with Elephantiasis." *Cent. f. Bakt.*, I. Orig., Vol. XLIX.

Elephantiasis—*continued*

may be identified with the *Micrococcus pyogenes albus*, and they are not prepared to accept Le Dantec's view as above stated. They regard the added coccal infection as merely a casual incident in the course of the disease, even when, as in Handley's case, they succeeded in finding it in the deep lymph of a limb affected by elephantiasis, at a time when no cutaneous lymphangitis was in active progress. They rather regard it as a residual infection after a previous attack of cutaneous lymphangitis. An interesting paper is that by Brochard,[1] who had an opportunity of studying the disease amongst an isolated island population of about 4000 persons. The main facts he adduces are the notable frequency of elephantiasis arabum on the Wallis Islands, the absence of diseases which are certainly filarial in origin, the abundance of cases of superficial abscess and inguinal adenitis, and the brevity of the attacks of elephantiasis. The author in certain cases found sheathed microfilariæ in the blood, but neither he nor his predecessor ever encountered adult filariæ in the islands. On this and on the clinical grounds mentioned, he concludes that the elephantiasis of the Wallis Islands, which appears to be quite typical, has nothing to do with filariasis, and inclines to the belief that both it and the suppurative and inflammatory condition occurring along with it are due to some micro-organism which has its habitat in the soil. Low [2] still continues a supporter of the *Filaria bancrofti* theory. Portions of his paper may be quoted here.

After dealing with some of the apparent fallacies he says :—

> The proof of the pudding lies in the fact, that where filariasis is common, elephantiasis is common ; where filariasis is rare, elephantiasis is rare ; where filariasis is absent, elephantiasis is absent, or at most is represented by a spurious case from time to time due to chronic erysipelas, tumours, or some other cause than the filaria. Lastly, if filarial lymphangitis is admitted to be due to the *F. bancrofti*, then elephantiasis must also be admitted, because one can trace the former step by step by insensible grades into the latter.

Again, speaking about the commencement of the disease, he quotes Corney of Fiji, who writes :—

> Elephantoid fever is, in my experience, an essential condition in the production of true elephantiasis, and it occurs sooner or later in a large majority of cases of varicose groin glands. Daniels refers to cases of elephantiasis without any pain or febrile attacks ; these I imagine to be very rare, and may possibly correspond with the cases of elephantiasis occurring in non-filarial countries.

and then continues :—

> My experiences are similar ; in the vast majority of cases the usual history is for the patient to have suffered previously with attacks of filarial lymphangitis, a little permanent thickening remaining after each, till a stage is reached when one calls the condition elephantiasis. There is no necessity to record such cases, therefore, but those rarer ones, quoted by Daniels and Manson, where the disease goes on after a single attack, or after none at all, without pain, are of extreme interest.

Records of cases of this kind are given, and their pathology is discussed. Amongst other points raised he states that :—

> In the ordinary cases of elephantiasis every one is more or less satisfied that the filaria *per se* does not cause the condition ; organisms apparently also help, and of these the streptococcus is the one most likely to assist. The absence of embryos from the blood in elephantiasis is easily explained by the pathological lesions found—the adults are long dead, and there are no embryos therefore to find their way into the blood. In heavily-infected countries it is quite feasible that such a case should get reinfected with filaria—the adults inhabiting some of the lymphatics in a different part of the body—and in that case embryos will again appear in the blood. I have noted this in several instances in St. Kitts, a heavily-infected area. *Post mortem* examinations in many instances do not help one much, as, if the case is one of long standing, age will have obliterated many of the characteristic changes that must have been present when the lesion started. Similarly, the dissection of elephantoid limbs, apart from showing the usual pathological lesions of thickening, hypertrophy, and solid œdema, do not reveal the etiology of the production of the condition.
>
> I carefully dissected four elephantiasis legs removed by operation in the West Indies, but found nothing to account satisfactorily for the condition present. In leaving the pathology and etiology of elephantiasis and some of the other filarial manifestations then, one must admit that there are many points by no means clear or definitely settled. Extended work is required for the solution of the different problems presented.

Turning now to the treatment of the condition we find Castellani again expatiating on his very excellent method of fibrolysin injections and bandaging. As this is now to be found in his own and other text-books we need not enlarge upon it here. It is a palliative measure, and his conclusions regarding it are :—

> (1) The treatment I have devised for elephantiasis—thiosinamin or fibrolysin injections and methodical bandaging, followed by removal of portions of the redundant skin when most of the fibrous tissue has been absorbed—is of utility in a certain number of cases.

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[1] Brochard, V. (June 8, 1910), "L'éléphantiasis arabum aux îles Wallis et la théorie filarienne." *Bull. Soc. Path. Exot.*

[2] Low, G. C. (March 15, 1911), "The Etiology of Elephantiasis." *Journal Tropical Medicine and Hygiene.*

Elephantiasis—*continued*

(2) The treatment has generally only a slight and temporary effect in recent cases when the disease is in the acute stage, with frequent attacks of filarial fever.

(3) The treatment gives much better and more lasting results in old-standing cases, especially in those of the verrucose type, characterised by the enormous neoformation of fibrous tissue and absence of fever.

(4) On the mode of action of the treatment I am not yet in a position to give a definite explanation. A partial explanation may, perhaps, be found in the well-marked, though transient, leucocytosis which generally follows each thiosinamin injection.

Handley's case has already been mentioned. A fuller account of the operation of lymphangioplasty and the results obtained will be found in the *Lancet* for January 2, 1910. Dubruel,[1] who is a believer in Le Dantec's view (*loc. cit.*), describes a method of treatment by giving perchloride of iron by the mouth, applying an ointment containing 10 per cent. sulphate of iron and by the use of anti-streptococcic serum. The latter, given in doses of 20 c.c. for 7 or 8 times at intervals of 3 to 15 days, gave satisfactory results, as did the perchloride of iron treatment. A reference to the operation for elephantiasis scroti may be given. Baldwin [2] has modified the usual method so as to be certain of getting enough skin. His short paper should be consulted for the surgical details. Further information is given by Branch [3] in a paper wherein he refers to Baldwin's article.

Additional Notes

Although he admits his personal experience of the disease is somewhat limited, Shattuck [4] has undertaken a review of the literature, and summarises his conclusions regarding the vexed question of etiology as follows :—

(1) The essential characteristics of typical acquired elephantiasis are lymphangiectasis, hyperplasia of connective tissue, and chronic œdema.

(2) The relation of these to each other in the production of elephantiasis is not clear.

(3) It appears that these changes may frequently be attributed to the interaction of stasis and of inflammation.

(4) Stasis always occurs early and persists.

(5) Inflammation may precede or follow stasis, or may not be manifest at any stage of the disease.

(6) Inflammation when present may be acute or chronic ; and is generally traceable to bacterial infection.

(7) Either chronic stasis or inflammation from any cause may predispose to elephantiasis, but even when they occur together, elephantiasis does not always result.

(8) There is reason to suppose that congenital weakness or anomalies of lymphatics may play an essential part in the production of some cases of elephantiasis ; and that such weakness or anomalies can be inherited.

(9) The filaria is an important factor in the production of endemic elephantiasis of some regions, but it is not essential to the occurrence of endemic elephantiasis.

(10) Elephantiasis in filarial regions results indirectly from filariasis through bacterial infection.

(11) Sporadic lymphatic elephantiasis and endemic elephantiasis are not essentially different.

Enteric Fever. One can only consider a mere fraction of the numerous references, and select for review, papers on bacteriology, on carriers, on the disease in the Tropics, and on prevention and treatment. A few notes on blood culture may be useful.

Bettencourt and Regalla [5] tested various methods, and found the use of bile best. One adds 1 to 2·5 c.c. of blood to 5 c.c. of bile, incubates, and after 24 hours plates out on Drigalski-Conradi. Epstein [6] finds 2 per cent. glucose broth, 2 per cent. glucose agar, and 0·2 per cent. solution of oxalate of ammonia all better than the above method, giving him respectively 80, 81·4, and 92 per cent. of positive results. He notes that the number of colonies which develops has no prognostic significance. Castellani, in order to reduce the bactericidal power of the blood, introduced the method of diluting it with fifty times its volume of nutrient broth. Gildemeister [7] finds sterile water does quite as well. By its use he once succeeded

[1] Dubruel, C. M. E. (July 21, 1910), "Essais de thérapeutique de l'éléphantiasis arabum." *Bull. Soc. Path. Exot.*

[2] Baldwin, F. A. (February 26, 1910), "The Operation for Elephantiasis Scroti." *British Medical Journal.*

[3] Branch, T. E. R. (May 16, 1910), "On Operation for Elephantiasis." *Journal Tropical Medicine and Hygiene.*

[4] Shattuck, G. C. (1910), "Etiology of Elephantiasis." *Collected Papers, American Society of Tropical Medicine.*

[5] Bettencourt, N., and Regalla, G. (1908), "L'hémoculture en bile dans le diagnostic de la fièvre typhoïde." *Arch. Inst. Bact. Camara Pestana.*, Vol. II., No. 1, Lisbon.

[6] Epstein, A. A. (1908), "Blood Cultures in Typhoid Fever." *Proceedings New York Pathological Society,* Vol. VIII.

[7] Gildemeister, E. (February, 1910), "Nachweis der Typhusbazillen im Blute durch Anreicherung in Wasser." *Arbeit a. d. K. Gesundheitsamt,* Vol. XXXIII., No. 3.

Enteric Fever—*continued*

in isolating *B. typhosus* when the bile method had failed. He used one part of blood to from eight to ten parts of sterile water, and believes the hæmolysis of the red cells aids the growth of the typhoid bacilli by liberating anti-bactericidal substances. Cummins and Cumming [1] investigated the matter, and concluded—

(1) That normal blood diluted from five to ten times in sterile water will serve as a culture medium for *Bacillus typhosus* when the bacilli are in sufficient number. (2) That this medium is fatal to small numbers of typhoid bacilli, owing probably to the bactericidal substances in the blood. This action would presumably be still greater in dealing with actual cases of enteric fever. (3) That 0·5 per cent. taurocholate of soda in sterile water forms, with the proteid of the added blood, a very efficient medium for blood culture in enteric fever.

Cummins [2] tested the efficacy of this bile salt water in cases where the blood was obtained by finger puncture, adding only about 0·5 c.c. of blood to 5 c.c. of the medium. A positive result was obtained in 40 per cent. of his cases, which compares comparatively favourably with 54 per cent. in a similar series of vein-puncture cases. The percentage was higher in the second week than later in the disease. No early cases were available. With reference to the various media used for isolating *B. typhosus* from the stools and urine of patients, and from water, etc., we find that Birt, in the *Lancet* of November 14, gave the composition of Conradi's brilliant green medium. He said that it

consisted of agar 30 grammes, Liebig's extract 20 grammes, peptone 10 grammes, and water 1000 cubic centimetres. Normal soda or phosphoric acid solution was added until the reaction became + 30, Eyre's scale, phenol-phthalein indicator. After sterilising, 1 cubic centimetre of a 1 in 1000 aqueous solution of brilliant green crystals, extra pure Höchst, obtainable from Messrs. Baker and Co., Holborn, and 1 cubic centimetre of a 1 per cent. solution of picric acid (Grübler) were added to 150 cubic centimetres of the agar. Sterilisation was not repeated, since the dyes were precipitated by autoclaving the agar. Malachite green media caused a loss of agglutinability of the typhoid bacillus which did not occur with brilliant green. Hence a bacteriological diagnosis might be made in a day. In 2,850 examinations of fæces by that method Conradi had isolated the typhoid bacillus 325 and the paratyphoid 35 times, and from 2,500 urine cultures he had recovered the typhoid bacillus on 105 and the paratyphoid on 26 occasions.

Werbitzki [3] recommends the use of China green (1·4 to 1·5 c.c. of a 0·2 per cent. solution to 100 c.c. of melted agar). It is said to inhibit the growth of *B. coli* to a much greater extent than the other preparations used.

Gaehtgens and Brückner [4] have compared the merits of a considerable number of media in 72 enteric cases, besides cases of paratyphoid and of carriers. They isolated the *B. typhosus* or *paratyphosus* by means of—

Endo's agar (Fuchsin)	in 50 per cent.
Werbitzki's agar (China green)	in 53 ,, ,,
Gaehtgen's agar (Caffein-fuchsin)	in 58 ,, ,,
Conradi's agar (Brilliant green)	in 59 ,, ,,
Lentz and Tietz's agar (Malachite green)	in 66 ,, ,,

The last named would therefore seem to be the best.

It contains 0·53 per cent. of a 0·5 per cent. alcoholic solution of pure malachite green in crystals. The reaction should be such that 10 c.c. of $\frac{N}{1}$ alkali are required to bring a litre of the agar-agar to the phenol-phthalein neutral point. It should be freshly prepared, since exposure to light acts deleteriously on the dye. The plates should be incubated twenty-four to forty-eight hours after inoculation. If the typhoid colonies are not well marked, a few drops of saline fluid are run over the surface of the agar. Endo plates are then spread with the emulsion. The *B. typhosus* was detected in the fæces of 50 per cent. of the enteric fever patients in the first or second week, and of 75 per cent. of those in the third week.

A medium which these two German observers did not find so good as the others is that of Padlewski,[5] which is a modified malachite green, but it has been favourably reported upon by Grimm, Werbitzki, and by Kathe and Blasius. The latter did not find Lentz and Tietz's method very successful. The following account of Padlewski's medium is taken from a review in the *Journal Royal Army Medical Corps* for July, 1910, which also gives details of the work of Kathe and Blasius with it.

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[1] Cummins, S. L., and Cumming, C. C. (June, 1910), "A Simple Method of Blood Culture in Enteric Fever." *Journal Royal Army Medical Corps.*

[2] Cummins, S. L. (February, 1911), "Blood Culture in Typhoid Fever." *Ibid.*

[3] Werbitzki, F. W. (1909), "Ein neuer Nährboden für den Nachweis von Typhusbazillen in Fäzes." *Arch. f. Hyg.*, Vol. LXIX., No. 2.

[4] Gaehtgens, W., and Brückner, G. (February 19, 1910), "Vergleichende Untersuchungen über einige neuere Typhusnährböden," etc. *Cent. f. Bakt.*, I. Orig., Vol. LIII., No. 5.

[5] Padlewski, L. (1908), "Eine neue Anwendungsmethode des Malachitgrünagars zum Nachweis von Bazillen der Typhusgruppe." *Ibid*, Vol. XLVII., No. 2.

Enteric Fever—*continued*

To a 3 per cent. agar, prepared with broth or meat extract, he adds 2 per cent. peptone and 3 per cent. ox-bile, liquefied by heat and filtered through cotton-wool, and 1 per cent. lactose dissolved in a small quantity of water. The reaction should be weakly alkaline to litmus. The agar should be nearly clear, though it is not necessary to filter it a second time after the addition of the bile. The mixture is put into flasks, 100 c.c. in each, and sterilised fractionally; 100 c.c. are liquefied, cooled to 60° C., and the following ingredients added: 0·5 c.c. of a 1 per cent. watery solution of malachite green, chemically pure Höchst, 0·5 c.c. of ox-bile, 0·75 c.c. to 1 c.c. of a 10 per cent. freshly prepared watery solution of sodium sulphite. It is poured into dishes which are left uncovered in the incubator for a quarter of an hour. The agar is of a pale yellow colour, without a tinge of green, since the dye has been decolorised by the sodium sulphite. The salt alone precipitates malachite green. The addition of bile prevents this. Typhoid colonies remain colourless; coli are deeply tinted green—hence the distinctions are well marked in twenty-four hours. The enteric colonies attain twice or three times the dimensions of those grown on the usual malachite green, and on Endo's agar. The borders are sinuous, the surface is delicately furrowed, finely granular, and is often terraced. The *B. coli* colonies are coarse, opaque, greenish-brown, and are destitute of furrows. Paratyphoid growths resemble typhoid. Streptococci and staphylococci are inhibited. Padlewski isolated the *B. typhosus* thirty times in forty-six examinations of dejecta on this medium. In fifteen comparative experiments he made with Drigalski-Conradi's, Endo's, and his method, he recovered the typhoid bacillus from excreta four times by the two former, and nine times by his own.

If the plates are prepared some days before use the agar may assume a greenish tint. This change rather facilitates than hinders the identification of the typhoid colonies, as they bleach the agar beneath them.

Jackson and Melia [1] strongly recommend the use of lactose-bile for the isolation of *B. typhosus* from water and milk followed by subsequent plating on Hesse's agar. They give the formula for the latter and the details of its preparation, together with certain cautions regarding its storage and use. The lactose-bile consists of sterilised, undiluted ox-gall (or an 11 per cent. solution of dry fresh ox-gall), to which has been added 1 per cent. of peptone and 1 per cent. of lactose. It is used in fermentation tubes.

Guth [2] of Hamburg has introduced a new alizarine, lactose and alkaline agar medium, on which *B. typhosus* forms blue colonies. Kathe [3] considers which is the most practical method for the bacteriological diagnosis of typhoid fever. He is in favour of blood culture and the Widal reaction. The detection of bacilli from the throat he considers of no value. Turning to other bacteriological papers the reader may be referred to Houston's water reports, especially those on research work, for much information regarding the vitality of *B. typhosus* in water, and the effects upon it of the storage of water. Some details will be found under the heading "Water," *page* 408.

The question of typhoid vaccine is in the main a bacteriological one. Probably the best general account of anti-typhoid inoculation is to be found in the Harben lectures by Leishman.[4] The preliminary experiments, methods of preparation, storage, standardisation, and use, are all detailed. Statistical results of inoculation in the army are presented, and in this connection one may direct attention to a useful paper by Maynard,[5] who, on a statistical basis, criticises the conclusions of Buist in 1908, and points out the sources of fallacy in the statistical methods usually employed. The figures quoted by Leishman, however, would appear to be above criticism, being based on a large number of cases, and very carefully collected and recorded by a special committee. Amongst 20,000 men there was a case incidence of 5·39 per 1000 among the protected, and of 30·4 among the unprotected. As Corker [6] points out in a recent paper, many of the cases shown among the protected must have occurred among men who had really ceased to be protected, for it would seem that two years may be taken as the maximum period of protection. Leishman also gives case-mortality statistics, which are favourable so far as they go. Indeed in twenty out of twenty-four units no inoculated man died from enteric fever, a most gratifying result. The lectures conclude with a brief note on vaccine-therapy. The results obtained are believed to justify further trial of this method of treatment. Lack of space will not permit of further references to anti-typhoid inoculation beyond the notice of a useful little note in the *British Medical Journal* for October 8, 1910, which says :—

There is a vast amount of data which goes to show that antityphoid inoculations reduce both case incidence and case mortality. In reply to the first question, it may therefore be said that it is advisable for a European

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[1] Jackson, W. W., and Melia, T. W. (April, 1909), "Differential Methods for detecting the Typhoid Bacillus in Infected Water and Milk." *Journal Infectious Diseases.*

[2] Guth, F. (July 24, 1909), "Zum Nachweis von Typhus- und Paratyphusbakterien." *Cent. f. Bakt.*, I. Orig., Vol. LI., No. 2.

[3] Kathe, H. (1910), "Die bakteriologische Typhusdiagnose." *Ibid*, Vol. LV., No. 5.

[4] Leishman, W. B. (July, August, and September 1910), "Anti-typhoid Inoculation." *Journal Royal Institute Public Health.*

[5] Maynard, G. D. (March, 1909), "Statistical Study of Anti-Typhoid Inoculation." *Biometrika*, Vol. VI., No. 4.

[6] Corker, T. M. (April, 1911), "The definition of a Unit's Protection by Anti-Typhoid Inoculation." *Journal Royal Army Medical Corps.*

Enteric Fever—*continued*

travelling to the East, to a district where enteric fever is rife, to be inoculated before departure. In reply to the second question—namely, where the material can be obtained, what apparatus is required, and how many inoculations are necessary—it may be pointed out that in this country Wright's vaccine is employed, while in Germany, Pfeiffer and Kol's vaccine is preferred. In the former case the vaccine prepared by the Lister Institute of Preventive Medicine can be obtained from Messrs. Allen and Hanbury's, while other well-known firms—for example, Messrs. Burroughs Wellcome and Co.—also produce and sell typhoid vaccines. The apparatus required is a good sterilisable hypodermic syringe. According to Wright, two injections should be given with an interval of from one to two weeks, 750 to 1000 million bacilli being injected at the first, and from 1,500 to 2000 million at the second, injection. In reply to the question, there is no reason to believe that antityphoid inoculation will in any way interfere with antivariola vaccination. Lastly, it is preferable to perform the first injection at least before the person starts, so that the malaise which follows this may have passed off before going on board ship. Many give both doses beforehand. The prevention is believed to last from eighteen months to two years, and for this reason there is no advantage to wait until the person has arrived, while the advantage of having the inoculation performed before starting is that the negative stage will have passed before arrival, and the protection will be fully developed.

The important question of carriers now claims attention, but before considering human carriers mention may be made of a paper by Mills,[1] who suggests that rats, from their love of filth, and possibly also dogs employed in ratting, may act as transporters of the virus. He cites some outbreaks in favour of this hypothesis, which certainly seems worthy of investigation. Courmont and Rochaix [2] have also recently advanced the view that the dog may play a part in spreading the fever.

The rôle of flies will be found discussed under the heading "Flies." One need only say here that the most important discovery in this direction is that flies can and do actually ingest the bacilli, which are to be found in their excreta. Indeed, from recent experiments with *B. pyocyaneus*, it is possible that flies may even transmit *B. typhosus* to their offspring through eggs, larvæ and pupæ. This, however, is merely a supposition at present. The literature on human carriers has become voluminous. Here we can only refer to a few interesting and recent papers, dealing more especially with the efforts made to treat such cases. As regards the army, the *Lancet* of January 8, 1910, directs attention to the report of the Director-General, Army Medical Service, which gives an account of experiments with cultures of lactic acid bacilli, anti-typhoid vaccine, sodium benzoate, and acid phosphate of soda. It cannot be said that any clear result was obtained. A somewhat similar article in the *British Medical Journal* of December 25, 1909, deals with Vincent's views on the subject. A portion may be quoted :—

> With the important exception of men serving in the kitchen or in the canteen, he thinks that the opportunity for the transmission of the disease by carriers is much less frequent in the army in time of peace than it is in civil life. Circumstances favourable to such transmission mainly arise from carelessness about the disposal of excreta ; and in the army these matters can be more rigidly supervised than is possible in civil life. He therefore proposes to deal with the carrier danger in the army by attention to three precautions. In the first place, he would require the medical officer of the unit, at all times and in all places, to treat the fæcal matter and the urine of soldiers as though they contained the typhoid bacillus, submitting the latrines to systematic, thorough, and constant disinfection. In the second place, he would not allow any man who has had typhoid fever, even at a remote date, or any man found by bacteriological examination to be a carrier of typhoid or paratyphoid bacilli, to be employed in the kitchens or canteens, or on work connected with the apparatus for the purification of drinking water ; and in the third place he would instruct such persons to avoid soiling their hands when defæcating, or, in certain circumstances, when micturating ; he would order them, on pain of punishment, to wash their hands after each defæcation, and he would treat those whose urine contained the typhoid bacillus with urotropine. These rules can, he admits, only be enforced under the ordinary conditions of life in barracks ; during manœuvres, or in time of war, precise observation of them would often be impossible and the risks of transmitting the disease would consequently be much greater.

Another "Army" paper is that by Cummins,[3] who divides persons who pass typhoid bacilli in their excreta into the following groups :—

> (1) Precocious Carriers.—Persons in the incubation period who are harbouring germs, but have not yet developed the disease.
>
> (2) Paradoxical Carriers.—Persons who have contracted typhoid bacilli without any resultant illness, and who continue to pass them in the excreta.
>
> (3) Typhoid Cases.—(*a*) Recognised ; (*b*) unrecognised ; (*c*) convalescent.
>
> (4) Chronic Carriers.—Persons who, subsequent to a recognised or unrecognised attack, or even after contact with cases, continue to pass typhoid bacilli either constantly or intermittently in the excreta.

He admits this classification is founded on that of Sacquépée,[4] whose review of the whole subject, both as regards typhoid and paratyphoid carriers, is well worthy of study, though

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[1] Mills, J. A. (January 21, 1911), "Typhoid Infection." *British Medical Journal.*

[2] Courmont, J., and Rochaix (1910), "Le Chien porteur de bacilles d' Eberth." *Semaine Médicale.*

[3] Cummins, S. L. (August 20, 1910), "Isolation of Disease Carriers and Methods of dealing with them." *British Medical Journal.*

[4] Sacquépée, E. (January 15, 1910), "Les Porteurs de Germes." *Bull. de l'Inst. Past.*

already in some respects a little out of date. Cummins states that it has been calculated that about 3 per cent. of all typhoid convalescents ultimately became carriers. He points out that most, but not all, carriers give the Widal test, and those that do, not usually in high dilution. A negative result in the examination of the excreta does not prove the case to be a non-carrier, as the bacilli are often only intermittently present. He mentions abortive cases of typhoid, and gives a reference to French military measures for dealing with such cases. Part of the method is described as follows :— Enteric Fever—*continued*

The men will parade in their barrack-rooms, and, as each is reached by the medical officer, he will loosen his clothes so as to display the thorax and abdomen, lie on his bed, and undergo a rapid but thorough examination, directed to the discovery of slight splenic enlargement, rose spots, gastric, hepatic, or intestinal symptoms, signs of bronchitis or pleurisy, furred tongue, redness or ulceration of tonsils or pharynx, etc. Inquiries will be made as to general fitness, diarrhœa, constipation, headache, and so forth; and the temperature will be recorded.

He points out in conclusion that the best prophylaxis against the production of typhoid carriers is the prevention of typhoid fever. As regards urotropine he finds that while it diminishes the number of bacilli excreted, it is in no sense curative. A practical bit of work is that by Gaehtgens,[1] which is reviewed by Birt [2] as follows :—

Gaehtgens has found that the usual mode of washing hands with soap, running water, and nail-brush, will reduce the number of typhoid and colon organisms on hands contaminated with typhoid dejecta, but will not eliminate them completely. The application of methylated spirit for half a minute is sufficient to destroy the *Bacillus typhosus* on the skin of the hands. Eau-de-Cologne is effective in a quarter of a minute, but 40 per cent. alcohol allows some of the bacilli to survive after two minutes contact. Antiformin, 2 per cent. crysoform, and 10 per cent. peroxide of hydrogen are not germicidal to the typhoid bacillus. The reviewer has ascertained that if a loop of an agar or broth culture of the *B. typhosus* is added to a few drops of methylated spirit, or spirit of wine, subcultures in broth or on agar remain sterile, though made immediately.

Ledingham's special report to the Local Government Board, reviewed in the *Lancet* of December 3, 1910, gives the prevalence of carriers in a general mixed population as about 3 per 1000, but a little consideration shows that the danger from the average carrier would appear to be almost negligible. It is what may be called the "virulent carrier" we have to fear, the man, or more probably the woman, with a high infective potency, due possibly to concurrent physiological or pathological conditions, or perhaps to simpler causes, opportunities of conveying infection to others, etc. In this connection a paragraph or two from a valuable address on the subject by Theodore Thomson [3] may well be quoted. He says :—

What, therefore, we would have the bacteriologist tell us is how we are to distinguish our types of carrier, so that we may know how to deal with each appropriately. In the search for the carrier, the detection of the *Bacillus typhosus* is accepted as proof of his condition; but it would seem that some types of this bacillus are harmful, others are harmless, while yet others may be in one or other of several intermediate grades. Are these variations due to the presence or the absence, as the case may be, of some other micro-organism influencing the action of the bacillus; and if so, what is that micro-organism? Or, if they are due to other conditions, can we be enlightened as to the nature of these conditions? These are the problems for the bacteriologist, the solution of which will be welcomed by the epidemiologist.

The duration of infectivity in enteric fever forms the subject of a paper by Harris,[4] who in his research found MacConkey's bile salt, neutral-red agar the most reliable medium. His results are presented in the form of tables, and it is noteworthy that a great variability exists in the period when a negative result was obtained. In some cases this was 40 to 50 days. In one instance bacilli were present 78 days after the temperature had fallen to normal. The persistence of infection bears no relation to physical signs. In all, 27 cases are analysed.

A very useful résumé of some of the main points in Ledingham's report to which we have already referred is given in the *British Medical Journal* for March 11, 1911, as follows :—

Briefly put, the facts are that the bacilli may be passed, more or less continually, by several classes of persons apparently in good health. The incubation period of the disease may last in an infected person from five to forty-five days, and during this period infection of contacts is probably very common; similarly the discharge of bacilli may continue for decades after the attack. People in contact with a patient or another carrier may become temporary or chronic carriers without necessarily suffering from the disease. Another most important fact is that some cases presenting symptoms which may lead them to be classed as influenza or diarrhœa, are in reality examples of atypical typhoid fever. It is shown that the relationship between gall-stone disease and the carrier state is very intimate —an observation which confirms work done many years ago on the etiology of gall-stones. Our conception of the epidemiology, pathology, and even the clinical manifestations of typhoid fever, have undergone radical changes, and some very interesting questions are raised by the new knowledge. There is, first, the fundamental problem—the paradox—why should one person be invaded by virulent typhoid bacilli and suffer no ill effects whilst another

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[1] Gaehtgens, W. (1910), "Die Händedesinfektion bei Typhusbazillenträgern." *Arch. f. Hyg.*

[2] Birt, C. (October, 1910), Review in *Journal Royal Army Medical Corps.*

[3] Thomson, T. (November, 1910), "The Enteric Fever Carrier." *Proceedings Royal Society of Medicine*, Vol. IV., No. 1.

[4] Harris, A. (March 11, 1911), "Notes on the Duration of Infectivity of Enteric Fever." *Lancet*

Enteric Fever—*continued*

individual readily falls a victim to the disease? The answer apparently is not that the "carrier" is well provided with immune bodies, for, as a matter of fact, he seems to possess very little of these substances; he, or more often she, is not immune, for a fatal typhoid septicæmia may ensue. The theory elaborated by Wolff-Eisner and others, that the fever and its symptoms result only when the host has elaborated sufficient immune bodies to kill the parasite and liberate the endotoxins contained in its body, offers a possible explanation. Again, the fact that on one occasion alone over 200 individuals were infected by typhoid fever, owing to their milk being polluted with the excrement of one milker, shows how perilously easy may be the path of the bacillus from one man's bowel to another man's mouth. It shows that the campaign for elaborate cleanliness in food preparation, so often urged by the medical press, and so often derided by the general public as a medical fad, is justified in every particular. That other diseases, such as epidemic diarrhœa and dysentery, may be spread in this manner is more than probable. The question of typhoid in children evidently deserves renewed attention; there would seem to be some relation between infantile mortality and the prevalence of typhoid fever in a community.

The unsatisfactory treatment of carrier cases has already been mentioned. As the Director-General, A. M. S., says, the best result is likely to be obtained by injecting a patient with a vaccine prepared from the particular strain of the typhoid bacillus, which has infected him. Clements and Dawson [1] report such a case, where, apparently, cure resulted after six doses (125 to 600 millions) of a vaccine prepared from a *B. typhosus* isolated from the patient's fæces. The treatment began on February 23, and terminated on May 10.

Turning to other bacteriological questions, we find that Galvagno and Calderini [2] found that Eberth's bacillus, obtained from typhoid cases, can survive for 30 days in a latrine, and 25 days in a soil tub. After allowing the bacillus to grow under these conditions for 10 days they spread out the infected material over a piece of ground, and noted that the bacilli remained alive for 20 days when on the surface, and 40 days when in the deeper layers. These observations require confirmation and repetition under tropical conditions, as they have an important bearing on the trenching of sewage and on fly infection. Using pure cultures of *B. typhosus*, Firth found that in sewage-polluted soil the bacillus did not live longer than 74 days. In raw Thames water Houston noted that 99 per cent. of the typhoid bacilli disappeared during the first week of storage, but a few specially resistant forms sometimes persisted for several months. These observations are mentioned by Horrocks [3] when recording his own results of similar experiments with the urine and fæces of carriers and of recent cases of typhoid fever. His conclusions, which differ from those of Galvagno and Calderini, may be stated:—

> The experiments seem to indicate that the duration of life of the *B. typhosus*, as at present recognised, is very short under natural conditions; it is unlikely that the artificial conditions in a sterile test-tube, under which the typhoid bacillus survived for over a year, will find a parallel in nature. Whenever typhoid urine and fæces gain access to wells, springs, or cesspools, it seems probable that the action of the associated bacteria will cause the typhoid bacillus to disappear in a few days.
>
> Soil bacteria appear to have similar destructive power. Also, when fæcal material is lightly covered with earth, or exposed to the atmosphere, the colon bacilli present exercise a marked inimical influence on the typhoid bacilli. If the dejecta contain many *B. coli*, millions of typhoid bacilli disappear in two or three days, and even if the typhoid bacilli are a thousand times more numerous than the *B. coli*, a similar result follows in about a week.

His results as regards variation of the *B. typhosus* need not be considered beyond noting that he certainly appeared to obtain a real variation of the bacillus into a coli type.

A great deal of useful information about carriers, culture methods, etc., will be found in the special "enteric" number of the *Journal Royal Army Medical Corps* for April, 1910.

Of special interest are the recent researches of Metchnikoff and Besredka,[4] who find that it is possible to produce typhoid fever by the experimental method, but that only the anthropoid apes present a marked susceptibility to the virus administered by the mouth. The lower monkeys cannot be infected except in exceptional cases. Rodents are refractory. The virus of the fever is the bacillus itself. There does not exist a "filtration" virus capable of playing a rôle in the etiology of the disease. In the disease produced experimentally, vaccination methods are inoperative as protective agents.

We will now discuss a few general papers dealing with the disease in tropical regions. Of these none are more useful than the series which appeared in the *Lancet* during the early part of 1901 under the heading "Sanitation in India." They deal for the most part with the

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[1] Clements, R. W., and Dawson, A. (April, 1911), "Report on the Treatment of a Chronic Typhoid Carrier by a Specific Vaccine." *Journal Royal Army Medical Corps.*

[2] Galvagno, O., and Calderini, W. (1908) "Lebensdauer und Virulenz des Typhusbazillus in Gruben, Tonnen und im Boden." *Zeit. f. Hyg. u. Infekt.*, Vol. LXI.

[3] Horrocks, W. H. (March, 1911), "On the Viability and Possible Variation of the *Bacillus typhosus*." *Journal Royal Army Medical Corps.*

[4] Metchnikoff, E., and Besredka, A. (March 25, 1911), "Recherches sur la Fièvre Typhoïde Expérimentale." *Ann. de l'Inst. Past.*

prevalence of disease amongst British troops, and we can only refer to a few of the interesting facts collected by the "Special Correspondent." For instance, it is stated that— Enteric Fever—*continued*

The increased susceptibility of young soldiers and recent arrivals in India is probably due to a combination of the following causes: (*a*) The normal or physiological susceptibility of Europeans to contract enteric fever in all parts of the world at a more or less fixed age—namely, 20 to 25 years. (*b*) The special tropical susceptibility caused by changes brought about by the transference from a temperate to a tropical climate weakening the resisting powers of the tissues and their antibacterial or phagocytic properties. These catabolic changes often manifest themselves by catarrh of the respiratory or digestive tract, causing slight bronchitis or diarrhœa respectively. Both these conditions greatly favour the entrance of the enteric fever bacillus to the blood, either through the respiratory tract or through the digestive tract by means of food or liquids. (*c*) Want of experience, and therefore want of care, in regard to diet, exercise, and general care of health, with the result that the men get out of condition and consequently become more liable to develop the disease; while they are also more likely to be careless as to the sources of drinks and food which they may partake of outside barracks. (*d*) Other predisposing causes: (1) over-fatigue, over-exertion, and exposure to the tropical sun with an empty stomach, such as rifle range or shikar in the morning without *chota hazri* (early breakfast); (2) any form of debility; and (3) any form of catarrh of the intestines or air passages.

The young are particularly predisposed to contract the disease; nevertheless, an organism healthy and vigorous, hardened by exercise, and fed on good nourishing food, possesses the power of resistance in a marked degree.

The important question of the prevalence of the disease amongst the natives of India is fully dealt with, and it is stated that although the problem as to whether enteric fever is or is not a common disease among natives in India is as yet scientifically *sub judice*, it is evident that medical officers now hold a general opinion that enteric fever exists among natives, especially children, to a degree which was not suspected. It is, however, noted that the Gurkha, whose food and habits bear closer similarity to those of the British soldier than those of other native soldiers, is more liable to the disease, a fact suggestive of the influence which diet may exercise on the liability to the fever.

It is interesting to note that there is a greater prevalence amongst mounted troops as compared with infantry.

It is suggested that the increased prevalence for enteric fever from which the mounted troops suffer in India is in some way due to the animals with which they are brought into daily contact. These animals are chiefly horses, of course, but mules, bullocks, and elephants are also met with to a very much less extent. Although it has not been proved that any of the above classes of animals suffer from enteric fever or that the disease can be experimentally produced in them by inoculation, yet it has been stated that certain other animals may, in rare instances, suffer from a disease indistinguishable clinically and pathologically from enteric fever, such as rabbits and white rats. As the water-supply used by mounted troops for their animals is often, if not always, liable to pollution, and as it is believed that enteric fever bacilli can pass living and unchanged through their intestines, or perhaps even multiply and become more virulent, a very wide field of infection to man by means of infected stable litter, flies, soil, dust and water is opened.

Again, speaking of an outbreak at Mhow, it is stated that

it was thought that this increased prevalence amongst mounted troops would seem to point to the fact that either: (*a*) there is some connection between horses and enteric fever, or (*b*) that the comparatively harder work of the mounted branches is a contributory agent; or (*c*) that the larger number of natives employed by a mounted corps opens the way to more frequent infection; or (*d*) that the number of animals in the neighbourhood of barracks foul and infect the ground and atmosphere. With reference to (*a*) it may be stated that evidence is not wanting to prove the fact that horses foul and infect the ground in the vicinity of barracks and that of their lines and riding-schools in particular.

There is a good chapter on sources of infection. Aerated waters are first considered. Amongst other notes, for instance, as to the dirty uses to which empty bottles may be put, this passage occurs:—

It is a popular belief that aerated waters, being charged with carbonic acid gas, are free from germs, and that the same care or supervision is not so necessary as is needed in connection with ordinary drinking water. This is most fallacious and dangerous reasoning, as living enteric bacilli have been found in aerated waters as long as eleven days after manufacture (Slater), and infection may thus occur at any time during this period. Hewlett, however, appears to think that the *Bacillus typhosus* cannot survive longer than a fortnight in water aerated with CO_2, and for this reason it is perhaps advisable to store soda-water for some time before use in the presence of epidemics of enteric fever. Duclaux states that, "to be safe, mineral waters should be stored for at least a fortnight before use."

Dust is now believed to be one of the most active channels by which enteric fever is spread in India. The work of Clauditz, who succeeded in obtaining experimentally a strain of *B. typhosus* which does not die out in soil, is mentioned, while it is suggested that the *B. typhosus* may exist in soil in some hitherto undiscovered form.

Aldridge recovered typhoid bacilli in India from earth contaminated by the urine of patients suffering from typhoid bacilluria, on the first, fourth, and ninth day of drying. Harrison has recovered typhoid bacilli from Indian dust after 77½ hours, during 23 hours of which the dust was exposed to the direct rays of the Indian sun at Kasauli (Punjab).

Enteric Fever—*continued*

Finally, the following conclusions arrived at by Firth and Horrocks are quoted :—

(1) That the *Bacillus typhosus* is capable of surviving in moist soil sometimes as long as 74 days, and that this survival is independent of either pollution or the reverse, but is mainly dependent upon the amount of moisture present ; (2) that from ordinary soil kept damp with rain-water the bacillus could be recovered on the sixty-seventh day, with dilute raw sewage on the fifty-fourth day, and with dilute sterile sewage on the seventy-fourth day; (3) that infective material could be readily carried about from dried soil and sand by air currents ; (4) that infected dry soil, if blown about as dust, is capable of infecting distant objects after twenty-four days from the time of desiccation.

A very complete chapter is that on the rôle of flies, and evidence is advanced which shows that in certain places at least the increase in the number of flies corresponded closely with the period of enteric fever prevalence. The dangers from infected clothing and blankets are fully exposed, and interesting information is given regarding the unsatisfactory washing arrangements in India, where there are three ways at least by which clothing, etc., may become contaminated when at the wash :—

(1) By being washed in polluted water, the existing pollution of the water being often added to by that of the clothes washed at the time or beforehand ;

(2) By being hung up to dry near sources of infection ; and

(3) By being stored before delivery in the washermen's houses.

The dangers of dirty kitchen cloths are specially insisted upon.

Some of these points had already been brought forward by Thomson [1] in his consideration of enteric fever in the native Indian army, or rather by Spencer in his comments thereon. For instance the latter says :—

The more I see of enteric fever in India, the less I am inclined to call it a specific disease as usually understood when one speaks of specific fevers, and I have drawn some attention to the subject in my previous writings. To satisfy the demands of scientific accuracy in diagnosis, it seems to me that the only course now left is to isolate the bacillus from the blood and identify it by its cultural tests.

Spencer is a believer in the rôle of allied germs of the typhoid-coli group, and is inclined to think that occasionally one of these allied organisms can undergo evolution in the human intestines and become transformed into the genuine bacillus of Eberth. He lays stress on the habits of life as a cause, and Thomson is equally strong on the influence of meat-eating as a predisposing factor. In a later paper [2] he returns to this subject, and also says, " The idea that natives are saturated with the disease is one to which our experience and the evidence adduced do not compel us to subscribe." He believes natives possess an immunity which may be due to racial inheritance, or may be naturally innate, and he cites the Arabs, Egyptians, Sudanese and Japanese as types of races enjoying immunity, and who are non-proteid in excess vegetarians anyhow under their natural conditions of life. I confess my experience in the Sudan confirms this view, but, until the pyrexias of infancy and childhood in the Tropics are properly worked out, it will be difficult to make dogmatic and irrefutable statements on this important question.

An interesting French discussion on a paper by Spencer will be found in the *Bulletin de la Société de Pathologie Exotique* for November, 1908. We have not time to review it, but the general view regarding native immunity was that it is racial in origin.

A very important piece of work is that by Semple and Greig,[3] who, as the result of a special inquiry in India, concluded :—

(1) That the *Bacillus typhosus* continues to be excreted for long periods in the urine and fæces of a certain percentage of patients convalescent from enteric fever.

(2) That the number of bacilli excreted in the urine is very large.

(3) That the excretion of the bacilli in the urine and fæces is markedly intermittent.

(4) That the "chronic bacilli carrier" exists in different units in India, and can cause epidemics and cases of enteric fever.

(5) That enteric fever orderlies may become " chronic bacilli carriers."

(6) That enteric fever is a septicæmia from the outset of the disease, and that the most accurate method of making a diagnosis is by blood culture.

(7) That paratyphoid fever exists in India, but the number of cases is, in comparison with infection by *B. typhosus*, small. The *B. para yphosus* A. (Brion-Kayser) is a commoner cause of paratyphoid infection than *B. paratyphosus* B. (Schottmüller) in India.

(8) That *B. typhosus* is present in the bile of cases of enteric fever in very large numbers.

(9) That in India the saprophytic existence of the *B. typhosus* outside the human host is short.

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[1] Thomson, G. S. (August, 1908), " Enteric Fever in the Native Army." *Indian Medical Gazette.*

[2] *Idem* (November, 1908), " Enteric Incidence in India and its Lessons." *Journal Royal Army Medical Corps.*

[3] Semple, D., and Greig, E. P. W. (1908), " An Enquiry on Enteric Fever in India." *Scientific Memoirs of the Government of India*, No. 32.

Enteric Fever—*continued*

Hamilton [1] has met with cases of enteric fever in infants in India, and in two cases believed infection to be due to the addition of contaminated raw meat juice to the dietary. He gives the symptoms in infants, and speaks very highly of the value of whey in the treatment.

Turning from India to Africa, we find Johnson [2] giving an account of the disease as seen in Nairobi, British East Africa. In some respects it appears to resemble that met with in the Sudan. He says :—

There are certain particulars in which the disease, as it affects those Europeans whom I have treated, differs from the disease as met with in Europe.

(1) Diarrhœa less frequently happens. In ten cases, perhaps eleven, treated in the hospital none suffered from it. As a rule, there are either one or occasionally two stools a day, or constipation exists, which requires treatment. I do not think I am inaccurate in saying that at some time or other in every case the inaction of the bowels calls for treatment.

(2) Hæmorrhage was seen once only in this number of cases, and it was fairly profuse.

(3) The pyrexia is of an irregular type, and approaches more nearly to a remittent fever than to a continued one.

(4) The exanthem is not seen in more than half the cases, and then it is very slightly marked.

(5) Thrombosis of veins is common. Among the ten cases it was observed on three occasions, and another case which was admitted for phlebitis and returned as such was, I think, an instance of enteric, the earlier stages having been passed.

(6) The Widal reaction is not always to be obtained, even though the case proves by every clinical sign and symptom to be one of enteric fever.

(7) Half of the cases occur in February and March, which are the driest and hottest months of the year, and when the dust storms are an almost intolerable nuisance. At this period the number of people who suffer from sore throats, quinsies, etc., is great, and in this connection Dr. Gee's remark that sore throat attends the first few days of typhoid fever with a frequency which is remarkable, and may even lead to perplexities in diagnosis, is recalled.

(8) Another peculiarity is that all of the patients whom I have attended with this disease were comparatively newcomers, none of them having been in this country for more than three years, and many of them not for so long, thus bearing out the idea that acclimatization has much to do with the incidence of the disease. The majority of the cases were under thirty years of age.

Although there is nothing very new in it, a paper by Vaughan [3] gives a very comprehensive account of the prophylactic measures employed in the Panama Canal Zone. Coming nearer home, we note Phillips' [4] paper on the disease in Egypt. He differs from Sandwith in believing that the disease is common, though usually mild, and that all grades of society are attacked. He says that spots are rare and constipation the rule. He thinks the mildness of the attacks is chiefly due to attacks in infancy and childhood, and to hereditary immunity of a partial nature. I confess this hypothesis does not strongly appeal to one, and it is interesting to contrast Egyptian with Indian views.

Returning to the Canal Zone two recent American papers by Brown [5] and Deeks [6] respectively claim attention. The conclusions of both are very similar. Those of Brown are given in detail :—

(1) Clinical typhoid fever can be caused by a great variety of organisms other than the *Bacillus typhosus*.

(2) Clinically, it is impossible to separate fevers caused by the *Bacillus typhosus* from those produced by paracolon and closely allied organisms.

(3) Systematic blood cultures, and bacteriological separations, are the only means of differentiating these fevers one from the other.

(4) The employment of semi-solid media has been largely responsible for the results obtained.

(5) The organisms are present in the circulating blood within the first twelve days of illness, or within the first ten or twelve days after a second infection.

(6) The results show that about 50 per cent. of the so-called "typhoids" are in reality due to paracolon.

(7) Serum reactions are absolutely worthless in the diagnosis of typhoid and allied fevers.

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[1] Hamilton, A. F. (December, 1909), "Enteric Fever in Infancy." *Indian Medical Gazette.*

[2] Johnson, J. T. C. (December 15, 1909), "Enteric Fever as met with in Nairobi, British East Africa." *Journal Tropical Medicine and Hygiene.*

[3] Vaughan, E. I. (April, 1910), "A Problem in Typhoid Fever Prophylaxis, and the Solution of Same." *Transactions Society Tropical Medicine and Hygiene.*

[4] Phillips, L. (October 1, 1910), "Typhoid and Paratyphoid Fever in Egypt." *British Medical Journal.*

[5] Brown, T. R. (1909), "A Brief Review of some of the work done in Ancon Hospital on Typhoid and Allied Fevers." *Proceedings Canal Zone Medical Association.*

[6] Deeks, W. E. (1909), "Typhoid and Allied Fevers in Panama." *Ibid.*

Enteric Fever—*continued*

Those of Deeks which may be added to the list are, that temperatures and temperature curves have only a relative value in diagnosis, and his warning to remember malaria as a complication. Taking up another aspect of the disease we find the recent views of Coleman and Buxton as regards its pathogenesis quoted in the *Indian Medical Gazette* for January, 1910, as follows :—

> They believe that the atrium of the infection is in the lymphatic structure of the intestinal wall; from here the bacilli reach the lymphatic system and the spleen, where they seem able to grow, being here in a measure protected from the bactericidal power of the blood; after they have grown to a sufficient amount, corresponding to the period of incubation, they overflow into the blood, where, the bacilli undergoing bacteriolysis, the endotoxins are set free and cause the symptoms of the disease. Subsidence of the fever seems to depend on the cessation of the discharge of bacilli from the lymph glands into the blood, probably because the immunity processes have succeeded in checking the multiplication of the bacilli in lymphatic tissues. It is possible that those cases in which an intermittent temperature persists after the original febrile movement has subsided may be due to irregular discharge of bacilli from some lymphatic organ, in which the bacilli still continue to grow. Relapses probably arise in this way, for it is known that the spleen sometimes remains large after the subsidence of fever in patients, who subsequently relapse, and it may be that this enlargement indicates the local persistence of the infection which may later flare up as the immunity reaction wanes. That the resistance to the typhoid resistance does wane, especially as regards local rather than systemic resistance, is shown by the frequency with which, after recovery from systemic infection, local infections appear in the form of abscesses, cholecystitis, etc.

We have now considered the main aspects of the disease, its diagnosis and prophylaxis, from the tropical standpoint. Treatment in the Tropics does not greatly differ from that in temperate climates, and it is outside the scope of this Review to enter into the question of vaccine treatment, especially as this subject and many other points, such as typhoid bacilluria, the ophthalmic and cutaneous reactions in diagnosis, etc., will be found admirably set forth by Goodall in the *Medical Annuals* for 1909–10 and 1911. We will content ourselves with mentioning the irrigation method from which Spencer [1] claims excellent results, if begun in the first week of the illness. He employs a solution of permanganate of potash, one grain to a pint of warm water, and uses it systematically and daily. He believes it gets rid of toxins, and lessens the tendency to ulceration. Then there is the antipyretic method employed by Barker [2] in India, *i.e.* the rubbing in of 30 drops or so of creosote into the flanks to induce sweating. Fordham [3] also records its use, 20 drops in one or both axillæ, and 5 drops by the mouth floated on a diaphoretic mixture. A measure somewhat of the same nature is that advocated by Cheinisse,[4] who strongly recommends as an alternative to cold bathing the application of alcohol to the abdomen.

> He applies a compress, consisting of a quadruple fold of absorbent cotton wool, wrung out of alcohol sufficiently to prevent dripping. Over this he places a second compress of cold water, in order to weaken the alcohol a little, and so prevent irritation of the skin, the whole being covered by an impervious bandage. The water compress should be changed every hour, but the one containing alcohol may be allowed to remain double that time. It may be necessary to lubricate the skin with a little lanoline if irritation should occur, but such inconvenience has not been found to intervene with any degree of frequency. This treatment has been followed in twelve cases of enteric fever, and although the number is not great, the cases themselves were of considerable severity, and no untoward results were experienced. It has been particularly valuable in the case of children, where the tendency to heart weakness renders cold bathing dangerous; and the author recommends that his treatment should be invariably preferred in such cases.

We have mentioned one form of bowel irrigation. Arnold [5] uses another, apparently with great success, namely enemata of turpentine and olive oil, from the first day of treatment regularly at stated intervals until the temperature has been normal at least ten days. The following is the technique :—

> When the case first comes under observation, an enema of turpentine 1 ounce and olive oil 1 pint is given by a funnel and tube; and, the foot of the bed being well raised, the emulsion is allowed to find its way slowly up the bowel. On the next day, or the day after, the same quantities are repeated. In most instances the amount of turpentine may then be reduced to ½ ounce with olive oil 15 ounces; this is administered on alternate days throughout the whole course of the disease, and continued until convalescence is fairly established.
>
> A preliminary thorough cleansing of the bowel by a dose, or preferably small divided doses, of calomel, followed by castor oil, prepares the ground for the action of turpentine. The dose may be repeated more than once if necessary, alternating with the enemata.

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[1] Spencer, D. B. (January 13, 1909), "Sur la fièvre typhoïde et paratyphoïde aux Indes anglaises." *Bull. Soc. Path. Exot.*

[2] Barker, F. A. (August, 1909), "The action of Creosote in Reducing High Temperature in Enteric Fever." *Indian Medical Gazette.*

[3] Fordham, H. J. (October, 1909), "Creosote in High Temperatures." *Ibid.*

[4] Cheinisse, L. (November 17, 1909), "Traitement de la fièvre typhoïde par des applications d'alcool." *Semaine Médicale.*

[5] Arnold, W. J. J. (July 13, 1910), "Turpentine Enemata in the Treatment of Enteric Fever." *British Medical Journal.*

Enteric Fever—*continued*

Quinine is also given in small doses as a heart tonic and bactericide. One has many other references on all branches of the subject, but it is impossible to deal with more, and it is hoped that those reviewed will be of service, especially to those whose lot is cast in lands where enteric is alike common and severe.

Additional Notes

Bass and Watkins [1] have introduced a quick macroscopic typhoid agglutination test,

which they describe, after more than a year's experience and one hundred comparative tests, as being as accurate as the Widal reaction. The only materials required are a microscopic slide or piece of glass, a puncture needle, a medicine dropper, and one drop of a suspension of typhoid bacilli, and the time occupied in making the test is less than two minutes, and it may be performed at the bedside. The suspension is of the strength of 10,000 million dead bacilli per cubic centimetre in 1·7 per cent. solution of sodium chloride, to which 1 per cent. of liquor formaldehyde has been added. This test fluid can be easily prepared, and it is stable, and can be marketed as other reagents and test solutions are. The test is made by pricking the ear lobe or finger with a puncture needle, and diluting the blood by dissolving it in approximately four times its volume of water. One or two drops of this diluted blood are placed on the microscopic slide or other piece of glass, with an equal quantity of the test fluid, and the slide tilted from end to end so as to keep the mixture flowing backwards and forwards. If the reaction is positive, a greyish mealy sediment consisting of agglutinated bacilli, and easily seen by the naked eye, appears in less than a minute. The appearance is first noticed in the fluid around the edges, and tends to collect there. If the agitation of the slide is continued for a couple of minutes the clumps increase in size, but if there is no reaction in two minutes none will occur later, the mixture remaining clear and unchanged when the result is negative. The blood may be collected by squeezing out about a quarter of a drop from the puncture, touching the slide to it, and spreading it out, and, if no slides are at hand, one drop of blood may be collected in a bottle containing four drops of water. The advantages of this test over the usual method of obtaining the Widal reaction are that it takes only two minutes to perform, does not necessitate any laboratory experience or facilities, is inexpensive, and can be carried out every day if necessary at the bedside, giving immediate information for diagnosis.

Gillmann [2] describes a bedside Widal test. He uses a reagent tube 5 mm. × 3 cm. forty-eight drops of a twenty-four hours' broth culture, killed by the addition of 1 per cent. formalin, are mixed with two drops of the patient's serum, and observed for from three to five hours. One would not think *a priori* that such a method was very reliable.

A new method of diagnosing enteric fever bacteriologically is given by Mandelbaum.[3] It depends on the fact discovered by Kraus and Low, that *B. typhosus* produces a fine network of threads when grown in the presence of anti-typhoid serum, just as Pfaundler found that *B. coli* did when grown with its homologous serum. The test is carried out as follows :—

A tube of broth containing 2 per cent. sodium citrate, is inoculated with *B. typhosus*. One part of the patient's blood and ten to fifteen parts of this broth are drawn into a sedimentation pipette, which is then incubated at 37° C. for four hours. If the blood should have been abstracted from a typhoid patient or convalescent, the bacillus will have grown into long threads or clumps ; no isolated motile rods are then to be seen. Mandelbaum obtained this positive reaction in twelve people who were suffering from enteric fever, in some of whom the agglutination test, 1/25, was negative. The blood of those who had been convalescent for more than a year after the attack was somewhat weaker, for a few motile rods might be visible among the chains and clumps. He noted the reaction in a typhoid carrier. The bloods of seventy-five controls gave negative results. Mandelbaum states that typhoid and paratyphoid fever may be distinguished by examining the pipettes prepared with the respective bacilli at the end of twenty hours ; the difference between the growth of the infecting agent and that of the other will then have become still more accentuated. He claims that specific agglutinins can be distinguished from normal and coagglutinins by this procedure, even if their agglutination value be the same He draws attention to the value of the test in those febrile cases in which the Widal reaction is negative.

Stühmer [4]—

records a case in which typhoid bacilli were identified in the fluid obtained by lumbar puncture during life. The patient was a young man who was admitted into hospital with febrile symptoms, but showing none of the usual signs of typhoid fever—there was no eruption, no enlargement of the spleen, no intestinal symptoms. After admission into hospital, meningeal symptoms developed. Widal's agglutinative reaction with *B. typhosus* was obtained with a serum dilution of 1:50, but failed with a dilution of 1:100. The fæces appeared to be of normal quality, and *B. typhosus* could not be identified in them. Some cerebro-spinal fluid was evidently under some considerable pressure in the spinal canal; it was slightly turbid, and numerous bacilli, resembling *B. typhosus*, were identified microscopically in the sediment thrown down on centrifugation. Bacteriological proof of the nature of the bacillus present in the sediment was obtained, and the absence of *B. tuberculosis* from both sputum and fæces was proved. The patient recovered after an illness of eight weeks. The author has been able to collect the literature of only eight other cases in which the presence of *B. typhosus* has been demonstrated in the cerebro-spinal fluid during life.

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[1] Bass, C. C., and Watkins, J. A. (December 15, 1910), "A Quick Macroscopic Typhoid Agglutination Test." *Archives of Internal Medicine.* Quoted in Epitome, *British Medical Journal,* March 18, 1911.

[2] Gillmann, S. (1910), "The Bedside Widal Test." *Medical Record,* Vol. LXXVIII., No. 18.

[3] Mandelbaum, M. (January 25, 1910), "Zur Typhusdiagnose nach meiner Methode." *Münch. Med. Woch.*

[4] Stühmer, A. (February 14, 1911), "Typhusbazillen in der Zerebrospinalflüssigkeit." *Münch Med. Woch,* No. 7. Quoted in *Supplement Medical Officer,* April, 1911.

Enteric Fever— *continued*

The question as to whether infection can be derived from the sputum of typhoid fever patients has engaged the attention of Tenney,[1] who states that while the sputum does not frequently contain the typhoid bacillus, it does so occasionally, and hence it cannot be ignored as a source of infection.

Army surgeons and many others will be interested in a paper by Firth,[2] which may be said to be the last word on anti-enteric inoculation. It deals with statistics, and shows that the value of the method is nearly, if not wholly, beyond all doubt both from the point of view of freedom from attack, and of recovery after attack. His figures point also to the necessity for the adoption of a steady and persistent re-inoculation of all men who have been inoculated more than thirty months.

Fæces. A very useful paper is that by Royal[3] on pseudo-parasites in the excreta. He experimented on himself by ingesting various vegetables and fruits. As it would be interesting to repeat the work in tropical countries, his technique is quoted. He says :—

> As experimental work, I ingested large quantities of the different fruits and vegetables, making the diet for the day consist principally of one article. At various intervals following the ingestion of the different substances examinations of the stools were made, and especially after the end of twenty-four hours, this being the time generally required for the food to pass the length of the intestinal tract. A better rule is to take the second stool following the ingestion of the substance. The stools were collected in glass jars with a tightly fitting top, and a 4 per cent. solution of formaldehyde was added. This readily deodorises and softens the stools, although if left too long in formalin they become hardened. The colour, odour and consistency were noted before the addition of the 4 per cent. formaldehyde.
>
> Suspicious looking particles of the fæces were spread out on a slide and covered with a large cover-glass. Large slides are best adapted for this purpose, the fæces being spread out in a very thin layer. When an examination of all substances is desired, I have found that a very good way is to make an emulsion of the fæces and then allow the mixture to settle and dry on the slide. If a thin watery emulsion is made it was found that coarse vegetable remnants, cells and crystals formed the lower layer, parasites and eggs the middle, while in the upper layers were the bacteria, fat, vegetable cells, etc. These can be drawn up with a pipette and placed on a slide, spread out thin and covered with a large cover-glass. The slides are then examined under the two-thirds and one-sixth objective of the microscope, the higher power being used to bring out the detailed characteristics. These were then compared with the specimens prepared by treatment with potassium hydrate and identified as the same.

The potassium hydrate was a 5 per cent. solution, and the control substances sections of various fruits and vegetables. Pieces of thread were also placed in it for one day. He divides pseudo-parasites into two classes :—

(1) Free living animals introduced by accident. *Example:* Small nematodes living normally in the onion, also cases of gordius, the hair snake.

(2) Parts of substances of both plant and animal origin, used as food, which have not been destroyed by the action of the digestive juices. *Example:* Radulæ of common limpet, seeds of mulberry.

He notes that the fibres of banana have been mistaken for tape-worms, especially *Tænia nana* and *T. diminuta*, owing to the fact that they are made up of segments resembling tape-worm strobilæ. In oranges there are structures which bear a resemblance to certain trematodes. These are small cells which when partially digested may closely simulate the liver fluke. The same is true of lemon cells which, however, have double cell walls, while of course both orange and lemon cells lack mouths, oral suckers or intestines. Celery shreds look very like worms, amongst others *Necator americanus*. They consist of fibro-vascular bundles. In the same way onion fibres may deceive, being like *Agchylostoma duodenale* and *Ascaris mystax*. Microscopically the bundles are found arranged parallel to each other, and usually give the cellulose reactions as do those of celery.

Sauer-kraut, rhubarb, and pieces of common white sewing thread may all cause mistakes in diagnosis. So may dates, the fibro-vascular bundles of which closely resemble tape-worm segments. Oatmeal in the stools may also simulate the segments of worms.

A somewhat similar paper is that by Young[4] of Peking who, however, rather confines himself to a description of the plant structures which may be expected to appear in the stools, especially of man in the Orient. Cellulose, he notes, has the same empirical chemical formula as starch, but differs from the latter in not turning blue when treated with a watery solution of iodine. It does so, however, if treated with sulphuric acid and iodine, or by a mixture of

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[1] Tenney, E. S. (1910), "The Sputum of Typhoid Fever Patients as a Possible Source of Infection." *Collected Papers American Society of Tropical Medicine.*

[2] Firth, R. H. (June, 1911), "A Statistical Study of Anti-Enteric Inoculation." *Journal Royal Army Medical Corps.*

[3] Royal, M. A. (1908), "Pseudo-Parasites." *Bulletin of the State University of Iowa*, New Series, No. 182.

[4] Young, C. W. (November, 1910), "Some Vegetable Bodies found in the Fæces." *China Medical Journal.*

iodine, potassium iodide and chloride of zinc. One can only quote from the paper here and there. Thus the author says that pollen grains which are not digestible might be mistaken for eggs. Again the ascus of a mould might be mistaken for an egg shell, and the ascospores for a dividing ovum. The paper is certainly useful, and gives one an idea of the manifold substances which may be found in the excreta of vegetable eaters. I recall being nearly deceived by the close resemblance a single loop of a curious spiral double-walled fibre which was passed in fæces bore to a large thin-shelled egg. The rest of the loops were hidden by debris, etc., and the single oval loop with granular contents certainly suggested a parasitic ovum. Mere reference may be made to a paper by Kraus[1] on the examination of the fæces in the case of persons with digestive troubles. It is on the lines of that by Baumstark, quoted from in the first Review.

Fæces— *continued*

An account of the benzidin, the aloin, and the guaiac tests for occult blood in the fæces is given by Cammidge.[2] A recent method given by Boos[3] is as follows :—

A reagent is prepared by reducing phenol-phthalein in alkaline solution by means of hydrogen. One gm. of phenol-phthalein and 25 gms. of potassium hydroxide are dissolved in 100 c.c. of water; 10 gms. of zinc dust are added, and the mixture is warmed, with agitation, until it becomes colourless. It is filtered while warm, and a small excess of zinc is added to the filtrate as a preservative. To detect blood in fæces a portion is diluted to a liquid consistence, treated with acetic acid, and then with ether, mixing the latter cautiously to avoid emulsification. After separation the ether layer is treated with 20 drops of the above reagent and 3 to 4 drops of hydrogen peroxide solution. In the presence of blood a colour, varying from rose to deep red according to the amount of blood present, will be developed.

The following is Taylor's[4] method for obtaining stained specimens of the ova of intestinal parasites in the stools.

(1) To a teaspoonful of fæces add 1½ oz. of water or saline solution in a conical glass. Break up the fæces thoroughly and allow to stand until the solid matter settles. Pipette off the supernatant fluid and add more saline solution, and again mix and allow to settle. Repeat this a third time. If a centrifuge is obtainable it may be used to hurry the sedimentation.

(2) With a pipette pick up some of the solid matter from the lowest layer of the deposit and make several moderately thick smears on slides.

(3) Dry and fix the smears by heat.

(4) Stain for 15 seconds with the following solution :—

Orange G.	4 grammes
4 per cent. solution of acetic acid	100 c.c.

(5) Wash in water.

(6) Dry thoroughly by heat.

(7) Mount in Canada balsam.

If permanent specimens are not wanted, the driedstained film is smeared with cedar oil and examined without a cover-glass.

The clearing with cedar oil or mounting in balsam is essential, and makes a wonderful difference in the appearance of the film, the mass of refractile material usually present in the uncleared film disappearing almost entirely from view.

Additional Note

A very useful paper which will be found more fully discussed under the section "Parasites" is that of Hall[5] on a comparative study of methods of examining fæces for evidences of parasitism. He gives his own technique which is somewhat lengthy, but which he finds best for routine examinations of various kinds of fæces. It serves both for worms and coccidia, but has not been tested for other protozoa.

Fevers. This is a large subject, and so far as the Sudan is concerned receives attention in a special paper in the Fourth Report of these Laboratories, Vol. A.

Manson[6] deals with the diagnosis of fever in patients coming from the Tropics. He utters a warning against supposing that because a fever has been contracted in or is occurring

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[1] Kraus, O. (July 9, 1910), "The Examination of Fæces in Medical Practice." *Lancet.*

[2] Cammidge, P. J. (August 13, 1910), "Tests for Occult Blood in the Fæces." *British Medical Journal.*

[3] Boos, J. (1911), *Apoth. Zeit.*, quoted in *Pharmaceutical Journal*, April 8, 1911.

[4] Taylor, J. (April, 1911), "The Examination of the Fæces for Ova of Intestinal Parasites." *Indian Medical Gazette.*

[5] Hall, M. C. (1911), "A Comparative Study of Methods of Examining Fæces for Evidences of Parasitism." *Bulletin No.* 35, *Department of Agriculture, U.S.A., Bureau of Animal Industry.*

[6] Manson, P. (March 20, 1909), "Diagnosis of Fever in Persons from the Tropics." *British Medical Journal.*

Fevers—*continued*

in a patient from the Tropics it must of necessity be a tropical fever. The first things to be considered in such a patient are tuberculosis, syphilis, typhoid, malignant disease and sepsis. He then proceeds to take up some of the more important tropical fevers in detail, *i.e.* malaria, that associated with liver abscess, Malta fever, kala-azar, trypanosomiasis, relapsing fever, and elephantoid fever. He concludes with a brief consideration of multiple infections, the possibility of which, as, for example, malaria and trypanosomiasis, should never be forgotten. Home [1] has a paper on a fever occurring on board ships at Malta, which he believes to be due to overcrowding. It is difficult in these days to believe that this condition can be more than a predisposing cause of fever. An interesting paper in the *Lancet* of May 15, 1909, deals with the biological significance of fever. It would seem that in infections where phagocytosis plays a part in protection, the raised temperature is beneficial and assists that process. It also aids the production of bacteriolysins and antitoxins. Rolly, whose paper is one of those under consideration, concludes

> that if the temperature remains raised only a moderate degree above the normal it exerts on the whole more beneficial than harmful effects, and that fever represents a reactive process on the part of the body whereby it attempts to combat the bacterium causing the disease, or to neutralise its toxic products more rapidly. That the temperature sometimes rises to an excessive height, and in so doing may exert directly harmful effects, does not negative this view of the nature of the febrile reaction, but may be regarded as an instance of the "over-compensation" which was shown by Weigert to be a common biological characteristic, especially under pathological conditions; and this was adopted by Ehrlich as an important part of his theory of immunity.

Wilson,[2] in a paper on certain Punjab fevers, describes as a specific entity Simple Continued Fever, or Heat Fever, or the Three-Day Fever of Rogers. His patients

> all complained of more or less headache, usually general, though sometimes frontal, sometimes occipital, with pains in the back. Headache was the first thing felt by the patient, sometimes accompanied by an admitted feeling of chilliness, seldom by a definite rigor. Thirst, anorexia, and a dry, hot skin were other prominent symptoms. The temperature varied from about 101° F. to 105° F., 103° F. and 104° F., being common; the pulse rate varied with the temperature, and was somewhat throbbing when that was high. The treatment usually consisted of a purge (of 3 grains of calomel, with or followed by a dose of white mixture), a diaphoretic mixture, and, if the temperature was high, cold sponging or wet pack. The blood in nearly all the cases was searched for malarial parasites, and no quinine was given. Under this treatment the fever gradually subsided, so that the temperature would reach normal usually on the third day, some cases on the second day, in hospital. The temperature used to fall with a continuous slope down to normal (though this slope might be disguised by the cold sponging or wet pack), and this is the most characteristic feature of this fever. In a certain number of cases this slope was interrupted by the evening temperature on the second day being no lower or a little higher than that in the morning. Patients were generally discharged after five to seven days in hospital. There were practically no relapses, though a man might occasionally come in again with a second attack.

As regards etiology the author says that the one constant condition present when these fever cases occurred was an uncomfortable degree of heat, and this was regarded as the cause. He discusses its mode of action, saying :—

> How the heat produces the fever is, of course, a difficult question. It may be by simply upsetting the thermotaxic centres in some way or other. There is little or nothing to suggest that a strange microbe has an immediate hand in its production. There are some reasons for the suspicion that most, if not all, the heat-strokes that occur during the hot weather are due to an exacerbation, or rather a hyperpyrexia, of this fever. Some cases admitted to hospital for what was apparently heat fever have suddenly passed into heat-stroke. Heat-strokes seem to be most numerous when heat fevers are prevalent, and most patients, on recovery from heat-strokes, admitted having felt ill before the attack. Should this suspicion turn out to be correct, this fever will assume a greater importance than it at present occupies, for in the Punjab, after enteric fever, more deaths result from heat-stroke than from any other disease.

In the light of other work I think it is quite possible that these were cases of Phlebotomus Fever, but it is only reasonable to suppose that heat may in some way or other cause a febrile condition.

Spencer [3] has recorded a case, apparently of this type which, however, passed into a kind of chronic condition with anæmia and rheumatic symptoms. From the patient's blood a short, fat, non-motile, Gram-negative bacillus was isolated, which did not ferment the more common sugars and produced alkali in litmus milk. It was non-pathogenic to rabbits and guinea-pigs. It did not agglutinate with typhoid, paratyphoid, A and B, and Malta fever sera.

Roberts [4] again describes the condition in India, which he has named Acute Tubercular Fever. He finds tubercle bacilli excreted from time to time in the urine, very seldom during

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[1] Home, W. E. (April, 1909), "On the Discrimination of Unrecognised Diseases, and on a Disease of Overcrowding in Ships, especially at Malta." *Proceedings Royal Society of Medicine.*

[2] Wilson, G. (June, 1909), "Notes on the Fevers prevalent at Ferozepore in the Punjab, India." *Journal Royal Army Medical Corps.*

[3] Spencer, T. W. (August, 1909), "A Note on a Case of Simple Continued Fever, with Recovery of an Intermediate Organism from the Blood." *Ibid.*

[4] Roberts, J. R. (August, 1909), "Experiences in Tubercular Disease." *Indian Medical Gazette.*

Fevers—*continued*

the course of a case, and very irregularly. He has never succeeded in infecting guinea-pigs by injection of the urine, and as it is very laborious to separate tubercle bacilli from other acid-fast bacilli in the urine, and from streptothrix, this urine examination is of little avail. One has to rely on the clinical symptoms and the special cutaneous and ophthalmic reactions. The chief symptom is

a continued temperature of long duration, from a fortnight to four or five weeks, an evening rise, a morning fall, with a maximum of 103° to 104°; often it is remittent, never falling to normal, or it is intermittent with a fall to 98°, reminding one of an enteric chart, or what has been called "simple continued fever." Other symptoms are on the whole remarkable by their absence; a certain proportion of cases develop an enlargement of the liver, a certain amount of meteorism, and the bowels are constipated. There is every degree between a simple and mild type to a severe and prolonged one, reminding the observer of acute generalised tuberculosis; but the great majority are not severe. Further, the mortality is low, and recovery the usual termination.

Those cases which become cachectic are suitable for treatment with tuberculin R.

Clayton [1] discusses the Seven-Day Fever of eastern ports, concludes that infection is conveyed by some biting insect, probably *Culex fatigans*, and that the disease is in reality a sporadic form of Dengue.

A suggestive paper is that by Whitmore [2] on fevers in the Philippines. Amongst other notes he says :—

I have also seen a number of cases of fever which differed clinically from typhoid, malaria, and dengue. During the past year I saw two cases of fever with sudden onset, an irregular fever of about two weeks' duration, with no bowel disturbance, no eruption, and no marked degree of emaciation after the fever was over. The blood serum of these patients did not agglutinate any of my stock typhoid or paratyphoid cultures, but from the blood of each patient I obtained an organism which agglutinated at 1 in 20, but not completely at 1 in 40 with the corresponding serum. These two organisms were pathogenic, and differed in morphology and some cultural characteristics from the typhoid bacillus.

From this it is evident that I am of the opinion that we have some cases of fever here which are due to infection with members of the abdominal group other than the typhoid bacillus, and that there are strains of the typhoid bacillus which are distinguished only by the agglutination test; further, it is probable that the failure of the agglutination test in some undoubted cases of typhoid fever may in part be accounted for by our not having the particular strain which is causing the disease. If such should prove to be the case we would have to broaden the term "typhoid fever," or create a number of "paratyphoid fevers."

I think most of those who have experience of fevers in the Tropics will agree with this finding, and in this connection one may cite the cases recorded by Archibald,[3] in which an organism of the *B. cloacæ* type was isolated from the blood. Whitmore also describes a "simple" or "simple continued" fever as follows :—

The onset of this fever is usually sudden, with prolonged chilly feelings, but rarely a severe chill. The temperature rises suddenly or by steps for two or three days to 103°–104° or even 106°, the face is flushed from the start in three or four days, *and, while the temperature is still high,* a rose red macular eruption appears over the entire trunk and limbs, but the eruption may be absent or transient. There is no sweating, the skin itches intensely, the conjunctivæ are injected, and there is pain in the eyes. The eruption does not appear on the palms of the hands or the soles of the feet. As the eruption comes out completely, the temperature drops, and in forty-eight to sixty hours the temperature is normal, the eruption has disappeared, and the patient feels well, without pains or after effects except that he is weak. Repeated blood examinations do not show malarial organisms, and quinine has no effect on the fever. At no time is there any more pain than would be occasioned by any acute infection when the temperature range is so high, and there are no pains afterward.

I fancy this would nowadays be classed as Phlebotomus Fever (*vide page* 248), though later on the author is inclined to regard it as Rogers' Seven-Day Fever. The urticarial fever of the Yangtse Valley described by Lambert [4] need merely be mentioned, as it only possesses a local interest. It and other undifferentiated fevers of China are discussed by Jeffreys and Maxwell in their *Diseases of China*.

A curious condition possibly worthy of mention is Rat-bite Fever, described originally by Horder and then by Middleton.[5] The fever is irregular, comes and goes, and may be associated with the presence of a measly rash. A useful paper on fevers, and more especially

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[1] Clayton, H. F. A. (February, 1910), "Notes on Seven-Day Fever of the Eastern Ports, etc." *Journal Royal Army Medical Corps.*

[2] Whitmore, E. R. (1909), "Observations on Fevers in the Philippine Islands." *Transactions Bombay Medical Congress.*

[3] Archibald, R. G. (1911), "Four Cases of Pyrexia due to Infection with a Bacillus of the *B. cloacæ* Type." *Fourth Report, Wellcome Tropical Research Laboratories*, Vol. A.

[4] Lambert, A. C. (April, 1910), "Notes on some cases of Fever with an Urticarial Rash occurring in the Yangtse Valley." *Transactions Society Tropical Medicine and Hygiene.*

[5] Middleton, G. S. (June 11, 1910), "Rat-bite Fever." *Lancet.*

Fevers—*continued*

on the short duration form in China, is that by Hume.[1] He classifies the majority of puzzling fevers as follows :—

A. Typhoid Colon Group. *B*. Dengue Group. *C*. Influenza Group.

Under *A* we note :—

(1) Cases that are clinically typhoid in symptomatology, however abrupt their onset and mild or brief the temperature course, and in which the serum reaction is positive with *B. typhosus*, or cultures yield this organism.

(2) Cases clinically similar to the above, but giving serum-reaction with or yielding cultures of *B. paratyphosus*. In this sub-group should be included Goodhue's cases of "Hawaiian Fever."

(3) Cases clinically typhoid, due to infection with *B. enteritidis*, such as those reported from Bombay by Row.

(4) Cases of fever due to infection with *B. coli*, proved by cultures from urine or blood, together with agglutination reaction, even in high dilutions.

In addition he mentions "Ichang," a local Chinese fever, and Seven-Day Fever.

Under *B* he puts the Three-Day Fever, which may very well be Phlebotomus Fever. Under *C* he notes that the lungs and throat are affected in over 90 per cent. of cases of tropical influenza.

Cousland [2] gives an account of "Low Fever" in China. This is what Rogers calls "Low Fever of European Immigrants in India," but it would seem to vary a good deal in type. The author likens it to the more chronic forms of kala-azar, and suggests it is due to a protozoal parasite. There does not, however, seem to be any splenic enlargement, or indeed any marked physical signs. A change of air would appear to be a certain cure.

Conor and Bruch [3] have recently described an eruptive fever observed in Tunis. They regard it as a specific entity, and propose for it the name *Fièvre boutonneuse de Tunisie*. This suggests the type of the rash which appears with the fever, and has a general distribution. The spots are peculiar, being neither macules nor papules, nor lenticular spots nor nodosities. They are rose-red or dark red, partly disappearing under pressure, about the size of a lentil, and not confluent. The skin patches between them are normal. The fever may last a fortnight, and may be accompanied by headache, nausea, vomiting and joint pains. Convalescence is short, but the rash persists after the temperature falls. The authors record seven cases, all more or less conforming to this type. Inoculation of the blood of patients into monkeys proved negative.

At a later date, Conor and Hayat [4] placed on record some new facts regarding this fever. The onset is usually abrupt, with rigors. There is constipation. The conjunctivæ are injected, the eyes red and brilliant. The stools are fetid, and there is insomnia. The rash appears first on the abdomen, and is not itchy or painful on pressure. In all their patients the rash affected the palms of the hands and the soles of the feet. The illness is not a serious one, and does not leave much malaise. There is no desquamation, only a little pigmentation when the *boutons* vanish. The blood does not agglutinate *B. typhosus* or *paratyphosus* (A or B). In two cases an incomplete agglutination in low dilution was observed with the *Micrococcus melitensis*. The leucocyte formula shows a lymphocytosis of about 35 per cent. The authors differentiate the disease from various kinds of erythema, from measles, from typhus fever, and especially from the condition described by Brill in the United States, which is of a serious nature with intense headache, feeble morning remissions, marked prostration and an enlarged spleen. The rash, however, is like that in the Tunisian affection, and there are some other points of resemblance. They also distinguish the fever from Phlebotomus Fever and from Dengue. It will be seen that these observations are important, and that in Northern Africa at least it is worth while to be on the lookout for such a condition. I have once seen a case in a British soldier in Khartoum recalling it in some measure. The condition at the time was regarded as rheumatic.

Recently there has been some discussion as to whether or not there is such a thing as "Round Worm Fever." Apparently there is. Hehir [5] states that

the onset is insidious and without rigors; the patient has felt indisposed for some days previously; there is usually a slightly coated tongue, loss of appetite, some constipation and headache, and there may be nausea and

[1] Hume, E. H. (May, 1910), "A Note on the Classification of Fever in Central China." *China Medical Journal.*

[2] Cousland, P. H. (November, 1910), "Low Fever." *Ibid.*

[3] Conor, A., and Bruch, A. (October 12, 1910), "Une fièvre éruptive observée en Tunisie." *Bull. Soc. Path. Exot.*

[4] Conor, A., and Hayat, A. (December 14, 1910), "Nouveaux faits concernant la fièvre boutonneuse de Tunisie." *Ibid.*

[5] Hehir, P. (August, 1910), "Remarks on Ascariasis. Is there a Round Worm Fever?" *Indian Medical Gazette.*

wandering pains, or discomfort about the umbilical region. The temperature rises from 101° to 102·5° F., reaching its maximum on the second or third day. After a dose of calomel, followed by a drachm of pulv. jalapæ co., or a seidlitz powder, the fever disappears abruptly on the third or fourth day. If the nature of the condition is suspected on the first day, santonin, followed by a purgative, given, and the worms expelled, the fever abates on the second or the third day, and does not return. If the condition is not recognised and no aperient is given, the fever, with slight constitutional symptoms, may continue for five or six days, and then disappear by lysis, in some cases to return at irregular intervals of from five to six weeks to six months. Blood examination reveals eosinophilia (up to 20 per cent.), leucocytosis, and occasionally slight anæmia. **Fevers—** *continued*

He gives an interesting account of how infection may be acquired in India, and mentions cases of profound toxic poisoning in children which apparently were wholly due to round worms. Schaffter,[1] agreeing and commenting on this paper, states that pain, combined sometimes with swelling in one or both knee-joints, may be a symptom of round worm infection in the Deccan. Savant [2] states that in a sea-coast town in the Deccan the condition is most common amongst fish-eaters. In addition to fever there may be severe colic. Reference may be made to a paper by Smithson [3] on a condition called Mossman fever which occurs in North Queensland. The pyrexia is accompanied by enlargement of the posterior or subscapular group of axillary glands. They become tender. The disease lasts for 10 to 14 days, and affects sugar-cane cutters almost exclusively. The blood is normal. The death-rate is very low. In fatal cases a typhoid state supervenes. The author suggests that some insect found amongst sugar-cane is possibly to blame. Statham [4] records an outbreak of fever in South Africa in three cases of which bacteria were isolated, which, though possessing many of the features of the typhoid-colon group of bacteria, fermented saccharose markedly, and did not affect dulcite. The type of fever was as follows : Onset more sudden than typhoid, pyrexial period (including the pre-hospital fever), probably seven to ten days ; headache and pain in the body, dirty tongue, constipation, spleen tender, but not enlarged. In half the cases a curious and profuse rash was present. The reader must refer to the paper for details. The organisms isolated belonged to the *B. lactis aerogenes* and *B. cloacæ* group. It is possible the water-supply was to blame, but the precise source of the outbreak was not traced. Reference may also be made to the papers by Brown and Deeks, quoted under " Enteric Fever."

The " Spotted Fever of the Rocky Mountains " is an interesting disease which, however, cannot be considered here. The following references will guide the reader to some recent papers on the subject: *Journal Tropical Medicine and Hygiene*, April 15 and June 15, 1909. *Bulletin Johns Hopkins Hospital*, May, 1909. *Bulletin of the Pasteur Institute*, December 15, 1909, February 28 and October 15, 1910. *Journal Tropical Medicine and Hygiene*, May 2 and 16, and June 1, 1910. Also *Experimental Station Records*, No. 8, June 17, 1910.

Finally attention may be directed to the second volume of the *Traité de Pathologie Exotique Clinique et Therapeutique*, which is entitled " *Parapaludisme et Fièvres des Pays chauds*," and which deals with a great number of the less important fevers. One specially notes Red Sea Fever, the Endemic Fevers of Massowah, and the Climatic Fever of the Antilles. There is also a note on the Pseudo-Dengue of Cochin-China.

Additional Notes

Under a paper on paratyphoid fever in South Africa, M'Naught [5] mentions Brill's fever, which he believes is common in South Africa, and which is probably due to a specific organism. Here is his description of the symptoms observed before his attention had been drawn to Brill's discovery :—

(1) The onset is sudden, and is accompanied by particularly severe headache, pains in the back and limbs, dark flush on cheeks, injected conjunctivæ, and suffused eyes. Sometimes the patient has been out of sorts for a few days before the onset of distinct symptoms, but usually the disease sets in quite suddenly.

(2) A characteristic dark red maculo-papular rash, not unlike the rash of German measles, appears all over the trunk and limbs. I have found this rash present on the soles and palms in all cases in which I had an opportunity of looking for it. Interspersed with the characteristic rash are sometimes found lighter red spots like rose spots. The rash leaves brown stains when it fades. It appears earlier than the rash of typhoid fever, sometimes coming out on the second or third day of illness.

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[1] Schaffter, C. F. (November, 1910), " Remarks on Ascariasis. Is there a Round Worm Fever ? " *Indian Medical Gazette.*

[2] Savant, S. V. (November, 1910), " Ascariasis." *Ibid.*

[3] Smithson, O. (December 1, 1910), " Mossman Fever." *Journal Tropical Medicine and Hygiene.*

[4] Statham, J. C. B. (December, 1910), " A Small Outbreak of Fever due to Bacteria having unusual Cultural Characteristics." *Journal Royal Army Medical Corps.*

[5] M'Naught, J. G. (May, 1911), " Paratyphoid Fever in South Africa." *Ibid.*

Fevers— *continued*

(3) The tongue is coated, but not usually dry or brown. Constipation is usual; the motions have a dark brown colour. The spleen is generally enlarged. There may be some abdominal fulness but not marked distension.

(4) The fever lasts from ten to fourteen days as a rule. It usually comes down by rapid lysis, but may do so by crisis. Convalescence is rapid, and there are no relapses.

(5) Though the patient often appears to be extremely ill during the first week of the disease, yet I do not know of it ever proving fatal.

A valuable article is one by Robertson [1] on the blood picture in disease. The paper must be read as a whole, but we quote what he says about two of the short unclassified fevers of what he calls the enteric group, as not only are these notes useful in themselves, but they give an idea of the scope and nature of the article, which is well illustrated by typical temperature charts :—

Examining, then, unclassified fevers of short duration in this enteric group, we find that, especially during September and October, but generally through the second half of the year, we are constantly meeting with fevers of one, two, three or four days' duration, which present a definite family likeness in symptoms and in their blood picture. The attack is sometimes ushered in with a definite rigor or even series of rigors, but in the simpler cases this is not a feature of the infection. Headache, slight pains in the limbs and body with constipation are the clinical features, and the temperature rises in the evening to 100° or 101°. Treated with a smart purge, the case promptly recovers, to relapse again weeks or months after if no change in the habits and circumstances of the patient has been made. These cases last generally two to three days, but may extend without any very definite severity to a week or more before assistance is sought. In some patients toleration of the albumose seems to be established, and constipation with slight feverishness is sometimes complained of as the only sign of ill-health, or the temperature may rise for one night only, and such cases are casually returned as "Ephemeral Fever," or "Malaria."

My attention was drawn to this very large class of cases by the typical blood-count and the invariable history of constipation. I have a very large number of these counts, and their characteristic is the high lymphocyte percentage with a compensating neutrophile decrease. I find the lymphocytes are over 40 and the neutrophiles under 50, or, practically speaking, about 45 per cent. each of the total leucocytes.

The total blood-count shows if anything a slight leucopenia.

I have some fifty or sixty of these counts, always associated with the same train of symptoms, and varying very slightly in any single case from the average. The large mononuclears rise to a maximum normal only as a rule. Quinine has no effect, save to increase the headache. A simple smart purgative clears the case up at once. Nausea is not often complained of, but I have seen bilious vomiting in one unfortunate who got 160 grains of quinine before his blood film was submitted to me. These cases may be called "Constipational Fevers," but I consider them specific and due to coli intoxication of a mild nature. The term "Copræmic Fever" is perhaps most correct.

The next class is like this, but the fever is higher, running for *four days*, and intermitting between 103° and 99°. The onset is sudden, invariably associated with a rigor or series of rigors; the face and body generally are flushed and the skin is hot and dry, the eyes are suffused and injected, the tongue is thickly coated, with red tip and edges, and constipation is severe. Pains all over the body are complained of, but especially in the back and limbs. Many patients describe the former as "lumbago." On the 4th or 5th morning the symptoms clear, and convalescence is ushered in with the return of the skin and bowels to activity. It is, however, slow, and great prostration is invariable.

The blood-count is as in the last class exactly, so that for a time I was unable to differentiate this, which I believe to be specific intoxication by a definite member of the coli group, from the less severe and possibly more general infection of that indefinite congeries. Towards the third day the lymphocytes decrease, and the large mononuclears are much increased.

Coming now to the next number of the series, I agree with the author of *Fevers in the Tropics*, that the fever he has described as Seven-day Fever is probably but another of these specific coli infections. Here, again, associated with the common symptomatology is the typical high lymphocytes count of the enteric group of infections with, however, a more lasting blood picture. I have blood-counts in this condition which show over 60 per cent. lymphocytes during the last three days of the attack, and for a fortnight after it in one case I had an opportunity of examining. In the stage preceding this, the large mononuclears are also relatively increased. From the blood of one case I have isolated a motile organism of the coli communis type.

He discusses septic fevers, including the pneumonias, and has some excellent remarks on eosinophilia, quoting Ewing to the effect that—

The most comprehensive view of the significance of eosinophilia is that of Neusser and his pupils, who from extensive observations have found evidence that *the supply of eosinophile cells in the blood is controlled by the sympathetic nervous system, and that eosinophilia is the expression of sympathetic nervous irritation.* This irritation they believe may proceed from the generative organs, ovaries, uterus or prostate, disorders of which with their related neuroses are usually accompanied by eosinophilia; from the skin, diseases of which have furnished some of the best examples of eosinophilia; from the intestines, from which the toxæmia of intestinal parasites and that of gout, which Neusser regards as of intestinal autotoxic origin, give rise to marked eosinophilia.

He concludes by advising beginners to stick to one stain. For routine work he employs Giemsa. Not the least useful part of the paper are the appended tables of differential

[1] Robertson, A. W. (May, 1911), "Hæmateikona. The Significance of the Blood Picture in Disease." *Indian Medical Gazette.*

blood-counts met with in various conditions in India. Altogether this is a paper to be read, re-read, and remembered. Fevers—*continued*

Filariasis. This subject may conveniently be considered under two headings—(*a*) Human, (*b*) Animal; though it is not intended to say much about the latter.

(*a*) **Human.**

Filaria loa has been receiving a good deal of attention. Rodenwaldt [1] describes a case in which, apart from the usual local swellings, the symptoms were exceptionally severe. The patient was from the Cameroons, had ocular *F. loa*, and attributed his illness to drinking unboiled water. He denied ever having been bitten by mosquitoes. He had dull painful sensations in the arm, leg, and trunk, and also a sensation as if hundreds of worms were crawling about inside him. There was headache, and such a feeling of weakness that, *nolens volens*, he felt he must lie down, and he was finally reduced to a condition of despair. The neuralgic pains were sometimes so severe that antipyrin had to be injected. The author notes that the patient was an energetic and intelligent man, in no way neurasthenic. At no time did he show *Microfilaria diurna* in his blood, but it is suggested that the latter will make its appearance when the young wandering *F. loa* have passed into a resting condition.

Dufougere [2] records a case in a European from the Congo, who exhibited ocular *F. loa*, and whose blood showed a marked eosinophilia, and contained a very large number of embryos. A study of these latter showed them to correspond exactly with Manson's description of *Microfilaria diurna*, and also with that of the embryos found by Penaud and Livon in the uterine tubes of *F. loa* extracted from the eye. The author, therefore, believes that *F. diurna* is a microfilaria, of which the adult is *F. loa*. Nattan-Larrier and Parvu [3] have studied the eosinophilia associated with the Calabar swellings due to *F. loa*, and which they term "*œdèmes éosinophiliques*," because they find masses of eosinophiles in the cellular subcutaneous tissue at the site of the swellings. They are inclined to think that there is a local formation of eosinophiles, which then pass into the blood stream. They note that the eosinophilia of the general circulation at the time when the swellings are absent is 24 to 54 per cent. At the time of the swellings it is 40 to 70 per cent. Twice only had leucopenia been noted. Low [4] points out that it is now generally admitted that *F. diurna* embryos are really the young forms of *F. loa*, but states that they are apt to be confused with *F. bancrofti*, which may remain in the peripheral blood during the day, and indeed in Fiji and some other South Sea Islands a diurnal occurrence seems to be the usual thing for them. He gives the following distinguishing measurements :—

The genuine *F. diurna* embryos (*Microfilaria loa*) measure from ·210 to ·280 mm. in length (fresh living specimens) (average ·240 mm.), by ·0070 to ·0075 mm. in breadth, the V spot being situated ·060 to ·073 mm. from the head, the break (seen in stained specimens) being ·042 mm. from the same point. Embryos of *F. bancrofti* on the other hand measure from ·280 to ·320 mm. in length (a good average measurement being ·310 to ·317 mm.) by ·0075 to ·0084 mm. in breadth, the V spot being situated ·090 mm. from the head, the break in the cells ·050 mm. (or over) from the same point.

Clearly, therefore, the embryos of *F. bancrofti* are longer and slightly broader than those of *F. diurna*, though one must admit that as regards other anatomical points there is a striking similarity between the two.

He recommends the substitution of the term *Microfilaria loa* for *F. diurna*. The intermediate host still remains unknown, and it is not clear why, in some cases, though adult worms are wandering about the subcutaneous tissues no embryos are present in the blood; nor again, though embryos are present in the blood, why there are no signs of adults, and so on. He discusses these problems, mentions Calabar swellings, and states that he believes *F. loa* can also produce a complete, hard, and boardlike swelling of the forearm, a pruritis of the arm and severe ocular pain with photophobia. He gives four points in the diagnosis :—

(1) The actual presence of the worm. Has this been seen, or has one been extracted? If so, of course the diagnosis is complete.

(2) The presence of diurnal embryos in the peripheral blood exhibiting the measurements and characteristics described above.

(3) The actual presence or history of Calabar swellings.

(4) Eosinophilia with no explainable cause.

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[1] Rodenwaldt, E. (1910), "*Filaria loa*." *Archiv. f. Schiffs-u. Tropen-Hyg.*, Vol. XIV., No. 4.

[2] Dufougere, W. (May 11, 1910), "Sur un cas de *Filaria loa*." *Bull. Soc. Path. Exot.*

[3] Nattan-Larrier, L., and Parvu, M. (November, 1909), "La valeur de l'Éosinophilie chez les malades porteurs de 'Filaria Loa.'" *Arch. Mal. du cœur, des vaisseaux et du sang.*

[4] Low, G. C. (January 2, 1911), "*Filaria loa*." *Journal Tropical Medicine and Hygiene.*

Filariasis *—continued*

In analysing cases one does find all these four characteristics present from time to time (Sir Patrick Manson's case, already mentioned, on which I conducted the periodicity investigations, was one of these), but on the other hand it is equally, or even more frequent, to find one, two, or even three of these points absent.

A very careful description of *F. loa* has recently been given by Huffman and Wherry.[1] This was necessary, as the drawings or sketches of *F. loa* in most treatises on parasites are generally misleading. One cannot quote further from their paper, but there is a plate illustrating the chief points to which they refer. Huffman [2] has also made a study of the embryos of *F. loa* which he obtained from a live female *F. loa* fully matured with her uterus full of them. He agrees that they are identical with *F. diurna*, but was unable to repeat some of Manson's experiments. This paper is also illustrated, but Leiper does not regard the illustrations as of value. Leiper [3] mentions a remarkable case of scrotal infection with *F. loa*, twenty-one worms being obtained post mortem from the scrotum, which was of normal appearance. There was an enormous infection of the blood with embryos. Death was due to advanced cardiac disease.

Rodenwaldt [4] cites a case of seven years' duration where both *F. loa* and *F. diurna* were present, this being further proof of their relationship as adult and embryo.

Sergent and Foley [5] signalise the discovery of what they believe to be *F. perstans* in the blood of an indigenous inhabitant of Oran (Algeria) who had never quitted his country. They describe the parasite, and suggest that filariasis may possibly spread from tropical to northern Africa owing to greater facilities for communication. Conor [6] describes the finding of the embryos of *F. perstans* in the urine of a patient in Tunisia, but, as a reviewer points out in the *Journal of Tropical Medicine and Hygiene* for February 15, 1911, the grounds for concluding that these embryos are *F. perstans* are totally inadequate, and the measurements and anatomy would indicate that whatever else they may be, they are certainly not that parasite.

Parsons [7] gives an account of *F. volvulus* and of the fibroid subcutaneous tumours which it causes, and which are rather like dermoid tumours at first sight. On palpation they yield a peculiar testicular feeling owing to their structure. He concludes :—

(1) Time will probably show that *F. volvulus* is more common than has hitherto been supposed.

(2) Analogy would lead us to suspect that *F. volvulus* is transmitted by some blood-sucking insect.

(3) The geographical distribution of *F. volvulus*, as at present known, seems to correspond more or less with regions in Tropical Africa that are associated with such insects as have been proved to act as carrying agents in other parasitical affections.

(4) While the adult male worm has been studied more or less completely, this does not hold for the female worm. The difficulty lies in the extraction of the worm from the tumour; the tail portion is nearly always left imbedded in the fibrous stroma and defies detection. What seems to be needed is some macerating medium in which the tumour would disintegrate without the worms becoming destroyed.

As regards preservatives, a weak solution of formalin proved very satisfactory, in the author's case, for preserving the tumours during transit.

(5) Although the embryos of *F. volvulus* have not yet been found in the peripheral blood, it seems highly probable that some part of their existence must be spent in the general circulation.

Antoine [8] having submitted so-called fibrous cysts due to filariæ, these latter were examined by Raillet and Henry,[9] who found them to be *F. volvulus* which, however, should in their opinion read *Onchocerca volvulus*, owing to the appearance of the cuticle, the forms of the spicules, and the disposition of the papillæ. A full description of the male worm and a partial description of a damaged female are given.

Although it is not of a nature which can easily be reviewed properly in a work like the present, reference must be made to Fülleborn's [10] very complete monograph, which deals both

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[1] Huffman, O. V., and Wherry, W. B. (March, 1911), "A Description of Four *Filaria loa* from the same Patients." *Parasitology*, Vol. IV., No. 1.

[2] Huffman, O. V. (March, 1911), "The embryos of *Filaria loa*." *Ibid.*

[3] Leiper, R. T. (April 1, 1911), "A Remarkable Case of Scrotal Infection with *Filaria loa*." *Journal Tropical Medicine and Hygiene.*

[4] Rodenwaldt, E. (1911), "Zur Loa-Diurnafrage." *Archiv. f. Schiffs-u. Tropen-Hyg.*, Vol. XV., No. 4.

[5] Sergent, Ed., and Foley, H. (June 10, 1908), "Existence de *Filaria perstans* chez un indigène de l'Afrique du Nord." *Bull. Soc. Path. Exot.*

[6] Conor, A. (January 11, 1911), "Existence de *Filaria perstans* en Tunisie." *Ibid.*

[7] Parsons, A. C. (December, 1908), "*Filaria volvulus* Leuckart: its Distribution, Structure and Pathological Effects." *Parasitology*, Vol. I., No. 4.

[8] Antoine (February 9, 1910), "Kystes fibreux provoqués par les filaires." *Bull. Soc. Path. Exot.*

[9] Raillet, A., and Henry, A. (February 9, 1910), "Remarques à l'occasion de la Note de M. le Dr. Antoine." *Ibid.*

[10] Fülleborn, F. (1908), "Untersuchungen an menschlichen Filarien und deren Übertragung auf Stechmücken." *Beihefte Arch. f. Schiffs-u. Tropen-Hyg.*, No. 9.

with adult and with microfilariæ and with the question of the transmission of filariasis by mosquitoes. Methods of fixation and staining are given, and the numerous illustrations are likely to prove useful to any one working at filariasis. Filariasis —*continued*

Whyte [1] has a long paper on *F. sanguinis hominis nocturna*, in which he discusses periodicity and its association with eosinophilia. He gives the technique employed for counting the parasites, and shows—

(1) That variations are found in different individuals in the *maximum number* of circulating microfilariæ. In this short series of cases the maximum figure varied from 8 to 143 per centimetre.

(2) That variations are found in the *rate* at which the microfilariæ emerge from and retire to the lungs and larger arteries.

(3) That the hour at which the maximum number of microfilariæ appear in the blood is not, as has been frequently stated, always midnight, but that, on the other hand, the number is often *less* at that hour than it is both earlier and later.

(4) That the hour or hours at which the largest number of microfilariæ appear in the blood, though varying in different cases, will be found *caeteris paribus* fairly constant in repeated observations on the same case.

(5) That filariasis is associated with eosinophilia, and that the degree of eosinophilia will often correspond with the number of microfilariæ in the circulating blood.

The *F. philippinensis* of Craig mentioned in the last Review has been under discussion, and as the general opinion appears to be that the claim for specific rank made for it has not been justified, we need not further consider it here.

A paper by Brunwin [2] on filariasis in Fiji is worthy of note as, amongst other things, he comments on the fact that though the filaria present is *F. nocturna*, it appears in most cases in almost equal numbers in day and night blood. He also mentions and describes filarial fever, and is inclined to regard *Culex fatigans* as the transmitter of infection. He tested the toxic action of tea and opium on filariæ, and believes the comparative immunity of the Indian population in Fiji to be due to one or more of the following causes :—

(1) Avoidance of the locality of affected persons at night, such as by sleeping in separate houses.

(2) The use of mosquito screens.

(3) A pure water-supply.

(4) The use of mustard oil for the skin.

(5) Tea drinking.

(6) The use of opium.

Wise [3] describes some interesting filarial affections in British Guiana. One of these is acute filariasis of the testis and spermatic cord which produces a condition closely resembling peritonitis. It is apt to be overlooked. Usually a fullness and swelling just below Poupart's ligament are the only outward manifestations ; sometimes there is also a swelling and desquamation of the scrotum. The skin shows no lymphatic changes. The condition is most common on the right side, and attacks healthy muscular adults of both the black and East Indian races.

Post mortem, acute purulent hydrocele is often present. The lymphatic vessels and lymph glands are found affected. Streptococci are present in large numbers, and adult *F. bancrofti* are usually to be found at the junction of testis and epididymis. They are dead, and the eggs and larvæ are found outside the body of the parent worm. The worms, etc., are often shut off in a small abscess and are surrounded by pus. Treatment consists in early and free incision of tunica vaginalis and cord. Chyluria is also mentioned and described. Chyluric urines in British Guiana are free from fat. One case is recorded in which such a urine contained many living embryos. The milky opacity is due to a large proteid content. Wise has found adult *F. bancrofti* in the pelvis of the kidney, an interesting observation.

Rodenwaldt [4] enters fully into the differential characteristics of *Microfilaria nocturna* and *diurna* as evidenced by his process of vital staining, by ordinary dried and stained films, and after coloration with Azure II. and decolorisation by Nissl's method. The paper is well illustrated, and the most important differentiating structure is the so-called "internal body" which is only found in *Mf. nocturna*. A note in the *Journal Tropical Medicine and Hygiene*

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[1] Whyte, G. D. (June 15, 1909), "Filarial Periodicity and its Association with Eosinophilia." *Journal Tropical Medicine and Hygiene.*

[2] Brunwin, A. D. (December 15, 1909), "Some Aspects of Filariasis in Fiji." *Ibid.*

[3] Wise, R. K. (1909), In Report of Surgeon-General, British Guiana, for 1907–8.

[4] Rodenwaldt, E. (1909), "Differenzialdiagnose zwischen *Microfilaria nocturna* und *diurna*." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIII.

Filariasis —*continued*

for March 1, 1910, mentions that in a Danish-French leprosy report, dated July 8, 1909, the presence of *Filaria sanguinis hominis* in the stomachs of body lice has occasionally been noted. It is possible, therefore, that these insects act as transmitters as well as mosquitoes. A good account of the symptoms and post mortem findings in a case of infection with *Mf. bancrofti* is given by Niclot.[1] Levaditi and Stanesco [2] recommend the use of ricin for facilitating the discovery of filariæ in the blood. They use Merck's ricin, of which a solution of 1 per cent. in isotonic saline solution is prepared and placed in centrifuge tubes, 4 c.c. in each tube; the tubes are sealed and are then kept at 60° for an hour. When required for use a circular cut is made round the tube, and 20 to 30 drops of blood allowed to fall into the fluid. Agglutination commences immediately, and is complete in some minutes. When all the cells have fallen to the bottom of the tube, the supernatant fluid is placed in another tube and centrifuged. The supernatant liquid is again decanted, leaving one or two drops at the bottom of the tube which serve to dilute the clot. The deposit thus formed is aspirated and examined fresh, or stained with diluted Giemsa.

Brochard deals with eosinophilia in filariasis and elephantiasis, and amongst other conclusions notes that the amount present does not depend on the number of microfilaria in the circulation nor on the age or severity of the skin lesions. In filariasis alone it is about 18·7 per cent., in elephantiasis cases 14·5 to 15 per cent. He considers its presence an aid in diagnosis.

There is not much to be said about the treatment of human filariasis. Wellman and von Adelung [3] record the cure of a case of hæmatochyluria.

The treatment was introduced by Wherry and McDill, and consists in cinchonisation and subsequent exposure to X-rays. The patient was a Japanese, with no symptoms except the character of the urine and weakness. The urine was almost as turbid as milk, and had a decidedly bloody tinge. It contained no embryos, although the blood did. Fifty to seventy grains of quinine were given from December 28 to January 12: in the latter part of this period only 15 grains a day. X-ray exposures (12.-in. coil; direct current; Wehnelt interrupter; 6¾-in. bulbs—Friedlander and Gundelach—distance from target *to table top* 15 in., 3 in. vacuum, which sometimes ran up to 6 or 7 in. during treatment) were given on December 14, 1¼ mins.; December 22, 1 min.; December 31, 1 min.; January 7, 45 secs.; January 12, 31 secs. On January 14 the urine was perfectly clear; no albumin. On January 12 the embryos still persisted in the blood, but in very small numbers. The patient was practically cured, though time will show whether the cure was permanent or not. Time has now shown that the first case, that of Wherry and McDill,[4] has had no symptoms since 1904, while the second,[5] though still harbouring a few filaria, has been greatly benefited.

Warden [6] records a case of lymphatic obstruction due to *Mf. nocturna* which was greatly benefited by treatment with radium. An account of the treatment in French is given by Dr. Dominici, while Sir Havelock Charles was favourably impressed by its possibilities. Thiroux [7] testifies to the powerfully toxic action on blood filariæ of "emetic anilin," an anilin preparation of antimony. It destroys the parasites outright. He has had no success with atoxyl and excision of the lymphatic varices, but Lemoine, whom he quotes, reports a case apparently cured by these methods. At a later date Thiroux and D'Anfreville [8] again deal with the question. They admit they have not yet been able to bring about a complete disappearance of parasites, but record good results obtained by them in a case of infection with *F. perstans*. Werner [9] has recently tried intravenous injections of salvarsan in filariasis, but without any beneficial result and without any effect on the nematodes.

(*b*) **Animal.**

An account of what is known as "filariosis" of the tendons in the horse, a disease due to

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[1] Niclot, (June 8, 1910), "A propos d'un cas de filariose (*Microfilaria bancrofti*)." *Bull. Soc. Path. Exot.*

[2] Levaditi, C., and v. Stanesco (1906), "Sur un procédé facilitant la recherche des trypanosomes et des filaires dans le sang." *C. R. Soc. Biol.*, Vol. LXVII.

[3] Wellman, C., and von Adelung, E. (April 23, 1910), "A Case of Filarial Hæmatochyluria, treated after the method of Wherry and McDill, with apparent recovery." *Journal American Medical Association*, quoted in *Medical Annual*, 1911.

[4] McDill, J. R., and Wherry, W. B. (September, 1910), "Additional Notes on a Case of Apparent Cure of Filarial Hæmatochyluria. No return of Symptoms since May, 1904." *Bulletin Manila Medical Society.*

[5] Wellman, C., and von Adelung, E. (September, 1910). "A Second Case of Apparent Cure." *Ibid.*

[6] Warden, A. A. (July 24, 1902), "Note on the Treatment by Radium of Lymphatic Obstruction (Cervical, Submaxillary, and Axillary) in a Patient suffering from *Filaria nocturna*." *Lancet.*

[7] Thiroux, A. (March 9, 1910), "De l'action de l'Émétique d'Aniline sur la Filariose." *Bull. Soc. Path. Exot.*

[8] Thiroux, A., and D'Anfreville, L. (June 8, 1910), "L'Émétique d'Aniline dans la Filariose." *Ibid.*

[9] Werner, H. (1911), "Salvarsan bei Filarienerkrankung." *Archiv. f. Schiffs-u. Tropen-Hyg.*, Vol. XV., No. 4.

Filariasis —*continued*

Filaria reticulata, is given in the *Journal of Comparative Pathology and Therapeutics* for December, 1908. Useful notes on "worm nests" in cattle, and somewhat similar nodules due to nematodes in camels, are given in the Report of the Government Bureau of Microbiology for New South Wales, 1909, and by Cleland and Johnston.[1] Here, also, mention is made of the re-classification of the large genus *Filaria* by Stiles, and the establishment of the sub-genus *Onchocerca*. Under this genus come the species *O. reticulata* of horses, as above mentioned, and *O. gibsoni* of cattle, which produces the "worm nests." These two parasites are closely allied to the human *O. volvulus*. Casual mention is made of the *F. evansi* of camels, the adults of which are found in tangled masses plugging the pulmonary arteries, and are also present in the mesentery and spermatic artery, while the filaria embryo found in the blood of camels by the Sergents in Algiers, and by Mason in Egypt, are mentioned. Balfour [2] also describes microfilariæ from the camel in the Sudan, and also in a horse (*Mf. sanguinis equi africani*) and hare from that country. They have also been found in a Sudanese goat, but so far have not been described. *F. irritans*, the cause of summer sores in horses, is rather an important nematode. Contributions to its study have been made by Fayet and Moreau.[3]

A well illustrated account of the rare *F. osleri* found in the trachea and bronchi of dogs in India is given by Gaiger.[4] Leese [5] describes the presence of filariæ in the vitreous chamber of the eye of a camel in India, which also harboured *F. evansi*. The ocular parasites were found by Raillet to be a new species, and named by him *Thelagia leesei*. They probably were the cause of the ophthalmia which was present.

Filariæ of birds have received a good deal of attention. Those found in the fowl may be mentioned here. Thus there is Manson's filaria, now termed *Oxyspirura mansoni*. O'Zoux [6] gives an account of it as found in Réunion, and also the technique of obtaining the parasite from the eye of the bird. He also outlines its probable life-cycle, assigning to the embryos an intermediate host inhabiting the soil, and which is ingested by the fowl. Mathis and Leger [7] find this nematode common in Tonkin, and in addition describe a new embryo filaria belonging to an adult worm, which, they maintain, differs from Manson's parasite. The adult has not been discovered. The microfilaria may or may not exhibit a sheath, and has been named *Mf. seguini*. Mandel [8] describes and illustrates a blood filaria in a horse. He employed the vital staining of Fülleborn and Rodenwaldt, and was able to demonstrate an excretion pore, excretion cell, the internal body, the genital cell, and the genital pore. In general aspect the parasite resembles *Filaria sanguinis equi africani*. It was found in Berlin. Lebœuf and Ringenbach [9] describe microfilariæ in frogs and lizards from the Congo Free State, and also *Mf. perstans* in the chimpanzee. An excellent coloured plate adds interest to their paper.

Filters. The recent appearance of such a volume as that by Don and Chisholm [10] on *Modern Methods of Water Purification* renders any lengthy review of papers on filters unnecessary. Only a few which appear to be of special value will, therefore, be cited.

There have been several unfavourable reports on the Berkefeld filter, one of which received notice in the first Review. To this Wilson [11] took exception, stating that the filters had not been properly treated, having been sterilised at 120° C. for one hour in the metal cases supplied by the makers, this method tending to crack the cylinders or the cement of

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[1] Cleland, J. B., and Johnston, T. H. (December, 1910), "Worm Nests in Cattle due to *Filaria gibsoni*." *Journal Comparative Pathology and Therapeutics.*

[2] Balfour, A. (1911), "Veterinary Notes: Filariasis." *Fourth Report, Wellcome Tropical Research Laboratories*, Vol. A.; and *Journal Tropical Medicine and Hygiene*, April 1, 1910.

[3] Fayet and Moreau, A. (1908), "Contribution à l'étude de la *Filaria irritans*." *C. R. Soc. Biol.*, Vol. LXV., No. 24, and *Rec. de méd. vét.*, Vol. LXXXV., No. 18, quoted in *Journal Tropical Veterinary Science*, 1909.

[4] Gaiger, S. H. (October, 1909), "*Filaria osleri* in India." *Journal Tropical Veterinary Science.*

[5] Leese, A. S. (1910), "Filariæ in Vitreous Chamber of the Eye of a Camel—Ophthalmia." *Ibid*, Vol. V., No. 1.

[6] O'Zoux, M. L. (November 9, 1910), "L'Oxyspirure de Manson à la Réunion." *Bull. Soc. Path. Exot.*

[7] Mathis, C., and Leger, M. (1908), "Microfilaire de la poule." *C. R. Soc. Biol.*, Vol. LXVII., No. 29.

[8] Mandel, H. (December 17, 1910), "Über eine Blutfilarie des Pferdes." *Cent. f. Bakt.*, I. Orig., Vol. LVII., No. 1.

[9] Lebœuf, A., and Ringenbach (December 25, 1910), "Sur quelques Hématozoaires du Congo." *Ann. de l'Inst. Past.*

[10] Don, J., and Chisholm, J. (1911), *Modern Methods of Water Purification.* London.

[11] Wilson, A. (April, 1909), "On the Relative Efficacy of the Doulton, Berkefeld, and Brownlow Filters." *Journal of Hygiene.*

Filters— *continued*

the metal mounts. To this Bulloch and Craw [1] reply by fresh work and a new paper. Here are their conclusions :—

Transmission of Air

(1) The passage of air through the joint and wall of the Berkefeld filter does not seem to be materially affected by (*a*) boiling in water, or (*b*) autoclaving at 120° C., or (*c*) soaking new and used filters in water for twenty-four hours.

(2) These filters leaked, in general, at the neck or joint at lower pressures than at the wall, the joint from ½ to 6, the wall from 4 to 7 lbs. per square inch with new filters. Used filters showed leakage at the joint from 1 to 4½, and wall 2 to 6 lbs. per square inch.

(3) Simple immersion of a dry Berkefeld filter may give rise to a pressure of over 6 lbs. per square inch, and this caused immediate leaking at the joint. With autoclaved, comparatively moist filters a pressure of 3 lbs. per square inch was obtained with leakage at joint. We have thus an auto-transmission of air.

(4) At the pressure used in our experiments, viz. 0·9 lbs. per square inch, the large Berkefeld filters gave a yield of filtrate approximating to 0·4 gallons per hour. This is an exceptionally lenient test for a filter which the Berkefeld Company consider should give about 6 gallons an hour, *i.e.* 15 times as much.

Transmission of Micro-organisms

(5) Of two Berkefeld filters with porcelain nipples, one gave a contaminated filtrate from ordinary London tap water immediately, the other likewise after 3 hrs. 40 mins. These were new filters which had not been autoclaved but merely boiled one hour.

(6) Of three Berkefeld filters with metal nipples, two gave immediate contamination with tap water, and the third after 2 hrs. 40 mins. These filters were likewise new, and had only been boiled one hour.

(7) Two dried Berkefeld filters, one with metal and one with porcelain ends, on immersion of a portion of their walls in a water culture of *B. prodigiosus*, allowed this organism to pass into the interior of the filters.

(8) These results are entirely confirmatory of our former work, and effectually dispose of the objections raised in the private communications received from Messrs. Nordtmeyer and Andrew Wilson.

Schmidt [2] deals with the mechanism of bacterial filtration through the Berkefeld filter. Only a few of his eight conclusions will be noted. (*a*) Staphylococci and cocci nearest them in size never pass the filter ; the *Spirillum parvum* of Esmarch, the smallest of all bacteria visible under the microscope, passes the filter in 80 per cent. of cases where the filter candle is 2·5 cm. in thickness. In the first place the diameter of the organism determines its passage through the filter ; in the second place its mobility. (*b*) In most instances the filter passers are those organisms which, in the first phase of filtration, become imbedded in the filter. (*c*) Under certain conditions which he details, 4·4 per cent. of *B. fluorescens liquefaciens* traversed the filter, but no *B. paratyphosus* B. passed it. Under more stringent conditions 25 per cent. of the former, 44 per cent. of the latter, passed through, while 80 per cent. of *Sp. parvum* appeared in the filtrate. The best results were obtained with candles of 2½ cm. thickness. Grenet [3] has devised a method of measuring the pores of filter candles. He has been able to show that in the case of Chamberland bougies the micro-organisms may have dimensions greater than the diameter of the filter pores. When one plunges a dry bougie into water the water rushes into the capillary pores, and can carry micro-organisms into the substances of the candles. In this way they can pass through the filter. The author, therefore, recommends that before use the candles should be immersed in sterile water.

Turning now to the larger types of water filter, one finds an illustrated account of the new sand filters used in the French army, given in the *Journal Royal Army Medical Corps* for July, 1909. They are installed in barracks, the system being that of Miguel and Mouchet. The purifying bed is of fine sand, and it is worth noting that the filter must be installed in a dark place or where the light is diffused. Direct exposure to the rays of the sun favours the growth of algæ on the filter. These render the surface less permeable. For the same reason the filter must be protected from frost. Though a few bacteria are always present in the filtrate, they are innocuous and are derived from the lower layers of the drainage and supporting beds. The purifying bed effectually arrests pathogenic forms, and they do not increase there because no organic matter is available for their growth. Smith [4] reported on the Candy filters employed at Harrogate, and reported that, as compared with sand filters, (*a*) the Candy filters were under direct control and simple to operate ; (*b*) that they were more easily and efficiently cleansed, less water being required for the washing out per million gallons of filtered water ;

[1] Bulloch, W., and Craw, J. A. (April, 1909), "On the Transmission of Air and Micro-organisms through Berkefeld Filters." *Journal of Hygiene.*

[2] Schmidt, P. (1910), "Über den Mechanismus der Bakterienfiltration mit Berkefeldfiltern." *Zeit. f. Hyg. u. Infekt.*, Vol. LXV.

[3] Grenet, F. (November, 1910), "Étude sur la porosité des bougies filtrantes." *C. R. Acad. Sciences.*

[4] Smith, W. R. (September, 1908), "Report on an Inspection of the Water Supply of Harrogate." *Journal Royal Institute of Public Health.*

(*c*) that there was no absolute necessity for a period of resting, although this was desirable ; (*d*) that the filtering medium was practically indestructible, and that the filters were capable of destroying by oxidation the dissolved organic matter, removing iron in solution, effecting a material reduction in the objectionably brown colour of peaty water, and of effecting a high degree of bacterial purity ; and further, if necessary, in the case of a peaty water, with the view of preventing lead poisoning, the acid of the water could be neutralised by the introduction of suitable alkaline substances. Filters—*continued*

An illustrated German account of the Jewell mechanical filter installed at Königsberg is given by Friedberger,[1] together with tables of the tests to which they were submitted. It may be compared with the chapter on these filters in Don and Chisholm's work. As mechanical filters are still not as well known as they deserve to be, the following very brief description by Humphreys [2] of the process of filtration which they effect is here given.

Mechanical gravity sand filters depend for their efficiency on the formation of an inorganic jelly effected by the use of a coagulant, rather than an organic bacterial slime, as is the case in ordinary filter-beds. The process consists of chemical sedimentation rapidly secured by coagulating the impurities, including bacteria, into particles of such size that they are retained on or near the surface of the filtering material. The coagulant in general use is basic aluminium sulphate, formed by mixing aluminium sulphate (containing 17 per cent. Al_2O_3) with caustic soda, which on dissolution throws out aluminium hydrate as a suspended glutinous precipitate. The quantity used is generally 1 grain per gallon. Solutions of lime (85 per cent. CaO) and of iron have also been tried, and for bacterial efficiency and cost these are claimed to be superior to sulphate of alumina. The average rate of filtration of London supplies is about 41 gallons per diem per square foot of filter surface, whereas, when using mechanical filters with a coagulant it is from 66 to 132 gallons per square foot per diem. The maintenance of this high rate necessitates a filtering head from 10 to 14 ft. In order to control the rate of filtration each filter is fitted with an automatic controller that maintains a uniform rate of flow under all conditions. The sand recommended for use has an effective size of from about 0·46 to 0·5 mm., and a uniformity coefficient of 1·5 mm., which is obtained by twice washing and screening through sieves of 24 and 40 mesh respectively, using that which is passed by the former and retained by the latter. The total maintenance charges—labour, coals, oils, cleaning and repairs —worked out at 3*s.* 6½*d.* per 1,000,000 gallons.

Flies. In the first place we consider recent papers which deal with flies as disease carriers. One of the most important is that by Faichnie,[3] who has shown that when flies are bred in enteric excreta they contain the *B. typhosus* in their intestines, become carriers of the bacilli for the rest of their lives, and spread infection by means of their excreta. He says :—

Experience seems to show that infection conveyed by flies' legs, natural though it may appear from all the experiments carried out to prove its possibility, is not a common nor even a considerable cause of enteric fever, in time of peace, at any rate. On the other hand, infection by the excrement of flies bred in infected material explains many conclusions formerly difficult to accept. In a word, it is the breeding ground that constitutes the danger, not the ground where the flies feed.

If this be confirmed by further experiment and observation, the indications for sanitary measures will be narrowed down and become quite definite, especially if we bear in mind those two important observations, viz., the breeding of 4000 flies from one-sixth of a cubic foot of trenching ground, and the breeding of 500 flies from one evacuation of the human bowel. In privy-midden towns at home, whose enteric rates are, as a rule, higher than those of water-closet towns, the mere cleaning of the privies once a week, or even once a fortnight, during the autumn or summer, instead of once a month, should have a marked effect.

In a later paper he [4] gives the results of experiments in India. In 13 flies bred from a typhoid stool at least 6 contained typhoid bacilli in their intestines ; and the bacillus was recovered from the excrement and intestine of a fly sixteen days old. Similarly from a paratyphoid stool at least 4 flies out of 11 contained *B. paratyphosus* A. in their intestines. In each there was only one fly in which one or other bacillus was certainly not present. The interesting technique is given. To prevent contamination from the exterior of a fly it is, after being chloroformed, transfixed with a sterile needle and passed two or three times through the flame until its legs and wings are scorched. It is then put into sterile normal salt solution and stirred without breaking with a glass rod. One c.c. of this solution is seeded into MacConkey's broth for 48 hours. If this remains unchanged the fly is crushed with a sterile glass rod, and a drop of the fluid obtained plated. Ainsworth [5] has a paper, showing how at Poona and Kirker in India, the greatest number of cases of enteric fever coincides with the greatest prevalence of flies. His charts, though admittedly based on somewhat scanty data, bear out his contention that the fly is a carrier. The papers on "Sanitation in India," which

[1] Friedberger, E. (1908), "Versuche über die Verwendbarkeit der amerikanischen Schnellfiltration (Filter der Jewell Filter Company) für die Königsberger Wasserversorgung." *Zeit. f. Hyg. u Infekt.*, Vol. LXI.

[2] Humphreys, W. H. (1910), "Mechanical Gravity Filters." *Water*, Vol. XII.

[3] Faichnie, N. (November, 1909), "Fly-Borne Enteric Fever : The Source of Infection." *Journal Royal Army Medical Corps.*

[4] *Idem* (December, 1909), "*Bacillus typhosus* in Flies." *Ibid.*

[5] Ainsworth, R. B. (May, 1909), "The House-Fly as a Disease Carrier." *Ibid.*

Flies—*continued*

appeared in the *Lancet*, have already been referred to under "Enteric Fever." That dealing with flies as carriers of infection will be found in the number for February 20, 1909. Aldridge's work on the Indian representative of the common house-fly (*Musca domestica determinata*, Walker) is mentioned, and some of it may be quoted here. He found that this fly breeds in enormous numbers in filth trenches.

Warmth and a moderate degree of moisture appear to be the favouring conditions; the cold of winter, the rapid drying of the soil in midsummer, and saturation of the soil during the rains seem to be prejudicial to the survival of the larvæ. By turning up the soil of trenches of different ages the stages of development can easily be followed; they appear to be approximately as follows:—

	Hot weather Days	Cold weather Days
Ova	1	2
Larvæ	5	14
Pupæ	3	5

Full-grown flies are not, in most cases, to be found in large numbers at the trenches, no doubt because they do not find their natural food there; but the numbers of larvæ, pupæ, and young flies—some of them with their wings not yet expanded—to be seen on turning up the earth are so great as to make it difficult to avoid the conclusion that the majority of flies in cantonments are hatched there. For instance, in a sixth of a cubic foot of soil taken from a trench, 4,042 flies were experimentally incubated. It was further found that when the soil containing the larvæ was kept saturated with water no flies appeared. From observation it would appear that the eggs are laid in the filth in the latrines in barracks, and the larvæ are hatched out after it is put in the trenching ground. If, therefore, the eggs can be killed in the excrement by strong germicidal substances, the propagation of flies in this way will be put a stop to. In spite of its widespread distribution under varying climatic conditions, the house-fly is not easy to rear under artificial conditions; but, experimenting partly with the eggs of these and partly with those of the blow-fly (*calliphora*), Aldridge found that these eggs are somewhat resistant to most chemical substances; immersion for two hours in common salt 10 per cent., mercuric chloride 1 in 1000, or crude carbolic acid 2 per cent., failed to prevent the larvæ hatching out. On the other hand, immersion in any fluid for twenty-four hours seems to kill a considerable proportion of the eggs and all larvæ. It seems probable that a still larger proportion of the eggs would be destroyed by the putrefactive processes going on in sewage, while any larvæ hatched out would be destroyed in twenty-four hours.

Again—

The following evidence bearing on the relationship of fly prevalence to enteric fever incidence is not without interest. During the first half of 1905 the amount of enteric fever at Lucknow was much less than usual, the only recent years showing equally low figures being 1901–1902, when the low rates were accounted for by the small number of young soldiers arriving in India owing to the South African War. It was also unmistakable to any one familiar with the Lucknow barracks that the number of flies was markedly less than usual. A table compiled showed that while the number of flies at no time was very great in all parts of the barracks, yet the increase during the latter part of March and decrease at the end of May corresponded very closely with the period of enteric fever prevalence, allowing for the usual period of incubation.

Again, it was also noted that, with few exceptions, the flies found in the lines were *Musca domestica determinata*, while the only species bred from larvæ and pupæ taken from the trenching grounds belonged to the genera *Hylemyia* and *Uiidia*. It would therefore appear that in this instance, for some reason not at present apparent, the trenching grounds did not supply the enormous numbers of flies that were found in other years, and coincidently with this the amount of enteric fever was much below the average.

Smith[1] has extended his observation on flies breeding in human excrement in India. He finds that if the soil under the deposit in which they were hatched out is impermeable, the larvæ will travel considerable distances, at least as much as 10 feet, to find suitable ground in which to bury themselves. They travel not only at night, but under the full blaze of the Indian sun, and are often snapped up by birds. Sparrows, however, seem to disregard them. Ants appear to be their chief enemies. As many as 548 flies have been known to hatch out of a single deposit of human ordure enclosed in a net, and even so a good many maggots had escaped. He concludes:—

(1) No place upon which ordure is deposited can be said to be of itself unsuitable for the development of flies, provided flies can reach the ordure and provided the maggots can either by falling or crawling reach a place in which to pupate.

(2) For the larvæ of flies, forty-eight hours is a sufficiently long feeding time to permit of the post-maggot stages being gone through.

(3) After forty-eight hours the maggots do not require moisture beyond any which they may be supposed to get from the air.

In conclusion, I think it safe to suggest that in India, where the whole country is littered with fæces, the flies bred out of excrement deposited on the ground by men and animals are greatly in excess of the number from any other source, whether in or out of cantonments.

A good deal of general information about house and other flies in England, the species found in London, their breeding-places during the winter months, etc., will be found in the

[1] Smith, F. (July, 1908), "A Further Note on the Ways of Common Flies in India." *Journal Royal Army Medical Corps.*

Flies—*continued*

Preliminary Report to the Local Government Board on Flies as Carriers of Infection, which is largely quoted from Volume I., No. 4, of the *Journal of the Incorporated Society for the Destruction of Vermin*, 1909. The second preliminary report is reviewed in the *British Medical Journal* for October 16, 1909. One notices that Jepson states that flies can be marked by dusting them with coloured blackboard chalk, the best being brick-red. Graham-Smith investigated the presence of *B. coli* either on the surface or in the interior of flies, chiefly house-flies, and found a good many infected in certain localities. The third report is reviewed in the *Lancet* for October 1, 1910, and the *British Medical Journal* for October 22, 1910. From these we quote some passages :—

Dr. Graham-Smith's infection experiments show that non-spore-bearing bacteria do not usually survive more than a few hours on the fly's legs or wings. Nevertheless, such flies, allowed to walk over sterile agar plates, may cause infection for several days. This seems to be due to the fact that the flies frequently attempt to suck the surface of the plate, and in doing so infect it with the fluid regurgitated from the crop. When a fly tries to feed, for example, on sugar, dried milk or sputum, it first of all moistens the material with fluid from its proboscis and then sucks up the dissolved matter. Within the fly's crop non-spore-bearing bacteria often survive for several days, and they usually survive even longer in the intestines. The fæces deposited by such flies frequently contain the organisms in considerable numbers for two days, and are generally infective for a much longer period. It is therefore not so much the crude material carried on the fly's feet that is the source of danger, but rather the infected "vomit" (the fluid regurgitated from the crop) and the fæces which contain the pathogenic organisms for some time after the fly has fed upon the specifically contaminated material. No evidence has been obtained that multiplication of the organisms takes place in the crop or intestine of the fly. With regard to the actual infection experiments, a considerable number of organisms were used, amongst which may be mentioned *Bacillus typhosus*, *B. enteritidis* (Gærtner), *B. tuberculosis*, *B. diphtheriæ*, and *Vibrio cholerœ*. These represent most of the infections which flies have been accused of carrying.

Naturally, most interest attaches to the typhoid germ, and we receive the definite information that under the experimental conditions flies ingested typhoid bacilli into their intestine, and that these could usually be recovered two days afterwards, and in one case as long as six days afterwards. The bacilli were found in the flies' fæces during the space of two days. In the case of Gærtner's bacillus corresponding results were obtained, but the bacilli were not recovered from the fæces. The tubercle bacillus, from sputum, was found to live for three days in the intestine ; but if a pure culture were used, it could be recovered nearly a fortnight afterwards in the intestine. The diphtheria bacillus, as a rule, was much shorter lived, but in at least one case it was found nearly a week afterwards ; the cholera vibrio was isolated two days afterwards.

These results show conclusively that all these pathogenic organisms can be carried about in a living condition by flies for the space of a few days, provided they obtain an entrance into the intestine. It must, however, be remembered that these experiments have been made under exceptionally favourable conditions, the flies being fed on syrup containing pure cultures of the bacilli. Much less striking results are to be expected under natural conditions. The complication of climatic conditions, temperature, vitality and environment of the organism, and so forth, have all to be reckoned with.[1]

In this connection a paper by Bacot [2] is worthy of notice. He finds that :—

(1) Pupæ and imagines of *Musca domestica* bred from larvæ infected with *B. pyocyaneus* under conditions which exclude the chance of re-infection in the pupal or imaginal period undoubtedly remain infected with the bacillus. (2) In the imago the infection is maximal at emergence and then diminishes suddenly. (3) The possibility of a dangerously pathogenic micro-organism being taken up by the larva, and subsequently distributed by the fly, is one which deserves serious consideration.

Reference has already been made under "Enteric Fever," to the general review of the subject by Galli-Valerio.[3] It is full of information and has a good bibliography. An English paper of the same type is that by Hewitt.[4] Amongst the diseases mentioned as carried by the house-fly are those due to parasitic worms, enteric fever, anthrax, cholera, tuberculosis, ophthalmia, especially in Egypt, plague possibly, and certain septic infections. He does not mention dysentery as does Galli-Valerio, but cites the view of Kerr of Morocco, who believed he had seen the syphilitic virus conveyed, and the disease spread, by flies which had fed on luetic sores.

Another paper, already mentioned in connection with diarrhœa, is that by Nash.[5] It is not easy to find definite and specific instances in which flies in the neighbourhood of the sick have been proved to be infected, hence a paper by Bertarelli [6] is of special interest, in which he gives an account of an enteric fever epidemic in a family where the etiology of the disease was obscure. There was a great number of flies both in the sick-room and in the neighbouring

[1] Still another report with much interesting matter is dealt with in the *British Medical Journal* for August 19, 1911.

[2] Bacot, A. W. (March, 1911), "The persistence of *Bacillus pyocyaneus* in Pupæ and Imagines of *Musca domestica* raised from larvæ experimentally infected with the Bacillus." *Parasitology*, Vol. IV., No. 1.

[3] Galli-Valerio, B. (1910), "L'état actuel de nos connaissances sur le rôle des mouches dans la dissémination des maladies parasitaires et sur les moyens de lutte à employer contre elles." *Cent. f. Bakt.*, I. Orig., Vol. LIV., No. 3.

[4] Hewitt, C. G. (1909), "The Bionomics, Allies, Parasites, and the relation of *M. domestica* to Human Disease." *Quarterly Journal of Microscopical Science*, Vol. LIV., Part 3.

[5] Nash, J. T. C. (September, 1909), "House-Flies as Carriers of Disease." *Journal of Hygiene.*

[6] Bertarelli, E. (April 15, 1911), "Diffusione del tifo colle mosche, e mosche portatrici di bacilli specifici nelle case dei tifosi." Quoted in *Bull. de l'Inst. Past.*

Flies—*continued*

yard; 120 flies were caught in the former, and 35 in the latter. The examination was confined to the feet and head of the flies. The *B. typhosus* was found 8 times (6 times on the feet) on the 120 flies, and twice (on the feet) on the 35 flies. The insects were therefore in a condition to infect food and drink, and this doubtless explained the spread of the disease from the first case. But house-flies are not the only species operative. Dutton [1] of Pittsburg, U.S.A., incriminated a little fruit-fly (*Drosophila ampelophila*) which haunted a garbage can containing excreta, and from which he obtained cultures of *B. typhosus*. He also obtained cultures from 20 out of 500 human fleas which had been allowed to suck the blood of typhoid patients, and he is convinced that two cases were inoculated by house-fleas. The rôle of tsetse flies, stomoxys and tabanidæ, in the transmission of trypanosomiasis is dealt with elsewhere, as is that of Phlebotomus flies in Sand-Fly Fever. So is the suggested rôle of Simulidæ in pellagra. Here, however, we may note an account by Wigand [2] of poisoning in animals as the result of gnat (*Simulidæ*) bites. The condition was like blood-poisoning, the local swellings being accompanied by disturbance of circulation and a lowering of body temperature. Oxen overcome by great clouds of gnats might actually die in half-an-hour; usually, however, within 24 to 36 hours. Death appears to result from heart failure. Happily the insects attack the lower portions of the animal's body, and by smearing these with thick oil the flies are kept off. Treatment consists in the exhibition of cardiac stimulants. This curious plague occurs chiefly in Central Europe.

Some points regarding the bionomics of house-flies may now claim attention. They are mostly culled from papers already quoted. Thus both Hewitt's and Galli-Valerio's papers are full of information. We note only that house-flies do not normally fly great distances. They can, however, certainly fly something like 200 yards, and can also be wind-borne a long way. Hewitt seems to have found them $1\frac{1}{2}$ to 2 miles from any breeding-place. They can also fly at an altitude of 80 feet above the ground. Unfortunately lack of space forbids further references to these papers. Some interesting facts were determined by Jepson [3] as regards what becomes of flies in the winter in England. He found that :—

(1) Flies do not disappear altogether during the winter as popularly thought, but may be found in places where the temperature conditions, etc., are favourable.

Whether under such circumstances they ordinarily continue to breed as in the warmer months cannot be said, but that they *will* breed in the winter, provided that the necessary conditions are present, is evident from the foregoing experiments.

(2) The fact that the flies have been seen in coitû in great numbers, seems to favour the view that they may breed in these warm places in the winter, assuming that their breeding-places remained undisturbed during the larval stage.

(3) On the other hand, the fact that flies taken at this time of the year appear more hardy and long lived than those taken and kept under the same conditions in the summer, seems to support the view that the former may persist throughout the winter as adults.

(4) If, as seems probable, flies are only to be found in winter in isolated colonies in certain warm places, the possibility of an appreciable reduction in their numbers, or even perhaps of their extermination, may become somewhat more hopeful. In such places they could easily be destroyed, as even the slightest exposure during the cold months is fatal to them. This is seen to advantage in the above case, where the fall in temperature, occasioned by the putting out of the fires for the Easter vacation, caused the complete disappearance of the flies for a period of five weeks.

Stomoxys are so closely allied to house-flies that they may next receive attention. A list of those found in Abyssinia is given by Surcouf and Picard.[4] The reference is useful for workers in the Sudan. A most important paper is that by Roubaud,[5] who deals with the *Stomoxyidæ* of Dahomey. There the family is represented by the two genera *Stomoxys* and *Lyperosia*. The latter in the form of *L. irritans* forms the subject of an illustrated paper by Weiss.[6]

Roubaud deals in detail only with the former, and describes eight species, *i.e. Stomoxys calcitrans*, *korogivensis*, *brunnipes*, *bouvieri*, *glauca*, *boueti*, *pallida*, *inornata*, and supplies a synoptic table for them. As regards their nutrition, he notes that they all bite and suck

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[1] Dutton, W. F. (October 16, 1909), *Journal American Medical Association.*

[2] Wigand (November 26, 1908), *Berl. Tierärztl. Woch.* Quoted in *Journal Comparative Pathology and Therapeutics*, March, 1909.

[3] Jepson, F. P. (September 30, 1909), "The Breeding of the Common House-Fly (*Musca domestica*) during the Winter Months." *Journal of Economic Biology.*

[4] Surcouf, J., and Picard, F. (April, 1908), "Note sur les Diptères du genre Stomoxys en Abyssinie." *Bull. Soc. Path. Exot.*

[5] Roubaud, E. (February 8, 1911), "Études sur les Stomoxydes du Dahomey." *Ibid.*

[6] Weiss, A. (1910), "Quelques Points de la Biologie de *Lyperosia irritans*." *Arch. Instit. Past. de Tunis*, Vol. IV.

blood, but the only domestic species is the first named. It bites dogs and cats, goats and sheep, and also attacks cocks and ducks, feeding on their crests or other head appendages. Flies—*continued*

The blood food is indispensable for both sexes at all ages. The insects prefer moist localities, and temperature conditions appear to have much the same influence on them as on *Glossinæ*. He gives an account of their breeding habits. Eggs are deposited in the fresh excrement of herbivora, and also in ground soiled by the urine and dung of animals, and by their trampling about on it. Larvæ require nearly 3 months to develop fully, at an average temperature of 23° to 25° C. Hatching takes place in 7 to 8 days. He mentions some interesting facts about natural destruction through the agency of an *Entomophthorea* fungus, like the *Empusa* of the house-fly. Infection takes place by the mouth. The mycelium is able fully to develop in 24 hours. The fly does not usually survive more than five days after infection. The parasite specially attacks *St. calcitrans*, but is not peculiar to *Stomoxys*, as it can affect other *Muscidæ*, *i.e.* the house-fly. Tsetses, however, are entirely refractory, because they cannot suck up anything outside the circulating blood. Another enemy is to be found in the genus *Oxybelus* of the fossorial wasps.

Notes on *Simulidæ* in Italy are given by Sambon[1] in his paper on pellagra. They appear never to enter houses. Sanderson[2] also deals with these insects in the United States. Their life history in the White Mountains is not well known, but he gives an interesting account of the destruction of the larvæ in mountain streams by means of Phinotas oil, which is efficient because it sinks in water. Flies of the genus *Phlebotomus*, so-called "sand-flies," in reality moth-flies of the family *Psychodidæ*, have recently acquired prominence as the transmitters of the virus of Phlebotomus, Papataci, or Sand-Fly Fever. Howlett[3] has a paper on them in which he says :—

> If one makes an inspection of an average Indian bathroom, one usually notices on the window or walls some small hairy moth-like flies, with leaf-shaped hairy wings held so as to nearly cover the abdomen like a roof. These are Psychodids of the harmless genera *Psychoda* and *Pericoma*.
>
> In addition to these, one may also find sitting on the walls, more especially in rather shaded corners, other small flies resembling them in their general hairiness and inconspicuous greyish colour, but having much longer legs and a totally different resting-attitude. While the short-legged harmless Psychodids sit in what is roughly the same position that moths usually assume, these other Psychodid flies, which represent the blood-sucking genus *Phlebotomus*, stand with the body well raised on the long legs, the head down, the tail slightly depressed, and the wings well separated, their tips pointing outwards and upwards. If one of the flies be examined with a lens, two points especially catch the eye ; first, the insect's look of devilish determination, and second the often remarkably long palpi, which in some species are carried bent twice at right angles or more, so as to bring the terminal joint to about the level of the base of the proboscis.
>
> Except for slight differences in size and wing-venation the species are much alike, but they can be readily distinguished by microscopic examination of the structure of the male genital clasping-organs, which are particularly well-developed. It is extremely difficult to identify pinned specimens with certainty.

The larvæ, he notes, are very small, but they have been obtained from a small open drain channel, and in the partially dried mud in a channel leading from a well reservoir. He describes the eggs, which can be hatched quite easily in ordinary glass tubes loosely plugged with cotton wool, and while they require the surface of the glass to be slightly damp, care must be taken to avoid excess of moisture, and to exclude mould ; they are unable to survive even a very brief exposure to the dry air of the hot weather. The time for hatching varies according to the temperature, from 4 to 6 days in the hot weather to 14 days at the end of November at Pusa.

The most characteristic feature of the larvæ is the presence of two long bristles or spines situated on raised tubercles at the caudal extremity. They live in damp, but not very wet earth, and their food consists of green algal growths. The length of the larval life varies with the temperature and time of year. It has been noted as being from 14 to 48 days, that of the pupa 8 to 28 days. As regards their biting habits he remarks :—

> The flies not infrequently even crawl under the bedclothes in their lust for blood, and the bite is to most people extremely irritating. The irritation continues during the whole time that the fly is sucking, this time being about two and a half to three minutes when the operation is allowed to be completed without interruption. The effects vary in different individuals. On myself the bite results in a small reddish, pimply swelling, which persists for several days, the itching at first felt subsiding after a day or so. Children are especially attacked, and often seem to feel the irritation very much. Cattle, dogs, frogs, and caterpillars have also been observed to be sucked. The flies generally bite most freely in the early part of the night and just before dawn, but have

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[1] Sambon, L. W. (October 15, 1910), "Progress Report on the Investigation of Pellagra." *Journal Tropical Medicine and Hygiene.*

[2] Sanderson, E. D. (February, 1910), "Controlling the Black Fly in the White Mountains." *Journal of Economic Entomology.*

[3] Howlett, F. M. (1909), "Indian Sand-Flies." *Transactions Bombay Medical Congress.*

Flies— *continued*

apparently no very definite period, and I have been bitten in full light at 6.30 a.m. in September. There is no doubt that variations in humidity and temperature very greatly influence their biting propensities, and a sudden increase of humidity combined with a rise of temperature can generally be relied on to stimulate them to a special effort.

At night the insects are attracted by lights, but they do not care for very brilliant illumination. They congregate in bathrooms and latrines, and in the latter suck moisture from the filthy soil. The females only apparently suck blood. Annandale [1] gives a list of the known species as follows :—

Europe	*Phlebotomus papatasii*, Scopoli (S. Europe).
	,,	*minutus*, Rondani (S. Europe).
	,,	*mascittii*, Grassi (Italy).
	,,	*tipuliformis*, Meunier (fossil in Baltic amber).
America	,,	*vexator*, Coquillet (Maryland).
	,,	*cruciatus*, Coquillet (Guatemala).
Africa	,,	*duboscqui*, Neveu-Lemaire (Sudan).
Asia	,,	*papatasii*, Scopoli (Northern India ; ? Java).
	,,	*himalayensis*, sp. nov. (lower Himalayas).
	,,	*malabaricus*, sp. nov. (Travancore, S. India).
	,,	*perturbans*, Meijere (Java ; base of Eastern Himalayas).
	,,	*babu*, sq. nov. (plains of India).
	,,	*major*, sq. nov. (outer Himalayas ; Paresnath, W. Bengal).
	,,	*argentipes*, Annandale and Brunetti (plains of India).

In this connection see paper by King in the Fourth Report of these Laboratories, Vol. B. In Malta, to judge from an article by Marett,[2] the species would appear to have different breeding-places from those in India. He deals with *P. papatasii*, the best-known species, and quotes from Grassi's recent monograph, which states that " they breed in drains, and in dark cellars where the larvæ and pupæ can be found all accumulated together with refuse, stones, bricks, and more especially pieces of cretonne." Fungi and decaying vegetable matters, also house tanks, have likewise been given as breeding spots. The author examined various kinds of places, a garden pond, a garden wall, tree roots, tree bark, earth, etc., without finding larvæ. In wells, latrine tanks, ventilation shafts and manholes, he found *P. phalænoides*, a species not mentioned by Annandale, breeding out. Sand-flies breed out in a natural rock cleft in a cave, but the special place where larvæ were found was in stone walls, dry above ground level, but damp at the ground level and below it.

A useful kind of paper for reference is that by Gaiger,[3] who amongst other parasites of Indian domesticated animals gives a long list of biting diptera.

One can only refer very briefly to some other papers on *Tabanidæ* and allied flies. Drake-Brockman [4] mentions some of the blood-sucking diptera of eastern and south-western Abyssinia. Old [5] lists the blood-sucking flies found in Central Africa. Balfour [6] cites a new locality (Kordofan) for the fly *Auchmeromyia luteola*, the larva of which is the well-known Congo floor maggot, and mentions [7] one of the *Asilidæ* or robber flies as attacking man, also in Kordofan. The bite was a trifling one, did not cause pain, and only produced a little local irritation with slight œdema. A list of the pernicious flies of British Guiana as given by Wise is to be found in the *Journal of Tropical Medicine and Hygiene* for September 15, 1909, while a somewhat similar list, with some descriptive notes confined to *Tabanidæ* and *Stomoxyidæ*, is given by Pratt [8] as regards the Federated Malay States.*

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[1] Annandale, N. (March, 1910), *Records of the Indian Museum*, Vol. IV., No. 2. Calcutta. See also Nos. 2 and 3 of March 30, 1911, on *Indian Papataci.*

[2] Marett, P. J. (September, 1910), " Preliminary Report on the Investigation into the Breeding-Places of the Sand-Fly in Malta." *Journal Royal Army Medical Corps.*

[3] Gaiger, S. H. (1910), " A Preliminary Check List of the Parasites of Indian Domesticated Animals." *Journal Tropical Veterinary Science*, Vol. V., No. 1.

[4] Drake-Brockman, R. E. (April, 1910), " Notes on the Blood-sucking Diptera met with in Eastern and South-Eastern Abyssinia." *Bulletin of Entomological Research.*

[5] Old, J. E. S. (January 15, 1909), " Contribution to the Study of Trypanosomiasis and to the Geographical Distribution of some of the Blood-Sucking Insects, etc." *Journal Tropical Medicine and Hygiene.*

[6] Balfour, A. (February 15, 1909), " A New Locality for the Congo Floor Maggot." *Ibid.*

[7] *Idem* (March 15, 1909), " A New Biting Fly." *Ibid.*

[8] Pratt, H. C. (1909), " Distribution of Certain Species of Biting Flies in the Federated Malay States." *Journal Tropical Veterinary Science*, Vol. IV.

* Articles on the *Tabanidæ* of the so-called Oriental Region and on the Oriental blood-sucking *Muscidæ* will be found in the *Records of the Indian Museum* for March, 1911, and July, 1910, respectively.

A well-illustrated paper on a little known subject is that by King [1] on the breeding-places, breeding habits, and life-cycles of two Sudanese *Tabanidæ*. Flies—*continued*

Efforts are now being made to introduce fossorial wasps into certain localities for the purpose of reducing *Tabanidæ*. A note on the subject will be found in the *Bulletin of Entomological Research* for July, 1910, p. 156.

The horse-bot fly, *Gastrophilus equi*, is of such importance that the following short summary by Collinge of his observations on its eggs may be of use :—

(1) The egg of *Gastrophilus equi* (Fabr.) is provided with a pair of lip-like valves, by means of which it is firmly attached to the hair.

(2) After the larva has escaped the egg-shell adheres for some considerable time to the hair.

(3) The eggs are not taken into the mouth as stated by Froggatt.

(4) My experiments confirm and supplement those of Osborn, although the actual dates differ somewhat ; thus the largest number of eggs hatched from the sixteenth to the twentieth day, and none hatched after the thirty-sixth day.

(5) Without moisture or friction very few eggs hatch.

Here and there measures of prophylaxis and destruction as regards flies have already been mentioned, but a few additional papers may be cited. A note in the *Lancet* for November 14, 1908, recommends sulphur fumigation for kitchens infested with flies, and a later note on November 22, 1908, mentions Delamarre's method of placing dishes with 10 per cent. formalin about rooms where the flies are numerous. An improvement on this is the use of formol milk advocated by Trillat and Legendre.[2] A solution of 15 per cent. commercial formol, 20 per cent. milk, and 65 per cent. water is placed in plates or saucers about the room, but not on the floor.

Marchoux [3] testifies to the value of fowls as destroyers of the larvæ. The flesh of fowls frequenting manure heaps, etc., where flies breed, acquires an unpleasant taste, hence it is well to reserve a certain number for this work exclusively and not sacrifice them for the table. Clement recommends the use of a spray of Izal. It stupefies them so that they fall to the ground, where they can be swept or gathered up and consigned to the fire. The fly-flap is recommended by a correspondent in the *British Medical Journal* for September 3, 1910. It is best fashioned out of a newspaper folded and refolded until it is about 12 inches to 13 inches long, and $2\frac{1}{2}$ inches wide, well flattened out and tied with strong thread or string about $1\frac{1}{2}$ inches from each end. With practice this instrument can be got to kill flies without crushing them. It should be used at a distance of about 2 feet from the fly. A surprisingly large number of the insects can be destroyed by the skilful and persistent use of this fly-flap.

A good account of *Empusa muscæ*, the fly fungus, is given by Hewitt (*loc. cit.*). Infection is by means of spores falling on the insect and undergoing germination, the hypha piercing the chitin and penetrating the fat body. The blood sinuses then become infected and the fly is doomed. He also describes other parasites of the house-fly. Galli-Valerio (*loc. cit.*) deals fully with measures of prevention and destruction, citing Howard's work mentioned in the first Review. Petroleum and saprol are useful for killing larvæ in midden heaps, etc., and also, if properly used, for preventing ovipositing. Protection of food is strongly urged, and a list of colours is given showing which attract most flies. Clear green was the most favoured, citron yellow one of the least, as were blue, pale violet and dark brown. In Khartoum, I have noted that white cotton clothing attracts flies in the early afternoon. In the Tropics proper scavenging, the use of incinerators, sewage tanks for sewage trenches and instruction of the public on flies, their habits and their dangers, are the best means of controlling these pests.

Additional Notes

Recently Newstead [4] has issued a most important paper on the Papataci flies of the Maltese Islands. The species met with were *P. nigerrimus*, *minutus*, *perniciosus*, and *papatasii*. Two of these are new to science. A very full account, beautifully illustrated, is

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[1] King, H. H. (July, 1910), "Some Observations on the Bionomics of *Tabanus par*, Walk., and *Tabanus tæniola*, P. de B." *Bulletin of Entomological Research.*

[2] Trillat and Legendre, J. (December, 1908), "Sur la destruction des Mouches par le Formol." *Bull. Soc. Path. Exot.*

[3] Marchoux, M. (December, 1908), In discussion of above paper. *Ibid.*

[4] Newstead, R. (May, 1911), "The Papataci Flies (*Phlebotomus*) of the Maltese Islands." *Bulletin of Entomological Research.*

Flies—*continued*

given of the morphology of the genus *Phlebotomus*, and the four Maltese species are carefully described and figured. This, however, is not all. There are interesting notes on breeding-places which were most difficult to find, and mention is made of three main factors determining the choice of such a place—(*a*) the presence of organic matter ; (*b*) moisture, but not in excess ; and (*c*) the absence of light. The only places where Newstead found larvæ were in the crevices of loose rock, and in caves or catacombs. The habits and occurrence of the adult flies forms an interesting section, but it is too lengthy for extraction. As regards prophylactic measures Newstead gives the following formula (Crawford) as a good repellent :—

℞. Ol. anisi
Ol. eucalypti
Ol. terebinth āā grs. 3
Ung. acid. borac. *q. s.*

In Khartoum one has found eucalyptus oil alone rubbed on the ankles, wrists, etc., and sprinkled on the bedding, to be very effective. Spraying the dark portions and angles of bedrooms with 1 per cent. solution of formalin is effective if a fine spray is used. An excessive amount must not be applied. The free admission of light, moving air, and the use of biscuit-box traps are recommended as preventive measures.

The trap should be made in the form of a corner-cupboard in miniature, and should measure about 18 inches in length ; the basal portion should be left open, and the interior should be lined with dark cloth or similar material. These should be examined daily and the flies killed with ammonia fumes.

Pandit [1] gives the following directions for getting rid of house and other flies :—

(1) Heat a shovel or any similar article, and drop thereon 20 drops of carbolic acid. The vapour kills the flies.

(2) Dissolve one drachm of bichromate of potash in two ounces of water, and add a little sugar. Put some of this solution in shallow dishes and distribute them where needed. This is a cheap and perfectly reliable fly poison, which is not dangerous to human life.

(3) To quickly clear the room where there are many flies, burn pyrethrum powder in the room. This stupefies the flies, when they may be swept up and burnt.

The above were taken from an American work on the subject. Pittaluga [2] describes a new blood-sucking dipteron from West Africa which has been named *Œcacta hostilissima*. The paper is illustrated by a very poor photograph of the insect.

Food. As in the last Review we confine ourselves to papers dealing with food in the Tropics, tinned foods, or food suitable to travel. In the Tropics, perhaps even more than elsewhere, foods are apt to become mouldy, hence a paper headed, "Moulds in Foods: are they Wholesome ?" in the *Lancet* for February 20, 1909, is worthy of note.

"So far," it says, "there has not been much evidence to show that the ordinary moulds which find a favourable place for development in foods are *per se* injurious to health, but the subject is worthy of deeper investigation than it has hitherto received. The presence of mould implies staleness or age. It is well known, however, that the digestibility and palatability of not a few foods increase as they 'ripen.' We have already mentioned the instances of cheese and ham, and there are the further instances of 'hung' mutton and venison and game. By ripening we do not mean a state bordering on actual putrefaction, when such foods are described as 'high,' but a seasoned condition when the food becomes more tender, digestible, and appetising. At this period mould may be found, especially if the seasoning process has been allowed to develop in a damp place. It seems as though foods which are palatable only if eaten comparatively fresh, may act poisonously on the system when mouldy, and conversely it would appear that those foods which are eaten dried or cured, or which can be kept in a more or less dried state, are undamaged by mould. Cheese, after all, is more or less the dried nitrogenous portion of milk ; 'hung' mutton is mutton that is exposed for some time to a current of air, so that, at any rate, its surface is dry ; of hams the same thing may be said. In the opposite category would be placed the mouldy fruit or jam which are, of course, moist, or the biscuit which has been lying in a moist place, for neither a biscuit nor flour would go mouldy if kept dry. The reason partly why some like mould in Stilton cheese, while all resent the same mould in a strawberry, depends probably upon the question of moisture. The guiding principle appears to be—as far, at any rate, as the palate goes—that anything which is mouldy must not be wet. This conclusion still leaves open the point as to whether mould occurring on food, whether wet or dry, may not be dangerous, having regard to the relations which have appeared to exist between low organisms and disease. On the whole, there is reason for believing that the health would be better safeguarded if moulds were kept out of the diet."

In this connection, and especially as frozen meat is now largely imported into some tropical countries, allusion may be made to Klein's [3] report on the black spots found on chilled beef. These are due to a mycelium belonging to a fungus which he calls *Oidium carnis*. Happily

[1] Pandit, H. B. (May, 1911), "The Plague of Flies." *Indian Medical Gazette.*

[2] Pittaluga, G. (June 10, 1911), "*Œcacta hostilissima*, n. sp., ein neuer, blutsaugender Zweiflügler der Westküste Afrikas (Spanisch-Guinea)." *Cent. f. Bakt.*, I. Orig., Vol. LIX., No. 1.

[3] Klein, E. (1909), "The Nature of Black Spots on Chilled Beef," quoted in *Lancet*, September 4, 1909.

it is harmless, as it belongs to the moulds which cannot grow at the temperature of the animal body. Moreover, it does not injure the meat, though naturally it is unsightly. Food—*continued*

Caspari [1] deals with the diet of Europeans in the Tropics. The great object of the dietary should be to throw as little work on the body as possible; in short, to check heat production. A lessening of the dietary, somewhat in the nature of a chemical heat regulation, is in the Tropics not incompatible with a mode of life wherein the body work nearly equals that in temperate climates. A purely vegetable diet is not advisable. A mixed diet well cooked, varied and appetising, is recommended, but this is just what it is very often difficult or impossible to obtain. As regards alcohol, the author merely states that while in large quantities it is harmful, there is no reason why persons accustomed to take it in moderation should not do so in the Tropics. Prison medical officers and others interested in dietetic questions will find much of value in McCay's [2] report on Bengal Dietaries. The most interesting part to the general reader is that discussing Chittenden's views, and it was found that—

when it came to judging of the effects of such a dietary on physical development, capacity for labour, and resisting power to disease and infection, Chittenden's standards were not sufficient. The Bengali diet is contrasted with that of the Behari; the latter (in the jails and in the population generally) is about 2 grammes per head higher in nitrogenous metabolism than the former. "In accordance with this we find in the Behari a much better physical development, greater capabilities for muscular exertion, a distinctly greater degree of vivacity, briskness, and sprightliness of manner." His weight is 120 pounds, compared with the 110 pounds average of the Bengali. This results from the 10 per cent. higher nitrogenous metabolism. It is also pointed out that the low nitrogenous metabolism of the Bengali does not secure him from renal disease, the particular condition that Chittenden considers to be most likely to be avoided by protein economy, for renal disease is much more common among the working population of Bengal than in Europeans. A comparison is also made between the hill tribes to the same effect, and the conclusion is come to that "in those races where an assimilable protein, and particularly an animal protein, forms part of the ordinary diet, muscular development and good fighting qualities seem to be intimately related with the level of nitrogenous metabolism attained."

The question of danger arising from tin in canned foods is one which often presents itself. The experiments of Buchanan and Schryver [3] indicate that it does not exist. The possibility of chronic tin poisoning arising in this way is extremely remote, and may indeed be excluded. Wiley [4] criticises their report more from the ethical than any other standpoint, but seems to indicate that harm might result if the consumers of food containing tin were not in good health. The report itself showed that beef essence may be rendered turbid from the presence of dissolved tin, but in authenticated cases of tin poisoning the amount of tin present in the food ranged from 1·8 to 13 grains or more per lb.

Schryver [5] returns to the subject at a later date, and three of his more important conclusions may be stated :—

(1) As a result of the experiment by Lehmann on animals, and an experiment described above on a human being, it is concluded that there is but little likelihood of chronic tin poisoning resulting from ingestion of canned foods.

(2) Nevertheless, cases have been recorded in the literature describing symptoms of irritant poisoning following the ingestion of contaminated foods, and in certain of these cases the amount of metallic contamination has been ascertained.

(3) It is difficult to state the exact quantity of tin salts which will give rise to symptoms of irritant poisoning, and these toxic effects will vary greatly with circumstances. Quantities of tin approximating to two grains to the pound are, however, unusual and unnecessary, and any foodstuffs containing such quantities should be regarded with suspicion.

There is often blackening in the interior of tins containing preserved foods, and this has been the subject of research by Beveridge.[6] He says :—

The blackening is caused by some chemical change brought about by the action of certain substances in the food on the metal of the tin with which it is in contact during sterilisation. If we take a clean, bright, empty tin, tightly solder it up, and sterilise at 150° C., or even higher, for some hours, no discoloration results.

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[1] Caspari, W. (1910), "Die Ernährung der Europäer in den Tropen," quoted in *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIV., No. 21.

[2] McCay, D. (1910), "Investigations on Bengal Dietaries, with some Observations on the Influence of Dietary on the Physical Development and Well-being of the People of Bengal." *Scientific Memoirs of the Government of India*, No. 37.

[3] Buchanan, G. S., and Schryver, S. B. (1909), *Local Government Board (Medical Department) Report of Inspectors of Foods.*

[4] Wiley, H. W. (April 3, 1909), "Tin in Canned Foods." *Lancet.*

[5] Schryver, S. B. (November, 1909), "Some Investigations on the Toxicology of Tin, with Special Reference to the Metallic Contamination of Canned Foods." *Journal of Hygiene.*

[6] Beveridge, W. W. O. (1909), "Report on the Nature and Causes of the Blackening of the Interior of Tins." *Third Report of Committee on Physiological Effects of Food, Training and Clothing of the Soldier.*

Food— *continued*

Except in the case of putrid foods, such as meat, the blackening of the interior takes place during sterilisation only, and there is no evidence to show that any increase takes place, however long the tin of food is kept, so long as the contents remain sterile.

It is probable, therefore, that any danger from the absorption of metals, such as tin, increasing in amount on prolonged keeping, can be discounted.

In the case, however, of meats which have become putrid in their tins from the result of bacterial action, owing to their having acquired a higher acidity, and to the formation of certain gases, the metals derived from the tin may increase in amount. This is largely due to an actual erosion of the tin-plating itself.

The chief cause of the presence of metals, such as tin and zinc, in sound tins of preserved meat is attributable, in all probability, to the presence of the fluids used in soldering, or to solder accidentally gaining entrance during the final soldering of the tins.

The mere discoloration of the interior of the tins has no injurious effects whatever in itself, either to the consumer or to the food.

We have found that of the three metals, iron, zinc and tin, iron is more rapidly acted upon than zinc and zinc than tin, so that the purity and thickness of the tin-plating influences somewhat the extent of the blackening of the interior. When the tin-plating is thick, and consists of a good proportion of tin evenly distributed, very little blackening occurs during sterilisation properly conducted.

It is in thin, inferior plating that much blackening is more apt to occur.

and his conclusions are as follows :—

(1) Except in cases where the contents of the tin are blackened by contact, or where there is actual erosion of the metal, the discoloration of the tin is probably not in any way deleterious to the consumer, nor has it any injurious effect upon the food itself.

(2) Except in the case of bacterial fermentation, a high temperature above 110° C. appears to be essential.

(3) In putrid samples of tinned meats, blackening and erosion of the metal can easily be accounted for by bacterial fermentation, caused by anærobic spore-bearing bacilli, which form large quantities of H_2S, mercaptan bodies and acids ; these, reacting on the tin, form sulphides of the metals.

(4) Perfectly fresh meats having an acid reaction may be sterilised at even a high temperature (120° C. to 130° C.), without causing blackening of the tin.

(5) Where alkalinity of the food exists, from being tainted or from having become so during the pickling process, and where the heat of sterilisation is carried too far, much blackening of the interior is liable to result.

(6) Acidity of the contents, except where it exists in a high degree, does not cause the same amount of discoloration as in the case of foods having an alkaline reaction.

(7) Excess of fat, combined with a high degree of heat in the presence of superheated steam, is responsible for a certain amount of discoloration.

(8) Much blackening of the interior of tins of meat might be regarded as indicating, in some instances, that the food was not in a perfectly fresh condition before sterilisation, and that the manufacturers in consequence employed higher temperatures during sterilisation than ordinarily used, with a view to ensuring efficient sterility.

Pfuhl [1] some time ago drew attention to an important matter in connection with tinned foods. He found that bacteria recovered by him from the contents of tins of preserved food, and which, moreover, appertained to species incapable of surviving a temperature of 100° C. for more than a minute, must have gained entry to the tins after sterilisation. In spite of this there was no obvious defect in the soldering of the tins. He believes, then, that at the moment when the tins are sealed after sterilisation the internal pressure is sufficient to cause a minute leak through which the germs gain admission. This happens more often in large 4-lb. tins than in the smaller sorts.

More recent work by Beveridge and Fawcus in the valuable report (*loc. cit.*) from which we have already quoted may possibly furnish a different explanation, and certainly clears up a curious point that has long been a puzzle, namely, that tins of meat which have passed the tests applied by the makers, and have kept good for months or even years, sometimes suddenly become blown and unfit for use. This occurrence could hardly be due to injury of the tin through rust, as, if so, the gas produced by putrefaction, consequent on entrance of air organisms, would find its way out and no blowing would result. Major Beveridge, and with him Captain Fawcus, have found that an organism may be present in the meat at packing, may not be destroyed by the so-called sterilisation, may remain inert for long periods if the tins are stored at a low temperature, and finally, may develop if the temperature reaches 37° C., or thereabouts. This bacillus is non-pathogenic to animals, but decomposes the meat and renders it unfit for consumption. As it does not develop much below the body temperature, meat might be contaminated by it, and yet be kept for months without showing signs of decomposition or blowing if stored in a cool place, neither would the temperature of the "warm room," in which manufacturers deposit tinned foods for a short time as a testing chamber, be sufficient to cause growth of this bacillus. But if taken to a hot climate the whole consignment might speedily become unfit for use. The recommendation is accordingly made

[1] Pfuhl (1908), "Über die Verunreinigung des Inhalts von Konservenbüchsen nach der Sterilisation." *Zeit. f. Hyg. u. Infekt.*, Vol. LXI., No. 2.

that the temperature of the fluid in which canned-meat tins are sterilised should be raised to 120° C. (248° F.), and that this should be kept up for one hour. Food—*continued*

In this connection one would also direct attention to an article headed "Bacteria in Meat," in the *British Medical Journal* for January 28, 1911. It is of such importance that we quote it in full.

The possibility of bacterial infection of apparently sound meat from animals in prime condition is a matter of considerable importance in the interests of public health. The subject was first investigated little more than two years ago by Gærtner, who found that normal flesh from healthy animals might present bacteria even within three days after death, but they were entirely confined to the surface, and by the end of ten days they had not penetrated more than half an inch into the interior. Similar results were obtained by Forster, who found that the interior of the meat was quite germ-free. It was therefore concluded that healthy meat was free from bacterial infection in its interior, and that bacteria would only be met with there when there was an infective focus in some other organ. This opinion soon required modification; Conradi, by using an enrichment method of culture, was able to demonstrate the presence of bacteria in the interior of meat from a considerable percentage of sound carcasses. This result, confirmed by Mayer and Rommler, is of importance in the bacteriological inspection of meat, and necessitates the proviso that the presence of bacteria in the interior of flesh is no certain indication of a diseased condition. Further confirmation of this fact is afforded in a recent communication by Dr. Alfred Horn, of Leipzig, who has investigated the matter in both healthy and diseased animals. Using the enrichment method as well as the ordinary method, he has been able to show that, although the percentage of positive results is decidedly higher by the first method, a certain number of cases may be detected by the second. Thus in carcasses examined within twenty-four hours after death, the percentages of positive results were respectively 14 and 5·5; from three to six days after death the figures were 31 and 15, while up to 21 days after death 54 per cent. and 25 per cent. respectively of cases gave positive results. In the case of animals in which some marked septic condition was found, the figures do not show any notable difference. Over sixty examinations of such carcasses were made, in every case within two days after death, and the percentage of positive results was 31 by the enrichment method and 21 by the other. It is thus evident that bacteria are as likely to be found in the flesh of healthy animals as of diseased. The bacteria met with were for the most part cocci, although Gram-negative rods of the *coli* type were found in a considerable proportion of the cases, while anærobic organisms also occurred not infrequently. It is, perhaps, unfortunate that Dr. Horn did not attempt to characterise these bacteria further, but, on the other hand, he makes the definite statement that no typical members of the food poisoning group were present on any occasion. After investigating the effects of the method and circumstances of killing and the means of packing and transport, he comes to the conclusion that these exert a considerable influence on the bacterial contamination of meat. This is especially the case where, on account of disease, the animal has to be killed on the farm under the worst possible conditions, and where the intestine and its contents are allowed to remain in the carcass for a much longer time than is the case in a public slaughterhouse. As a further point of importance, he insists on the bacteriological examination of the spleen in all cases where disease is known or suspected. The importance of this lies in the fact that the spleen is a natural breeding ground for micro-organisms, and that in the event of a generalised septicæmic condition it is more likely to show the presence of bacteria than the muscles. In investigating this matter he examined over 200 animals in which some septic condition was present. The bacteriological examination of the spleen and muscles gave an identical result, either positive or negative, in three-quarters of the cases. In 9 per cent. the spleen was sterile, while the muscles were infected. Here Dr. Horn considers that we have to deal with a post-mortem invasion from the exterior, for it is not to be imagined that in a generalised infection the spleen would be entirely unaffected. On the other hand, 17 per cent. showed the spleen positive and the muscles negative, and in such cases he thinks it advisable that a further and more exhaustive examination of the muscles should be made. This opinion and recommendation was previously advanced by Müller in 1909.

A very interesting paper full of useful hints is that by Dearden [1] on the examination of canned food at the port of entry. He says:—

The examination on the quay is, of course, an external one, the process being one of inspection, percussion, palpation, and auscultation. Inspection shows any imperfect seams, whether there has been any "faking" and resoldering, if there are any perforations or broken flanges allowing contamination by air, and last, but not least, the existence of "blowing." Percussion yields a resonant note when air or gas is present in the tin, though this does not necessarily indicate that it is blown, but very often denotes an imperfectly filled tin, technically termed "slack." In certain instances of compressed corned beef I have found what I can best term a cracked sound along the sides, which indicates that air has entered, though no perforations may be actually visible; subsequent opening has showed decomposition. A dull sound with irregular convexity at the ends of the tins denotes overpacking. By palpation one is able to gauge up the amount of resistance, the extent of blowing, and to differentiate between this condition and the resiliency of the tin in doubtful cases. Auscultation is limited to shaking the tin near the ear, and it is by this means that one can tell whether the contents, if consisting of meat, are "sloppy" or "dry" and contracted. If, after external examination, the existence of blowing is still doubtful, perforation of the tin under water will settle the question, as after the bubbling is finished the ends will collapse and lose their elasticity if this has been present. It is not usual to open tins on the quay, but to bring them to the office for this purpose. On opening, one is guided by appearance and smell. The contents may be mouldy, and, in the case of meats, soft and "sloshy," or discoloured from metallic contamination. The "whiff" of decomposition is, of course, easily detected.

Later he deals with the greening of vegetables by the addition of copper, a subject more fully discussed by him in another paper.[2] One cannot review the paper at length or mention the views of authorities cited, but the following is the attitude adopted by the author

[1] Dearden, W. F. (October, 1909), "Examination of Canned Foods at the Port of Entry." *Journal Royal Institute of Public Health.*

[2] *Idem* (September, 1910), "The Artificial Greening of Preserved Vegetables." *Public Health.*

Food— *continued*

himself. "I regard the use of this particular substance (copper sulphate) for the artificial greening of vegetables as somewhat on a par with the use of boron preservatives for various articles of diet. In both cases there is a lack of pronounced evidence of injurious effect on actual consumers, and I think it may be stated that interference with digestion is the most that can be placed at the door of either practice with any certainty. I have, however, come to the conclusion that vegetables dosed with sulphate of copper may be classed as unwholesome, and thus brought within the operation of the Public Health Acts."

He believes there should be no 2 grains to the pound limit as has been suggested, and he puts in a plea for more rigid legislation as regards this and similar food adulterations.

As bananas are a tropical product it should not be out of place to quote Pritchard [1] on the value of banana flour as a food for infants. The crude flour is best, its nutritive properties are high, and with the exception of a lower proteid content, banana meal compares favourably as a food with most cereal flours. It should be given to infants in the form of a decoction as a diluent of cow's milk. This is made by rubbing up a heaped tablespoonful (1 ounce) of banana flour with a pint of water, and then boiling for five minutes. One advantage it possesses is the ease and rapidity with which it can be prepared.

A great deal of information about rice is to be obtained in Hamill's [2] report, more especially as regards polishing processes. He finds, however, that if only small quantities of the polishing materials, such as talc and steatite, remain in the rice, there is no reason to fear injurious results. He recommends an outside limit of 0·5 per cent. of mineral matter. Lowe and Taylor [3] think this is too large an amount, being 35 grains per pound, and mention a case of pancreatic calculus containing much silica and alumina which they seem to infer might result from the ingestion of adulterated rice. We have already referred under "Beri-Beri" to the review of Hooper's work on the rice plant in the *Indian Medical Gazette* for July, 1910.

Additional Notes

Gosh [4] has made observations on diet in India. These chiefly deal with the native dietary, but some concluding notes are worthy of attention. He says :—

> The diet of Europeans in India has also to be regarded. It is not sound practice to live on pure European diet in India, and to try to imitate the native of the place would be equally a folly. In a suitable mixed dietary the proportion of animal food should be less than 1 in 4. If this is exeeeded, an undue strain is imposed on the alimentary organs and the liver. The following seale of diet may be suggested as suited for Europeans per diem doing ordinary work :—

	Amount	Proteid	Fat	Carbohydrate
Bread	8 oz.	0·64 oz.	0·12 oz.	4 oz.
Meat	6 „	1·6 „	0·9 „	—
Cheese	1 „	0·31 „	0·28 „	—
Eggs	Two	0·1 „	0·23 „	—
Butter (Ghee)	3 oz.	0·03 „	2·7 „	—
Potatoes (or other vegetables)	8 „	0·44 „	0·36 „	2·8 oz.
Milk	8 „	0·32 „	0·28 „	0·37 „
Rice	4 „	0·4 „	0·032 „	3·3 „
Fish	3 „	0·54 „	0·09 „	—

It seems advisable to give a reference to papers by Rideal [5] on certain substances used to colour foodstuffs. They bid fair to be a useful addition to our knowledge, but so far the series is not complete. Another paper worthy of note owing to its bearing on beri-beri and allied conditions is that by Edie and Simpson [6] on the preparation of various foodstuffs with reference to its effect on their content of organic phosphorus compounds and its relation to disease. The paper deals mainly with wheat and rice, and, though only of a preliminary nature, brings out some interesting points.

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[1] Pritchard, E. (October 15, 1910), "Banana Flour as a Food for Infants." *British Medical Journal.*

[2] Hamill, J. M. (1909), "On Facing and other Methods of Preparing Rice for Sale." *Reports to the Local Government Board Food Report*, No. 8.

[3] Lowe, W. F., and Taylor, J. G. (June 18, 1910), "Faced Rice as a Danger to Health." *Lancet.*

[4] Gosh, B. N. (May, 1911), "Some Observations on Diet in India." *Journal Royal Institute of Public Health.*

[5] Rideal, S. (June 10 and 17, 1911), "An Investigation of Certain Substances Used in Colouring Foods." *Lancet.*

[6] Edie, E. S., and Simpson, G. C. E. (June 17, 1911), "The Preparation of Various Foodstuffs (espeeially Wheat and Rice): Its Effect on their Content of Organie Phosphorus Compounds and its Relation to Disease." *British Medical Journal.*

Food Poisoning. Perhaps the most notable advance as regards this important subject is the definite proof of its association with bacilli of the paratyphoid group. A few illustrative papers will be considered. Bainbridge [1] points out that the paratyphoid bacilli (A. and B.), *Bacillus aertryck*, *B. suipestifer*, *B. danysz*, *B. enteritidis* Gærtner, and *B. typhi murium* form a closely allied group of organisms, and that with the exception of *B. paratyphoid* (A.) they are morphologically and culturally indistinguishable from one another. He attempted differentiation by bacteriological methods, and concludes that—

(1) The members of the paratyphoid and food-poisoning group of bacilli fall into four sub-groups, namely :—

(*a*) *B. paratyphoid* (A.), which stands alone in both its cultural characters and its agglutination reactions.

(*b*) *B. paratyphoid* (B.), which is indistinguishable from *B. aertryck* and *B. suipestifer* in its cultural characters and (usually) in its agglutination reactions, but can be differentiated from these two organisms by the absorption method.

(*c*) *B. aertryck* and *B. suipestifer*, which cannot be differentiated from one another, and which appear to be merely strains of the same micro-organism.

(*d*) *B. enteritidis* Gærtner, and *B. danysz*, which can be easily distinguished from the preceding sub-groups by their agglutination reactions, but which are indistinguishable from one another, and apparently also are only strains of the same organism.

(2) The uniform application of the absorption method is essential for the recognition of *B. paratyphoid* (B.), and offers the only means by which it can be identified with certainty.

(3) *B. typhi murium* has no existence as a definite organism, since different strains alleged to be *B. typhi murium*, and obtained from accredited sources, were found to differ greatly in their bacteriological characters.

Fowler [2] describes an outbreak at Gibraltar affecting six persons seriously and causing one death. The poisoning was due to *B. paratyphosus*, B., and the symptoms were colic, vomiting, diarrhœa, headache, pains in the limbs, fever and marked depression. Although it could not be definitely proved, the flesh of geese was in all probability to blame, and it may have become infected after death in the case of some of the birds which had probably been ill before slaughter, and had been undrawn.

The most complete work on the subject is the monograph by Huebener,[3] which is, of course, in German, but a useful little work is Bolduan's [4] translation of Dieudonné's *Bacterial Food Poisoning*. It is outside the scope of this review to discuss works of this kind, but both volumes may be recommended.

An interesting report signed by Smith [5] is that on an outbreak of food infection due to the consumption of infected pork pies. The specific organism was shown to be *B. paratyphosus* B.; the infection took place in the bakery, and the source of infection was almost certainly the head cook, from whose fæces a similar organism was isolated.

Trommsdorff and others [6] have recently described in greater detail the bacteriological investigations conducted in connection with this Wrexham outbreak. They state :—

The examination of the excreta of the head cook gave abundant evidence of the presence of bacilli, which proved to belong to the hog-cholera group, and which were apparently identical with those in the pies and in the heart of the fatal human case. *Thus the blood of the head cook—who was said not to have eaten any of the pies, and who had not been ill in the least degree—gave a strong positive reaction, and eight weeks after the epidemic she was found to be excreting members of the hog-cholera group in her fæces. She might, therefore, be considered as a chronic bacillus carrier, and the direct cause of the infection.*

The head cook had apparently never passed through any typhoid-like illness, nor had she so far as is known ever caused a like outbreak before.

As she left the bakery at once, it was not possible to obtain a second specimen of her stools. From the urine of this woman (who had long suffered from cystitis) we likewise obtained a large number of apparently typhoid-like bacteria in pure culture.

We also obtained these same organisms from the specimen of Pie 1. It seems probable that the woman had transmitted her entire specific flora to the pies, although she was supposed personally to have had nothing to do with their making. How this transmission actually occurred it is of course impossible to say.

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[1] Bainbridge, F. A. (April, 1908), "On the Paratyphoid and Food Poisoning Bacilli, and on the Nature and Efficiency of certain Rat Viruses." *Journal of Pathology and Bacteriology*, Vol. XIII.

[2] Fowler, C. E. P. (September, 1909), "Outbreak of Food Poisoning after a Christmas Dinner." *Journal Royal Army Medical Corps.*

[3] Huebener, E. (1910). *Fleischvergiftungen und Paratyphusinfektionen*, Jena. Quoted in *Cent. f. Bakt.*, I. Ref., Vol. XLVIII.

[4] Bolduan, C. F. (1909), *Bacterial Food Poisoning.* New York.

[5] Smith, W. R. (December, 1910), "Report on an Outbreak of Food Infection at Wrexham." *Journal Royal Institute of Public Health.*

[6] Trommsdorff, R., Rajchman, L., and Porter, A. E. (March, 1911), "A Severe Outbreak of Food Infection caused by a Paratyphoid Carrier." *Journal of Hygiene.*

Food Poisoning —*continued*

Bainbridge [1] deals with the epidemiological aspect of the question in an important paper read before the Royal Society of Medicine (Epidemiological Section). His remarks on *B. paratyphosus*, A., and the fever it produces, which he mentions as being not uncommon in India, are useful, but will be dealt with later. Those on *B. paratyphosus*, B., are more important. The examination of a number of strains from different sources, mostly German, showed that there were two groups; one identical with standard strains of *B. suipestifer*, the other with standard strains of *B. paratyphosus*, B. The latter were all derived from cases of paratyphoid fever, and from chronic paratyphoid carriers, whereas all the strains derived from food or food poisoning were identical with *B. suipestifer*. It would therefore seem that the distribution of *B. paratyphosus*, B., is confined to man, and that it is *B. suipestifer* which is of interest to us at present, though Bainbridge states that its rôle in food poisoning is by no means clear. Still, he thinks that it probably actually does cause food poisoning, and in any case is always potentially dangerous to man. His remarks prior to reaching this conclusion may be quoted. He says :—

> In forming an opinion as to the relation of *Bacillus suipestifer* to "food poisoning," two groups of facts must be taken into consideration. On the one hand, this organism can frequently be isolated from the excreta of patients suffering from "food poisoning," while it is very rarely found in healthy people, at least in England. The outbreak can often be traced to a given article of food, and the same bacillus can be found in the food. On the other hand there is evidence that meat containing *Bacillus suipestifer* can sometimes be eaten without ill-effects, and that in other diseases it is merely a secondary invader and does not initiate the illness. It must be admitted, I think, that *Bacillus suipestifer* has some relation to "food poisoning," and that it must be either a secondary invader or a causal organism of the disease. If *Bacillus suipestifer* is a secondary invader in "food poisoning" in man, the primary cause of the disease may be either a filter passer or a ptomaine. There is no direct evidence for the presence of a filter passer; and, unlike filter-passer infections, "food poisoning" is not contagious. Nor has the hypothesis that "food poisoning" is caused by ptomaines received any support during the last few years. The evidence for this view is still slight and indefinite; and, so far as I know, no one has yet demonstrated the presence of ptomaines in food which had caused "food poisoning."

He then deals with *B. enteritidis gærtner*, and sums up as follows :—

> It thus appears that *Bacillus enteritidis*, *Bacillus suipestifer*, and *Bacillus paratyphosus*, B., can all give rise to the clinical symptoms of "food poisoning." In the case of *Bacillus paratyphosus*, B., the usual source of infection is probably food which has been contaminated by a human carrier; in the case of *Bacillus suipestifer* and *Bacillus enteritidis* (Gærtner) the source of infection is food derived from healthy or diseased animals, and containing these bacilli from the outset. The two latter organisms are probably responsible for the majority of food-poisoning outbreaks. In outbreaks associated with the presence of *Bacillus enteritidis* the incriminated food has usually been derived from diseased cattle; in outbreaks associated with *Bacillus suipestifer* the food has been derived from cattle or pigs. The possibility that such outbreaks may be caused by bacterial viruses must not be overlooked.
>
> In conclusion, it is obvious that these facts have a practical value for those who are called upon to investigate outbreaks of "food poisoning." It is of importance to ascertain what organism is present in such outbreaks, since that knowledge gives a clue to the most probable source of the infection. Depending upon the nature of the bacillus which is found, attention can be at once directed to the kind of food in which the bacillus usually occurs, or a search may be made for a human carrier.

The discussion on the paper is worthy of note, but too lengthy to be dealt with here. In reply the author said that he believed that with some experience one could diagnose paratyphoid fever as a rule, even when apparently it was like enteric fever. First, in paratyphoid fever the onset was sudden, and often there were vomiting and diarrhœa, neither of which were usual in typhoid. Secondly, there was labial herpes in 50 per cent. of cases of paratyphoid fever. Thirdly, the initial temperature rose rapidly in paratyphoid, and gradually fell. The question of the presence of toxins in cooked meat had not yet been settled. In one of the best recorded cases of a food-poisoning outbreak, careful search was made for toxins, and none were found. The question of post mortem infection of meat must arise in some cases where the processes carried out were not cleanly, but, apparently post mortem infection was rare, because in England the Gærtner bacillus was but rarely found in the intestines of animals.

As an example of food poisoning due to another bacillus of the group, we may cite a paper by Savage and Gunson,[2] where "pork-cheese" or brawn was to blame, or vegetables infected from it. Bacteriologically the cause was a Gærtner bacillus of the Aertryck sub-group, which was isolated from a fatal case. It was proved to be present in the meat before the brawn was made, and was doubtless associated with a local injury or disease of one leg from which the pig was suffering. An outbreak due to the infection of beef with *B. enteritidis gærtner* forms

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[1] Bainbridge, F. A. (February, 1911), "The Etiology and Epidemiology of Paratyphoid Fever and Food Poisoning." *Proceedings Royal Society of Medicine*, Vol. IV., No. 4.

[2] Savage, W. G., and Gunson, C. H. (November, 1908), "An Outbreak of Poisoning from Infected Brawn." *Journal of Hygiene.*

the subject of a valuable communication by McWeeney,[1] which we need not consider in detail. Nine young lives were lost, and the lessons taught by this disaster are, he says: First, it indicates the need there is for the abolition of the private slaughter-house, and for the inspection of all animals used for human food, both before, during, and after slaughter; secondly, it emphasises the danger arising from the use of old stale scraps of meat, and especially of beef. If, on economic grounds, such left-over pieces *must* be used up, the only way of avoiding or diminishing the danger would seem to be very thorough and prolonged boiling. Ordinary examination of such meat may fail to discover any grounds for suspicion. **Food Poisoning** *—continued*

Papers on the subject will also be found reviewed in the *Bulletin of the Pasteur Institute* for June 15, 1910. In one of them *B. coli*, *B. proteus*, and certain micrococci are mentioned as accidentally pathogenic.

The other great cause of food poisoning is, of course, the *Bacillus botulinus*. One has fewer recent references to this organism, but an account of its toxin and antitoxin is given by Leuchs.[2] It is unlikely to interest the general reader. An outbreak of illness due to tinned meat, in which apparently toxins were to blame, is given by Beard,[3] but one doubts if the bacteriological examination which was made was sufficiently exhaustive.

Teyxeira [4] has investigated the causes of poisoning by preserved fish, fish pastes, etc., and as these, especially in the form of sardines, are common articles of diet in the Tropics, the review of his paper may be given in full :—

The author was able to confirm the presence of the following micro-organisms: *B. prodigiosus; B. botulinus* of van Emengem; *B. enteritidis* (Gærtner); *Penicillium glaucum*, and *Aspergillus glaucus*. The estimation of lead by the Fresenius-Babo method showed in one case that the soldering of the tin contained 50·6 per cent. of lead. The examination for ptomaines according to the Stas-Otto process, improved by Baschieri, gave a positive result in two cases. For the estimation 120 grm. of the fish, together with 100 grm. of the oil in which they lay, were taken. Tun-fish "Barbate Mark": 0·1096 grm. of a very bitter acrid crystalline substance was isolated; slightly soluble in water, readily soluble in alcohol, strong alkaline reaction, melting point 30° C. $H_2Pt.Cl_6$ produced a gold-yellow crystalline precipitate, and the usual alkaloid reagents gave a precipitate. Nitric acid produced a red coloration; no change with concentrated or dilute sulphuric acid. Physiological examination showed signs of poisoning, but not of a fatal character.

Tun-fish "Gubbio Mark": 0·2109 grm. of an amorphous dirty-white mass was isolated, possessing an irritant odour and astringent taste; alkaline reaction, soluble in water, slightly soluble in alcohol, soluble in chloroform, insoluble in ether, petroleum-ether and amyl alcohol. Precipitates were obtained with the usual alkaloid reagents. Nitric acid produced a straw-yellow coloration; sulphuric acid (1.20), bluish colour, carbonisation with strong sulphuric acid. Physiological examination did not give fatal results.

Goundou. Branch [5] records a case from the West Indies, the first met with in 14 years' experience there. He appears to think it may be an expression of syphilis. Orpen [6] describes, with excellent illustrations, an unusual case in Sierra Leone. The nasal tumours were of five years' growth, and followed a severe attack of yaws, and constant severe headache. The patient denied having had syphilis. A year after the appearance of the nasal growths a third tumour developed in the left malar region. A discharge from the right nostril and severe cephalgia were other late symptoms. Orpen found anosmia present, and thinks the third tumour, which is the peculiar feature of the case, may be of antral origin. The tibiæ were curved. A photograph also shows a unilateral case. Shircore [7] mentions a case in Nyasaland, which he thinks was goundou, and where the exciting cause was the entry of a small fly into one nostril. A week afterwards blood and larvæ were discharged from the nose, and then pain appeared in the nasal bones, followed by swelling. One cannot help thinking this may have been merely a case of nasal myiasis. Burrows records and figures a case from Sierra Leone. The bony growths were quite hard and smooth to the touch. They apparently sprang from the free edge of the nasal bones, and did not involve the nasal processes of the superior maxillæ. They were constricted at the base. There does not seem to have been much advance in our knowledge of the etiology of this condition. Bouffard,[8] however, has recorded a case in a

[1] McWeeney, E. J. (May 15, 1909), "Observations on an Outbreak of Meat Poisoning at Limerick." *British Medical Journal.*

[2] Leuchs, J. (1910), "Beiträge zur Kenntnis des Toxins und Antitoxins des *Bacillus botulinus*." *Zeit. f. Hyg. u. Infekt.*, Vol. LXV.

[3] Beard, J. (December 3, 1910), "Notes upon an Outbreak of Illness due to Tinned Meat in the City of Carlisle." *Lancet.*

[4] Teyxeira, G., quoted in *Journal Royal Institute of Public Health*, March, 1911.

[5] Branch, C. W. (March, 1909), "Case of Goundou in the West Indies." *Journal Tropical Medicine and Hygiene.*

[6] Orpen, R. W. (February 3, 1908), "An Unusual Case of Goundou." *Annals of Tropical Medicine and Parasitology.*

[7] Shircore, J. O. (February 26, 1910), "Goundou." *British Medical Journal.*

[8] Bouffard (April 14, 1909), "Autopsie d'un cas de Goundou chez le cynocéphale." *Bull. Soc. Path. Exot.*

Goundou— *continued*

cynocephalus monkey. At the autopsy the growths, which appeared limited during life, were found in reality to affect all the bones of the head. The nasal tumours were only outshoots of a generalised osseous hypertrophy of the skull. Such a condition would explain Orpen's third tumour. Nattan-Larrier, commenting on Bouffard's case, stated that it showed that there was no connection between goundou and yaws or syphilis. Brumpt mentioned a pseudo-goundou due to yaws, which he had seen amongst the Shilluks of the Upper White Nile. Quite recently Marchoux and Mesnil[1] have reported a similar condition in monkeys. It was, however, more general, the extremities being enlarged and the long bones curved. In the case of the skulls there was no encroachment on the cranial cavity, the increase being external. The authors go very carefully into the condition, which is a rarefying hypertrophic osteitis. They are unable to say if the condition is the same as goundou in man. They mention the occurrence of the disease in South America. In Brazil it was seen in a young white girl. Nattan-Larrier classes the condition with acromegaly and Paget's disease. Letulle showed the skull of a child belonging to the ancient race of Incas which exhibited a condition identical with, or closely resembling, goundou. In the case of the monkeys the authors are endeavouring to clear up the etiology.

Additional Note

Leger[2] has made a further contribution to our knowledge of the histo-pathology of goundou. He studied tissues derived from the two monkeys above mentioned, and came to the conclusion that the condition is due to a production of active embryonic elements caused by an irritation of the medullary tissue, and comparable to an actual inflammatory state which results in rarefaction of bone, and later in an osteosclerosis due to excessive production of fibrous tissue accompanied by over-production of bony tissue.

Guinea-Worm. Bartet[3] has written of an urticaria, either generalised or localised, accompanying dracontiasis. He observed the condition in Upper Dahomey, the eruption preceding the escape of the worm from its host. It may be accompanied by a kind of gastric crisis with fever, prostration, nausea, vomiting, etc. In a later paper[4] he seeks to explain the pathology of the condition which, along with the blisters and pruritis that may accompany *D. medinensis* infection, he thinks may be due to the secretion of a liquid from the worm itself intended to favour its escape from its host. He notes that in cases where urticaria appears the worm has a flattened ribbon-like aspect.

Graham[5] gives a brief account of the disease on the Gold Coast. When speaking of prophylaxis he says that it is very probable the infection is only acquired during one or two months of the year, and that water collections, dangerous at these periods, might be used with impunity at other times. Further, he thinks it likely that only a special species of cyclops can transmit the disease, and that if this species of cyclops is absent from a water-supply it can be safely used. In this connection reference may be made to the description of several species of cyclops furnished by Brady.[6] It is well illustrated. Cummins[7] deals with guinea-worm in the Anglo-Egyptian Sudan. He notes Leiper's work on the passage of the liberated embryos through the stomach wall of their host, and mentions Castellani's view that the males and females come together in the tissues about the mesentery. After connection the males die off, while the impregnated females seek the surface of the body, usually in the lower limbs. His paper views the subject mostly from a military point of view, but as regards preventive measures he remarks :—

> Prophylaxis can be attempted along two lines: by filtration of the water, and by preventing the infection of pools. The cyclops, being a large organism, is stopped by the coarsest kind of filtration, and all you have to do is to get your troops to strain their drinking water through khaki, or any fairly dense material. This can be done in cantonments, but that is just where the disease is not contracted. It is in the pools, refilled by the early rains,

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[1] Marchoux, E., and Mesnil, F. (March 8, 1911), "Ostéite hypertrophique généralisée des singes avec lésions rappelant le Goundou." *Bull. Soc. Path. Exot.*

[2] Leger, A. (April 12, 1911), "Contribution à l'étude de l'histo-pathologie du Goundou." *Ibid.*

[3] Bartet, A. (May 13, 1908), "L'Urticaire dans la Dracunculose." *Ibid.*

[4] *Idem* (June 10, 1908), "Essais de Pathogénie de l'urticaire dans la Dracunculose." *Ibid.*

[5] Graham, W. H. (December 1, 1908), "Report on Guinea-Worm." *Journal Tropical Medicine and Hygiene.*

[6] Brady, G. S. (July 25, 1910), "On some Species of Cyclops and other Entomostraca collected by Dr. J. M. Dalziel in Northern Nigeria." *Annals Tropical Medicine and Parasitology*, Vol. IV., No. 2.

[7] Cummins, S. L. (January, 1911), "Notes on Guinea-Worm in the Sudan." *Journal Royal Army Medical Corps.*

Guinea-Worm—*continued*

that the cyclops abounds, and these pools, infected by natives, who enter them for ablution purposes and to fill water-vessels, are often the only water-supply on the line of march in infected districts.

You will note that June and July, the months of the early rains, are the months of greatest prevalence of the local lesion. The native liberates embryos from his parasite into the pool whence his water-supply is drawn. These, after a sojourn in the cyclops host, return to the human stomach, and thus pave the way for a fresh infection of the pools in the succeeding year.

The real prophylaxis consists in preventing infection of the pools. This can be approached by building troughs for the natives to draw water from, and policing the banks of the pools to prevent people entering the water. This is a counsel of perfection. It cannot be effectually carried out except near stations, or, in other words, places where a good water-supply is already at the disposal of troops. It is on the line of march or on detached duty that infection of troops will occur.

Still, although the disease is difficult to prevent, much may be done to lessen its incidence. Nobody wants to get guinea-worm, and if once the native can be convinced that a given measure will prevent it, there is a chance of his mending his ways. In the meantime it is well worth while for a military administration, with its eye on possible operations in infected areas, to improve the sources of water-supply along strategical roads, to have combatant officers instructed in the causation and prevention of the disease, and to attempt the isolation of infected civilians during the two or three dangerous months of the year.

As regards treatment he does not favour injection of perchloride of mercury, which is very apt to lead to abscess formation, when it is the pus, not the perchloride, which kills the larvæ. He believes in employing traction where the worm is in a safe position, and the water douche for all worms in the vicinity of joints. After the embryos have been extruded the dead worm can be pulled out without difficulty, or, if not accessible, is soon absorbed by the tissues. Leiper's [1] paper on guinea-worm in domesticated animals is a useful contribution to the literature. He says :—

One of the most curious anomalies in the geographical distribution of dracontiasis has been the absence of the disease in Africa south of the Equator, although endemic northwards from the line to the Tropic of Cancer. It has been suggested that possibly the particular species of cyclops essential to the development of the parasite may not occur in the southern half of the Continent. Quite recently, however, a mature guinea-worm has been found by Mr. C. Grey at Broken Hill, North-West Rhodesia, in a leopard. I am indebted to Sir Patrick Manson for the specimen, and for kind permission to record it. In a letter dated November 27, 1909, Mr. Grey says : "The leopard appeared to have guinea-worm. I killed it the night before last near my house, but could not get at it till yesterday morning. On skinning it I found pieces of worm visible in eight or nine places in the connective tissue, and appearing to come from beneath it. The first worm I noticed was sticking out of the bullet-hole in the shoulder. The leopard was in good condition, and had a very good coat. I have never heard of the guinea-worm being found in man here. The doctor here has never had a case. I send a piece of the worm and some films."

The piece of worm sent resembles exactly the guinea-worms found in human beings on the West Coast of Africa. In appearance it is white and glistening ; in length, 45 cm. ; breadth, 1·5 mm. Both extremities are missing unfortunately. The body is filled by a single uterine tube crowded with embryos, which correspond exactly in size and structure with those of *Dracunculus medinensis* from man.

He then deals fully with the literature of guinea-worm in the lower animals, and concludes that the guinea-worm can infect and attain maturity in the dog and horse, if not in all the domesticated animals. Gaiger,[2] noting that there were only two records of guinea-worm in the dog in India, mentions five other instances of such infection. Emily [3] has recorded a case of encysted guinea-worm, the little tumour being found attached to a hernial sac with which it very probably was in communication. He states that it is not uncommon in guinea-worm regions to find negroes with little hard tumours due to calcified parasites. He mentions the intermediate host as being *Cyclops quadricornis*. Leiper [4] notes the native tradition that the guinea-worm can attain its full maturity outside the body. He regards this as extremely improbable, but, as showing how one might be deceived, he mentions having been sent a species of *Mermis*, a nematode found in earth and which closely resembles the guinea-worm. In West Africa the natives look upon it as a mature Dracunculus. But little has been said about treatment, and there is not much advance to chronicle, save perhaps the use of chinosol by subcutaneous injection as recommended by Acton.[5] It is a potassium salt of a compound oxychinoline and sulphuric acid, and is soluble, diffusible, and non-poisonous in the quantities usually employed.

It is a very powerful bactericide and antiseptic ; 15 grains to the pint of water is equivalent in every respect to a 1–40 solution of carbolic acid. An important point to note is that it should always be dispensed in pure soft water, any hardness in the water tends to split the chinosol into an oxychinoline, which is toxic, therefore it is

[1] Leiper, R. T. (March 1, 1910), "Guinea-Worm in Domesticated Animals." *Journal Tropical Medicine and Hygiene.*

[2] Gaiger, S. H. (1910), "*Filaria medinensis* in the Dog." *Journal Tropical Veterinary Science*, Vol. V., No. 3.

[3] Emily (December 14, 1910), "Note au sujet d'une petite tumeur constituée par un 'Ver de Guinée' enkysté." *Bull. Soc. Path. Exot.*

[4] Leiper, R. T. (March 1, 1911), "Note on the Native Tradition that the 'Guinea-Worm' can attain Maturity outside the Body." *Journal Tropical Medicine and Hygiene.*

[5] Acton, H. W. (July, 1910), "The Treatment of *Filaria medinensis* by Subcutaneous Injection of Chinosol." *Indian Medical Gazette.*

Guinea-Worm— *continued*

better to use distilled water. For subcutaneous injections 1 drachm of a 1 per cent. solution is used, but for a gargle or spray 1·4 grains in an ounce of water diluted with an equal quantity of warm water is usually employed. When used in connection with this parasite, an equal quantity of this 1 per cent. solution is injected on all four sides of the swelling; the total quantity used is 1 drachm, the object being to bathe the worm in this fluid, and by so doing kill it. The skin is first carefully sterilised in the usual manner, the strong mixture advocated by Cheyne (1–20 carbolic and 1–1000 $HgCl_2$ equal parts) being the antiseptic employed, and compresses of 1–2000 $HgCl_2$ are then applied for 12 hours. A long injection needle is introduced as near as possible to the swelling, and kept about half an inch below the skin, parallel with and along the whole length of the swelling. The needle is now slowly withdrawn, and in doing so 15 mins. of this 1 per cent. solution is evenly distributed along its track. When the point of it has nearly been withdrawn, it is then swung round and introduced at right angles to the first line of injection, when another 15 mins. are injected on its withdrawal. This process is repeated on the opposite side, so that the injection area forms a square and includes the whole of the guinea-worm swelling. When no suppuration was present, uniform results were obtained by this method. If the guinea-worm had not come to the surface a single injection of 1 drachm given in the above fashion caused its immediate death, and in four or five days the whole swelling had disappeared owing to the fact that the worm had been absorbed like a piece of aseptic catgut. On the second day after the injection the man was usually fit for his ordinary work. If the worm, however, had reached the surface, but no sepsis was present, the injection into the tissues killed the worm, and it could safely be wound out the next day, and if by chance it broke during this process no harm was done, the worm being absorbed *in situ* and the small superficial wound rapidly healed in a few days. If suppuration was present and the case seen early, the injection killed the worm if not already dead, and markedly influenced the suppurative process, so that healing of the wound might be anticipated in eight to twelve days.

Nineteen cases with only one failure, and that of an accidental nature, are recorded. Cases take about one-fourth of the time to treat, as compared with those subjected to Emily's perchloride injection, and asepsis is easier.

Bellet,[1] before extraction, recommends cocaine injections (1 to 3 c.c. of a 1 per cent. solution of the hydrochlorate, both into the body of the worm and into its tract subcutaneously. This serves to paralyse the movement of the parasite, and, combined with bicarbonate of soda compresses (15 grammes to the litre), has yielded good results, enabling extraction sometimes to be performed at one sitting. Only a few cases, however, are recorded. Possibly a combination of cocainisation and chinosol injection would yield the best results.

Hæmatozoa. It is neither possible nor indeed advisable to attempt a review of the numerous papers dealing with the discovery of new species of protozoal blood parasites in various kinds of animals. Well-nigh every month sees the list extended. Here we deal with new human hæmatozoa, with general papers on these parasites, and with any thought to be of special interest—*i.e.* those describing new genera or throwing light on developmental problems.

Taking human blood first, *Sergentella hominis*, as it is now called, the vermicular parasite exhibiting periodicity, and found by the Sergents in human blood in Algeria, has now found its way into the text-books. It was mentioned in our first Review. Of a somewhat similar type are the crescentic and vacuolated bodies discovered by Castellani and Willey in human febrile cases in Ceylon, and mentioned and figured in Castellani and Chalmers'[2] valuable manual. Their nature and significance are unknown.

Hoefer,[3] in a case of anæmia at Leipsic in a woman who had never been away from the neighbourhood of that city, found an hæmatozoon of varying forms, which he illustrates by a coloured plate. It stained like a malarial parasite, showed chromatin, occurred in the red cells as rings or as curved pyriform bodies, and also apparently as a large blue staining mass, dotted with fine chromatin granules, rather like a benign tertian parasite, but devoid of pigment. In the plasma, double, possibly dividing, free forms were found which in some instances showed two nuclei each, and were either pear or somewhat spindle-shaped. Another free form suggested a vermicule. The author is inclined to think it should be classed with Hartmann's "Binucleata allied to Achromaticus and Piroplasma." The patient admitted having been much bitten by mosquitoes in the neighbourhood of the town.

Of new blood protozoa in animals the *Endotrypanum schaudinni* found by Mesnil and Brimont[4] in a sloth (*Chalœpus didactylus*) is of special interest. The parasites were eight to eleven microns in length and two to four in breadth. The body was rounded at one end and drawn out at the other, which was usually prolonged into a filament. No pigment was seen. A body, staining red, was evidently the macronucleus. Near it was an elongated smaller

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[1] Bellet, E. (November 11, 1908), "De l'extirpation du Ver de Guinée apres cocaïnisation." *Bull. Soc. Path. Exot.*

[2] Castellani, A., and Chalmers, A. J. (1910), *Manual of Tropical Medicine.* London.

[3] Hoefer, P. A. (June 14, 1910), "Über ein unbekanntes Protozoon im menschlichen Blute bei einem Falle von Anämie." *Cent. f. Bakt.*, I. Orig., Vol. LV.

[4] Mesnil, F., and Brimont, E. (December 5, 1908), "Sur un hématozoaire nouveau (*Endotrypanum*, n. gen.) d'un Édenté de Guyane." *C. R. Soc. Biol.*, Vol. LXV.

Hæmatozoa—*continued*

body, very clearly seen in the depth of the cell; sometimes it lay in front, sometimes at the side; this was evidently the micronucleus. All the forms seen were endoglobular. The hæmatozoa were rather large for the cell; when the anterior filament was straight the wall of the cell formed a sort of spur. The invaded cell was not altered in any other way. The authors suggest that part of the parasite's life is spent free in the plasma. Once two were found in one cell. No multiplication forms were seen.

The authors think that, like *Leishmania*, this type is intermediate between the trypanosomes and the *Hæmocytozoa;* they suggest that it is near the trypanosomes of the *dimorphon-congolense* group, and point out that Höhnel has seen endoglobular forms of *T. congolense*.

Another new genus of hæmatozoa in animals has been named *Toxoplasma*. The best known species is *Toxoplasma cuniculi*, first found by Splendore [1] in rabbits, and associated with lesions resembling those of kala-azar. Carini [2] has worked with this parasite. He finds it often causes death, and that, post mortem, small nodules are found in the liver and spleen. Dogs and fowls are refractory to infection by inoculation. In rabbits, guinea-pigs, and white rats, subcutaneous or endovenous inoculation may or may not give positive results. Pigeons are most easily infected. They die in 15 to 20 days, and the parasites multiply abundantly in their organs, especially in the spleen and liver. The parasites are rather like Leishmania, but do not possess micronuclei (blepharoplasts). Dividing forms are frequently seen, and masses suggesting schizogony. In a later communication Carini [3] gives illustrations of the parasite as met with in inoculated pigeons. Splendore [4] has recently written again on the subject. He has succeeded in infecting several species of birds and frogs. Cross-shaped forms of the parasite sometimes present gregariniform movements. The parasite has a flagellated stage and may be encountered within the red cells. A karyosome can be demonstrated when the iron-hæmatoxylin method of staining is employed.

Other toxoplasmata have been described, *i.e.* that of the gondi, a North African rodent, by Nicolle and Manceaux,[5] and named by them *T. gondii;* that named *T. talpæ* found by Mine in Japan and described by Prowazek,[6] and finally that found in the dog in Turin by Mello.[7] The last named is specially interesting, in view of the discovery of Leishmania in dogs. A very important piece of work was that performed by Miller [8] on the life history of *Hepatozoon perniciosum*, a parasite allied to, if not identical with, *H. muris*, the hæmogregarine of the leucocytes of the Norway rat. Miller found the parasite in white rats, and besides proving that asexual reproduction (stage of schizonts and merozoites) takes place in the liver cells, he found that sexual reproduction (sporogony) occurred in a gamasid mite, *Lelaps echidninus*, parasitic upon the rat and feeding on its blood. The most interesting point is that infection of the rat takes place owing to its ingestion of the mite when the sporozoites in the latter are freed by the action of the duodenal juices, become motile vermicules, penetrate the villi, enter the blood-stream, are carried to the liver, and start in the hepatic cells the cycle of schizogony. The mites leave the rats during the day, and only return to them at night, a fact which readily explains the transmission of infection. The disease produced in the white rats is fatal, and is characterised by severe anæmia. It has been proposed by Porter [9] to class this type of parasite affecting the white cells of mammals under the new generic name *Leucocytogregarina*, and there seems a tendency to accept this classification, though *Hepatozoa* (Miller) might be more correct. It is certainly convenient and, while fairly descriptive, separates these hæmatozoa from the *Leucocytozoa*, which are parasites of birds, and which have recently come greatly into prominence. Sambon [10] has dealt with them at some length, dealing both with their development and with the different species. Of special interest is that in the red

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[1] Splendore, A. (1908), "Un nuovo protozoo parasita dei conigli, etc." *Rev. la Soc. Scient. de S. Paulo.*

[2] Carini, A. (October 13, 1909), "Reproduction expérimentale de la toxoplasmose du Lapin." *Bull. Soc. Path. Exot.*

[3] *Idem* (November 10, 1909). *Ibid.*

[4] Splendore, A. (February 17, 1910), "*Toxoplasma cuniculi.*" *Rev. la Soc. Scient. de S. Paulo.*

[5] Nicolle, C., and Manceaux, L. (1909), "Sur un protozoaire nouveau du Gondi." *Arch. de l'Inst. Past. Tunis.*

[6] v. Prowazek, S. (1910), "Parasitische Protozoen aus Japan, gesammelt von Herrn Dr. Mine in Fukuoka." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIV., No. 10.

[7] Mello, U. (June 8, 1910), "Un cas de toxoplasmose du Chien observé à Turin." *Bull. Soc. Path. Exot.*

[8] Miller, W. W. (1908), "*Hepatozoon perniciosum* (N. G., N. Sp.), A hæmogregarine pathogenic for White Rats, etc." Bulletin XLVI. *Treasury Department. Public Health and Marine Hospital Service of U.S.A.*

[9] Porter, A. (October, 1909), "Leucocytozoa." *Science Progress.*

[10] Sambon, L. W. (August 15, and November 2, 1908, and February 1, 1909), "Remarks on the Avian Hæmoprotozoa of the Genus Leucocytozoon." *Journal Tropical Medicine and Hygiene.*

Hæmatozoa— *continued*

grouse, sporogony taking place in a fly. Since the date of his paper many new species have been found in various parts of the world. Wenyon,[1] criticising some of Porter's (*loc. cit.*) remarks, also enters into a detailed description of the group. It may perhaps be useful to give his two lists, one stating the characters of the *Leucocytozoa*, the other those of the so-called *Leucocytogregarina*.

A. *Leucocytozoa.*

(1) They are exclusively parasites of birds, for though Carini has described a *Leucocytozoon* from an amphibian, it is exceedingly doubtful if this is a *Leucocytozoon*, as it does not exhibit the sexual dimorphism which is such a distinctive characteristic of the avian parasites.

(2) They are parasitic in cells which have been variously interpreted as leucocytes, red blood corpuscles, immature red blood corpuscles, etc.

(3) They have the peculiar property of causing the host-cell to assume a characteristic spindle form. The parasites themselves surround the nucleus of the host-cell which is found at the middle of the spindle.

(4) Three forms of the parasite can generally be recognised in the peripheral blood, large, deeply staining parasites which are the female gametocytes, pale staining parasites which are male gametocytes, and lastly young forms which are possibly immature gametocytes.

(5) The male gametocyte develops into a Polymitus, or in other words it forms male gametes, which are narrow whip-like organisms resembling the male gametes of the malarial parasites. These male gametes fertilise the female gamete, and a motile zygote results.

(6) The nucleus resembles that of Halteridium. The male nucleus consists of chromatin granules scattered about the centre of the parasite. The female nucleus is a more compact group of chromatin granules, in the midst of which, or to one side, is a granule definitely marked off from the rest by its larger size. It is possible that this granule is a karyosome.

(7) The parasites are devoid of pigment, they are not enclosed in any cyst, they never leave the host-cell to move about in the blood plasma as do the hæmogregarines; the asexual mode of reproduction is unknown, nor is there any knowledge of the further development of the zygote and of the mode of transmission (*vide*, however, paper by Mayer, quoted below).

B. *Leucocytogregarina.*

(1) They are parasitic in leucocytes of mammals.

(2) They do not alter the shape of the host-cell to any extent, though they may cause considerable change in its nucleus.

(3) There is no sexual differentiation to be compared with that existing in the bird parasites.

(4) The nucleus is characteristic, and resembles that of hæmogregarines. It is quite unlike the nucleus of the *Leucocytozoon*, and in staining reaction approaches that of the nucleus of the host-cell.

(5) A cyst (cytocyst) is frequently, though not invariably, present. Within the cyst the parasite lies as a cylindrical body, completely filling the cyst, or as an elongate vermicule doubled upon itself in the shape of a U.

(6) The parasites may leave their host-cell and their cyst and move about in the plasma as minute gregarines.

(7) Asexual multiplication is by schizogony in a cell of some internal organ.

(8) Sexual development has only been completely described in one case, namely, in the case of the leucocytic parasite of the rat. It has been described, but less completely, for the similar parasite of dogs.

We turn now to other parasites of bird's blood, namely the *Hæmoproteidæ*, formerly known as *Halteridia*, or *Hæmamœbæ*, a fact which one finds still confuses students of these hæmatozoa. *Hæmoproteus columbæ* is perhaps the most interesting of these, for its life-cycle in its intermediate host. *Lynchia maura* has been fully worked out by the Sergents,[2] who have conducted much research on this and other avian hæmatozoa. Their paper and those occurring with it are well worthy of study. Aragao [3] has also worked at this subject, and his conclusions serve to refute Schaudinn's well-known view, that the hæmoproteidæ are stages in the life history of trypanosomes. Work confirmatory of Schaudinn's is, however, not lacking. Woodcock will be found quoted as showing that a hæmoproteus of the chaffinch becomes in certain phases a little trypanosome. Readers should, therefore, be referred to his latest paper,[4] wherein it will be found (*page* 679) that he has modified his view, and no longer believes the tiny trypanosomes were developed directly from the Halteridia. The part of the paper with which we are specially concerned is the "Note on Halteridium fringillæ (Labbé)," a parasite which formed the subject of a previous article,[5] and in which he found nuclear dimorphism,

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[1] Wenyon, C. M. (April, 1910), "Some Remarks on the Genus Leucocytozoon." *Parasitology.*

[2] Sergent, Ed. and Et. (1910), "Études sur les hématozoaires d'oiseaux." *Recherches Expérimentales sur la Pathologie Algérienne*, 1902–1909.

[3] Aragao, H. de B. (1908), "Über den Entwicklungsgang und die Übertragung von *Haemoproteus columbae.*" *Arch. f. Protist.*, Vol. XII.

[4] Woodcock, H. M. (November, 1910), "Studies on Avian Hæmoprotozoa." *Quarterly Journal of Microscopical Science.*

[5] *Idem* (1909), "On the Occurrence of Nuclear Dimorphism in a Halteridium Parasitic in the Chaffinch," etc. *Ibid.*

as did Schaudinn in *H. noctuæ*, and as Berliner [1] has since done. It is this discovery which he thinks shows a close relationship between Halteridium and the hæmoflagellates. Other work confirmatory of Schaudinn's is that of Mayer,[2] who has found a Halteridium of the owl which undergoes flagellate development in certain mosquitoes. His paper is well illustrated, and he thinks the name Hæmoproteus should be reserved for Halteridia forms which undergo a different development and develop in different intermediate hosts. He describes also a partial development of a leucocytozoon. As the papers cited give very full bibliographies one does not propose to review other similar articles. The question as to whether Schaudinn was right or wrong is still apparently unsettled, but recent work points to his being correct, though I should not wonder if the recognition of the part possibly played by so-called "infective granules" in the life history of these and allied parasites may not clear up much that is obscure and puzzling. Hæmatozoa—*continued*

A good general paper on the hæmatozoa of fish, and one very well illustrated, is that by Neumann.[3] It is of special interest, because new forms of parasites are described, one of which that he has named *Globidium multifidium*, strongly recalling the yeast, which is the cause of epizootic lymphangitis in equines. An English paper on fish hæmatozoa is that by Henry,[4] who has also found new forms. Minchin and Woodcock [5] have also dealt with the subject in connection with fishes caught at Rovigno. There is a number of useful notes on technique in this paper and a reference also to the great Schaudinn question. One had intended reviewing papers on the plasmodia of birds and monkeys, but will rest content with a reference to another well-illustrated paper by Neumann,[6] which, as it gives an excellent account of the development of an avian plasmodium in a mosquito, is likely to be useful to those who may be tracing the development of the malarial parasite in anophelines.

We have said nothing about the hæmogregarines of cold-blooded animals, very many of which are now known. Reference to a single paper may be permitted, that by Reichenow,[7] because it deals with development and enters into the question of classification. He believes all hæmogregarines are Coccidia, and would place them in the family *Adeleidæ*. The hæmogregarines of mammalian red cells are included, but Miller's hepatozoon is kept apart. A French review of this article occurs in the *Bulletin of the Pasteur Institute* for December 30, 1910.

Additional Note

A very interesting new endoglobular blood parasite found in Russian polecats has been found and described, with a well-executed coloured plate, by Lebedeff and Tscharnotzky.[8] It appears to constitute a new genus and species, and has been named *Microsoma mustelæ*. The earliest stage in the red cell is like a tiny *anaplasma*, but the parasite, which at first consists wholly of chromatin, increases in size, develops a blue-staining cytoplasm, and finally occupies the whole host cell. What may be free forms are also described. The authors compare the condition not only with *anaplasma* but with Koch's bodies in East Coast Fever, the nature of which has recently been decided by Gonder. This new parasite would seem to be most closely related to the piroplasmata.

Heat Stroke. Simpson [9] has a paper on the solar element in sunstroke in its physical relations. The latter, he says, are apt to be forgotten. The paper is of a scientific nature, and must be studied as a whole, but a note on tinted glasses which it contains may be quoted.

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[1] Berliner, E. (1909), "Flagellaten-Studien." *Arch. f. Protist.*, Vol. XV.

[2] Mayer, Martin (1911), "Über ein Halteridium und Leucocytozoon des Waldkauzes und deren Weiterentwicklung in Stechmücken." *Ibid*, Vol. XXI.

[3] Neumann, R. O. (1909), "Studien über protozoische Parasiten im Blut von Meeresfischen." *Zeit. f. Hyg. u. Infekt.*

[4] Henry, H. (1910), "On the Hæmoprotozoa of British Sea-Fish (A Preliminary Note)." *Journal Pathology and Bacteriology*, Vol. XIV.

[5] Minchin, E. A., and Woodcock, H. M. (April, 1910), "Observations on Certain Blood Parasites of Fishes occurring at Rovigno." *Quarterly Journal of Microscopical Science.*

[6] Neumann, R. O. (1908), "Die Übertragung von *Plasmodium praecox* auf Kanarienvögel durch *Stegomyia fasciata*, etc." *Arch. f. Protist.*, Vol. XIII.

[7] Reichenow, E. (1910), "*Hæmogregarina stepanowi.* Die Entwicklungsgeschichte einer Hämogregarine." *Ibid*, Vol. XX.

[8] Lebedeff, W., and Tscharnotzky, A. (May 27, 1911), "Ein neuer Parasit im Blute des Iltis, *Microsoma mustelae.*" *Cent. f. Bakt.*, I. Orig., Vol. LVIII., No. 7.

[9] Simpson, R. J. S. (November, 1908), "The Solar Element in Sunstroke in its Physical Relations." *Journal Royal Army Medical Corps.*

Heat Stroke— *continued*

Speaking of wave-lengths which produce the sensation of light, the author says that their measurement is important from the general aspect, and, in particular, in view of the increased comfort, if not protection, afforded by smoked or blue glasses.

Most smoked glasses have, in fact, a faint yellowish tinge; there is therefore some absorption of the shorter wave-lengths as well as a general dimming of the whole spectrum; in blue glasses the same general absorption does not take place. Recently orange-tinted and yellow or "amethyst" glasses have been placed on the market, which are said to be as effective as the smoked glasses. It is, of course, quite obvious that the same theory cannot explain the beneficial results from the use of blue and of orange glasses, unless we assume that the effect in each case is purely mental. There is, however, no doubt that in a brilliant light the smoked glass is by far the most effective, and this must be due to the reduction in intensity of the whole spectrum, except possibly the longer wave-lengths.

Although one has unfortunately not had access to them, one gives references to two papers by Dufour,[1] which look as though they might be of interest or value. The latter [2] deals with results obtained by lumbar puncture. The recent output on the subject of insolation appears to have been very small.

Hydatid Disease. The majority of papers to which one has references are concerned with the fixation of complement test, and the precipitin reaction, which was just coming into use as a diagnostic agent at the time our last Review was written, and in which it received brief mention. Both have now proved their value, as many papers demonstrate. Happily for our purpose, Eckenstein [3] has recently written a useful review on the principal papers, dealing with the application of the Bordet-Gengou reaction. He gives an account of the different methods employed, especially as regards the preparation of antigen. He refers the reader to a previous paper by himself and Sabrazes [4] on the technique of the test, but gives the essential details shortly as follows :—

Before use the antigen must be diluted with salt solution. The correct dilution is found by testing the hydatid fluid with different sera, as is done with the heart extract in the sero-reaction for syphilis. The dilution of the antigen which I am using is 1 in 5. Originally the fluid was used undiluted, but the results were inconstant. Thus on one occasion the undiluted fluid completely prevented hæmolysis with several sera obtained from patients, all of whom were free from hydatid disease.

Three rows of tubes are required, and the unit used is 100 c.mm. The following solutions are added :—

To tube 1 :—1 unit of serum, 1 unit of salt solution (9 per 1000), 1 unit of antigen.

To tube 2 :—1 unit of serum, 2 units of antigen.

To tube 3 :—1 unit of serum, 2 units of salt solution.

The tubes are incubated at 37° C. for about one and a half hours. One unit washed sheep's corpuscles (5 per cent.) is added to each tube, and the whole returned to the incubator until hæmolysis has taken place in the control tubes. The third tube serves as a control for the hæmolytic power of the serum examined. Each time it is advisable to test at least two sera obtained from healthy subjects in order to control the antigen.

A positive result is obtained when there is no hæmolysis in the first and second tubes, but hæmolysis in the third tube; a negative result when hæmolysis takes place in all three tubes.

The objection has been made to these simplified methods that human serum may contain substances which at one time favour hæmolysis, at another time prevent it (Weinberg); but, as we have shown elsewhere, in practice this does not prevent a result from being obtained in nearly all cases. Another objection is that the serum may contain such a small quantity of antibody that it is necessary to use a method which permits of the dosage of the complement and the minimal dose being employed. This may perhaps account for the negative result obtained in observation No. 12. Lippmann also refers to this, and recommends that a larger dose of serum should be used in such cases.

The excellent results obtained by Weinberg are mentioned, and the two conditions which may influence the reaction receive due notice. These are (1) the death or degeneration of the cyst; (2) operation; opinions vary as to the influence, if any, of these two factors on the test. For instance, Weinberg records cases in which the cysts were dead or undergoing degeneration, yet he obtained the reaction, as indeed he also did long after operation, especially if a portion of the cyst wall had been left behind. The nature of the reaction is discussed, but as views differ there is no need to consider this question here. Since this review, other papers have appeared confirming the value of the test. An interesting extract from Braunstein's [5]

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[1] Dufour, R. (1909), "Du liquide céphalo-rachidien hémorrhagique dans un cas d'insolation." *C. R. Soc. Biol.*

[2] *Idem* (1909), "Des résultats de la ponction lombaire dans l'insolation." *Revue neurol.*, Vol. XVII.

[3] Eckenstein, K. (August 6, 1910), "The Serum-Diagnosis of Hydatid Disease: Fixation of the Complement." *Lancet.*

[4] Eckenstein, K., and Sabrazès, J. (January 22, 1910), "Note on a Simple Method of Fixation of the Complement in Syphilis." *Ibid.*

[5] Braunstein, G. (1910), "Der Wert der spezifischen Komplementbindungsverfahren bei Echinokokkose des Menschen." *Wien. Klin. Woch.*, Vol. XXIII.

paper is given in the Epitome, *British Medical Journal*, for December 24, 1910, as follows :— Hydatid Disease—*continued*

The fluid contents of an echinococcus cyst, either from an animal or man, provide a satisfactory antigen which if ½ per cent. carbolic acid be added, can be kept for six months without losing its properties ; 0·4 c.cm. of antigen is used for the test. The blood serum in hydatid disease was found to have a general complement deviation action, and therefore a regulated amount of the serums both of the patient and of the control normal persons should be used ; the author used constantly smaller amounts, down to 0·01 c.cm. The cases tested can be divided into three groups. To the first belong three in which the examination was made during the patient's lifetime, and the correctness of the diagnosis based upon the reaction was confirmed at the subsequent operation. The most interesting case of this group was that of a woman 41 years of age who had complained for six years of pains in the stomach region. There was slight gastroptosis, and the liver, which was low down, was palpable to the right of the middle line, and became somewhat more prominent on deep inspiration. Repeated examination, combined with the use of Röntgen rays, failed to give confirmatory evidence of the presence of echinococcus disease. The reaction was positive with 0·06 c.cm. of serum, but Wassermann's reaction was also positive. The diagnosis was therefore doubtful between syphilis and hydatid disease, and the patient was advised either to undergo a long course of iodide treatment or to have an operation. The operation was chosen, and disclosed the presence of an hydatid cyst at the edge of the liver of the size of a child's fist. To the second group belong two cases in which the reaction was tested with blood obtained after death when the autopsy had shown the presence of hydatids. One case gave a positive reaction with 0·2 c.cm. of serum, the other negative even with 0·4 c.cm. of serum ; the negative reaction may perhaps be due to the fact that the cyst was surrounded by a hard, calcified capsule. In the three cases of the third group the reaction was tested at longer or shorter intervals after operation for hydatids. One case gave a positive reaction with 0·01 c.cm. of serum ten days after the operation. A second, tested a year after operation, was not definitely positive with 0·4 c.cm., but the case demonstrated the possibility of the presence, though in small quantities, of specific antibodies, even after so long an interval. In a third case a positive reaction was obtained two years after operation, but a fistula from an empyema which had developed three months after the operation was still discharging, and it is possible that the empyema was a result of an echinococcus injection, and the persistence of the fistula showed that the hydatid disease was not yet cured. The author holds that in cases of active echinococcus disease in man the complement fixation test is an extremely valuable help to diagnosis.

Taking now the second test, the precipitin reaction, which is said by Weinberg to be less reliable than the complement deviation tests, we find Welsh, Chapman and Storey [1] recording results from Australia. Two of these authors [2] had already recorded nine cases,

in eight of which blood from the hydatid patient was collected in sterile glass pipettes on the morning of the day of operation ; the hydatid fluid or cysts were obtained in sterile flasks in the afternoon ; the patient's serum and the hydatid fluid were allowed to stand overnight in a cool chamber ; and the test was made next morning about 24 hours after the blood had been collected. Control sera from healthy persons were taken at the same time as the sera to be tested, and were kept in the same manner. From 6 to 12 drops of serum were shaken up with one cubic centimetre of clear hydatid fluid, precautions to minimise bacterial infection being taken, and the tubes were allowed to stand for 24 hours at room temperature before the precipitates were read. In these circumstances, with one exception, the patient's serum never failed to give a positive reaction with the hydatid fluid removed from his tissues. The single exception, however, yielded a precipitate when the patient's serum was tested with the hydatid fluid obtained from another patient. While this was our usual procedure, we also tested the serum of some of the patients, collected before operation, with hydatid fluids taken from other patients, and we obtained positive precipitin reactions in cases in which subsequent operation revealed undoubted hydatid invasion ; and negative precipitin reactions in doubtful cases in which at operation hydatid cysts were not found. Notwithstanding our small series of cases, the fact that in every case the presence of the reaction corresponded with the presence of hydatid cysts, and the absence of the reaction with the absence of cysts, led us to the conclusion that in the precipitin reaction we had a valuable aid to the diagnosis of hydatid disease. We must, however, emphasise the fact that this striking evidence of the correlation of a specific precipitin reaction with hydatid invasion was obtained in the most favourable conditions of experiment, since usually the serum and the hydatid fluid were taken from the same patient and tested within 24 hours, or, when the serum and the hydatid fluid were obtained from different patients, the hydatid fluid had not often been kept for more than a few days.

In the second paper they mention the necessity of storing hydatid fluid, if the test was to become of general value, and their reports deal mainly with the interaction of hydatid fluids, (*a*) not derived from the patient whose serum was being tested, (*b*) of longer standing than those used in the first series of cases, and (*c*) subjected to various methods of treatment in order to preserve them in a sterile condition for many months. They found that—

(1) A precipitate was not obtained in any interaction between hydatid fluid and human serum from a patient not invaded by hydatid cysts.

(2) Having regard to the long duration and probable irregularity of the interchange of protein molecules between a hydatid cyst and its human host, and having regard also to the possible unsuitability of the hydatid fluid, we must expect a certain number of precipitin tests to fail to give a satisfactory precipitate, and this has been our experience.

(3) In the conditions of a diagnostic precipitin test as above described for patients suspected to harbour hydatid cysts, a negative reaction is inconclusive, but a positive reaction is conclusive of hydatid invasion, and the latter may be obtained in circumstances of clinical importance.

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[1] Welsh, D. A., Chapman, H. G., and Storey, J. C. (April 17, 1909), "Some Applications of the Precipitin Reaction in the Diagnosis of Hydatid Disease." *Lancet.*

[2] Welsh, D. A., and Chapman, H. G. (May 9, 1908), "The Precipitin Reaction in Hydatid Disease." *Ibid.*

Hydatid Disease— *continued*

In cases where both the precipitin and the Bordet-Gengou reaction had failed, Bettencourt,[1] adopting Noguchi's method for syphilis and employing a hæmolytic system of human red cells and rabbit-homo serum, has obtained positive reactions confirmed by operation. We have thus three new blood tests at our disposal for effecting a diagnosis. These, of course, may be supplemented by ordinary blood examination which shows eosinophilia to be present. Palazzo has recently reported a case with 68·3 per cent. of eosinophilia, the highest percentage yet recorded. The eosinophilia diminished, and finally disappeared after successful operation. Palazzo [2] believes that the neutrophiles are transformed into eosinophiles by the toxins of the hydatid cyst. Repeated examinations are necessary, as the eosinophilia may be intermittent. Syme [3] gives an interesting account of peculiar cases, and concludes with the following notes :—

> As regards treatment, no one method is universally applicable; but the treatment most generally satisfactory is removal of the mother cyst and daughter cysts if present, marsupialisation of the adventitia, and drainage. Cysts in the soft parts of the parietes may be dissected completely out and the incision closed, also omental cysts; when these are numerous, as is generally the case, repeated operations are necessary, as it is a great mistake to attempt too much at one operation. Care must be taken not to allow the contents to escape into the peritoneal cavity and get into the margins of the incision, as scolices may become implanted there and grow. Of this I have seen undoubted instances. Cysts in the spleen may be treated by removal of the mother and daughter cysts, dropping back the spleen, and closing the abdomen. Some lung and liver cysts, when small and barren, may be treated in the same way, but generally require marsupialisation. When liver cysts have invaded the lung, it is important, if possible, to evacuate the primary cyst through the abdomen.
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> Suppurating cysts have been almost universally treated by drainage; but Mr. Hamilton Russell has washed out the cyst, then filled the cavity with saline solution, and closed the adventitia closely and also the abdomen. I have never ventured to do this myself, though Mr. Russell reported a successful case. In bone, the cancellous tissue containing the cysts must be thoroughly gouged out; sometimes the whole portion of bone must be removed, leaving the periosteum, and in some very advanced cases in the lower limb amputation may be necessary. Such cases, however, are extremely rare.

One such was recorded, and figured in the Second Report of these Laboratories. A paper which surgeons are likely to find useful is that by Bird [4] of Melbourne. Madden [5] has recorded an interesting case of multiple retroperitoneal hydatid cyst met with in Egypt, where the disease is very rare. As Madden says :—

> Though the native Egyptian lives with his animals a great deal, the rarity of hydatid disease may be understood by quoting a paragraph from the note on the subject to which reference has already been made as follows : " Professor Looss has never found the tænia echinococcus in a stray dog in and about Cairo, but discovered it once in a small pet dog. It is possible that in the villages the dogs may harbour tænia, though there is but little chance of their being infected with the disease, as no slaughtering of animals affected with the disease in the cysticercus form takes place. Very little meat is eaten by the country people, and the only killing for food is done at the abattoirs. Even should a pariah dog become infected by eating cysts from cattle or sheep, he is so shy and wild that man runs very little risk of infection from him. He is the great scavenger of the village, and is never fondled or made a pet of in any way. The larval stage of the tænia echinococcus is occasionally met with in sheep and goats, and is exceedingly common in cattle and camels. This localisation to the herbivora is common in all countries in which the disease is found.

The disease is possibly commoner in the Sudan, though it is rare also in these regions if one is to judge from a paper on the subject by Christopherson,[6] who, apparently basing his opinion on a paper in *Allbutt's System of Medicine*, believes, in contradistinction to Madden, that the disease is not uncommon in Egypt. He mentions four cases only, originating in the Sudan and coming under his notice in the course of seven years. One of these had a hydatid cyst in the left ventricle.

Minett [7] records two cases of hydatid disease of the kidney from British Guiana. One of these had actually 600 small cysts in one kidney, only complete cysts being counted. He also mentions a case recorded by Wise in which hydatid cysts were present in practically every one of the viscera. Many of these cysts contained small calculi, most probably present as the result of osmosis.

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[1] Bettencourt, N. (January, 1911), " Le systéme hémolytique Lapin-Homme dans la séro-réaction du kiste hydatique." *Arch. Inst. Bact. Camara Pestana Lisbon*, Vol. III., No. 2.

[2] Palazzo, G. (1909), quoted in Epitome, *British Medical Journal*, October 9, 1909.

[3] Syme, G. A. (October 2, 1909), "Some Unusual Cases of Echinococcus (Hydatid) Cyst, with Remarks on Diagnosis and Treatment." *British Medical Journal.*

[4] Bird, F. D. (October 2, 1909), " Operations for Liver and Lung Hydatids." *Ibid.*

[5] Madden, F. C. (February 13, 1909), " An Interesting Case of Multiple Retroperitoneal Hydatid Cysts." *Lancet.*

[6] Christopherson, J. B. (November 1, 1909), " Case of Hydatid Cyst of the Left Ventricle, together with some Remarks on Hydatid Disease in the Anglo-Egyptian Sudan." *Journal Tropical Medicine and Hygiene.*

[7] Minett, E. P. (April 15, 1911), " Three Unusual Post-mortems from British Guiana." *Ibid.*

Hydatid Disease—*continued*

Tuffier and Martin [1] call attention to the danger of exploratory puncture in cases of hydatid of the lung. Often immediate death has followed, and Pasquier places the mortality at 63·8 per cent., though this rate, the authors hold, is unduly high. The fatal symptoms are those of asphyxia, the result really of drowning in the fluid contents of the cyst, which is believed to contract vigorously under the stimulus of the puncture, rupture, and flood the cavity in the lung with its contents, whence they make their way up any bronchi that may lead into the cavity, and reach the general system of air-passages. If exploratory puncture is decided upon in a suspected case, everything should be in readiness for immediate cutting down upon the cavity and giving its contents free exit externally.

Hydrophobia. In the first instance we consider some papers dealing with the Negri bodies, their significance and the technique for staining them. The subject is still more or less within the realms of controversy.

Da Costa,[2] in two cases, found what he believed to be Negri corpuscles in the supra-renal bodies of rabid guinea-pigs. He mentions that sometimes the supra-renal body is virulent in cases of mammalian hydrophobia.

Babes and Stefanesco [3] have studied the subject in inoculated dogs. They find that the Negri corpuscles appear later in the bulb and medulla than the fine grains described by Babes [4] in the protoplasm of the nerve cells first affected. They are satisfied that the latter and not the Negri bodies are the "active" parasites of rabies. Babes declares his diagnostic method, which depends on the demonstration of miliary perivascular or pericellular nodules in the central nervous system, to be superior to the diagnosis by means of Negri bodies. It is, he says, more rapid, more simple, and more certain. Harris [5] gives a method for staining Negri bodies. To judge by his photo-micrographs and coloured plate it yields good results. Here is the technique :—

In the routine examination, smears between two glass slides are made from the cornu ammonis, cerebellum, and cerebral cortex. Two slides are preferable to one slide and one cover-glass, as the thickness of the smear can be controlled more easily and there is less danger of soiling the hands. The smear is to be treated as follows :—

Fix in methyl alcohol one minute.
Wash briefly in water to remove the alcohol.
Immerse in an old saturated solution (95 per cent. alcohol) of alcohol soluble eosin from one to three minutes.
Wash two or three seconds in water to remove the excess of eosin.
Immerse in a fresh solution of Unna's alkaline methylene blue 5 to 15 seconds.
Wash briefly in water.
Decolourise in 95 per cent. alcohol; and follow with absolute alcohol, xylol and balsam, or blot and dry in the air.
The entire process requires less than five minutes.

The structure of the bodies is more sharply defined if the smear is not allowed to dry before being fixed and stained. Smears which have dried for several days or weeks cannot be stained satisfactorily.

The older the saturated solution of eosin (alcoholic), the more rapidly and intensely it stains. A solution less than two months old will not yield good results.

The methylene blue (Unna's) will produce a very disturbing precipitate if it be older than a week or two. The fresher the solution the more sharply defined are the "inner" bodies.

During the decolorisation the slides should be examined from time to time. Decolourise until only the nerve cells are blue and the red cells have become bright red. It has been our experience that when the red blood cells appear red, the nucleoli of the nerve cells a deep blue, and the protoplasm a pale blue, the Negri bodies will be seen coloured a light red with sharply defined dark bluish-red "inner" bodies. It is better to decolourise too much than too little. The results will be more uniform if the staining is done in staining dishes or jars.

The advantages of this method are :—

Strong contrast between Negri bodies, nerve cells, and blood cells; the absence of a granular precipitate, so disturbing in many methods as to render the recognition of the small-sized bodies impossible; rapidity and simplicity.

In the staining of material fixed in Zenker's fluid or acetone, the section should be stained three to five minutes in the eosin and thirty seconds to two minutes in the methylene blue. In sections the inner bodies appear a deep blue.

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[1] Tuffier and Martin (January 10, 1910), *Rev. de Chir.* Quoted in *Medical Annual*, 1911.

[2] Da Costa, A. C. (January 28, 1908), "Sur la présence de corpuscules de Negri dans la surrénale du cobaye rabique." *Bull. Soc. Portug. Sciences Naturelles.*

[3] Babes, V., and Stefanesco, E. (January 2, 1908), "Étude comparative sur l'apparition des lésions rabiques et des corpuscles de Negri." *C. R. Soc. Biol.*

[4] Babes, V. (January 2, 1908), "Sur le diagnostic histologique de la rage." *Ibid.*

[5] Harris, D. L. (December 18, 1908), "A Method for the Staining of Negri Bodies." *Journal Infectious Diseases.*

Hydrophobia— *continued*

Pace [1] is the author of an illustrated paper on parasites and pseudo-parasites of the nerve cells. In rabies he has found eosinophile formations occurring as—

(1) Very fine granules like a powder at the poles of the nerve cells.

(2) Larger granules having the same situation.

(3) Corpuscles enclosed in a kind of central morula and arranged about the nucleus in the form of a rosette.

He asks if these are Babes' granules which take on a black stain by a silver impregnation method, and states that very similar pseudo-parasites are found in the ganglion cells in the course of other diseases. He also gives an account of true parasites of nerve cells found in fish, etc.

Negri [2] finds that his corpuscles retain Gram's stain, a fact, he thinks, in favour of their being protozoa. He gives the technique for the staining method, which need not be quoted here. A very important publication is the *Bulletin of the Pasteur Institute of Southern India*. In its first number Cornwall and Pai [3] signalised the frequent presence of Negri bodies in the ganglionic layer of the retina in fixed virus, *i.e.* a virus exalted in virulence by serial passage through rabbits. They are usually very small, but have not been found in the retinæ of animals dying from other causes than rabies. They give the technique for their recognition in this situation :—

In the first place the eye should be extracted as soon after death as possible, for the retinal elements quickly undergo destructive changes, though these are less noticeable in the cells of the ganglionic layer with which we are particularly concerned than in the more delicate rods and cones. The eye may be fixed as a whole in acetic bichromate mixture, or the retina may first be dissected out and fixed alone. We found the latter a tiresome procedure and usually fixed the whole eye. After fixation the retina must be dissected out, and may either be made into a ball with collodion or lifted about as it is and embedded in paraffin in the usual way. The section should not be more than 4 μ–5 μ in thickness.

The best stain is Mann's mixture. To get certain results the eye must be fresh, the sections of the best and the staining perfect. The whole process is scarcely more laborious and difficult than getting a good preparation of any part of the brain. Negri bodies appear as brightly stained reddish dots in the pink cytoplasm of the cells of the ganglionic layer, often with an unstained area round them. They are seldom as much as 2 μ in diameter, and generally less. Not every cell contains the bodies, perhaps only 1 in 10 of those cells which are sufficiently well displayed to the view, but then it must be remembered that cells are only seen in thin section. As many as ten have been seen in one cell, but usually there are not more than one or two. Their distribution is irregular, but it does not seem that they are confined to, or are more numerous in, any particular region of the retina.

Even when no Negri bodies can be seen there is often considerable degeneration of the ganglion cells; the nucleus becomes indistinct or disappears, the cytoplasm vacuolated and the chromatic substance collects at the periphery of the cell. Occasionally one to five tiny, deeply stained blue dots, scarcely ·2 μ across, have been noticed in cells which do not contain Negri bodies, but their significance is unknown.

As regards routine examinations they present some very useful notes :—

Negri bodies were found in a portion of the brain in every case in which subdural inoculation gave a positive result, provided that the material had been sent in a proper fixing medium, *i.e.* acetic bichromate mixture. In more than one case Negri bodies were found in the fixed material, whereas the glycerine specimen failed to convey rabies. These brains had been sent from great distances during the hot weather, and had been from eight days to one month *en route*.

When material has to be sent great distances, it is probable that the microscopic method is superior to the inoculative.

If specimens arrived preserved only in glycerine they were fixed and sectioned in the usual way, but very poor preparations are thus obtained, and it is doubtful whether Negri bodies can always be recognised with certainty after the tissue has been soaked in glycerine two or more days. We failed, after this procedure, to recognise the bodies on some occasions though the inoculation was positive, but succeeded in others.

Tissue fixed in alcohol 90 per cent. or formalin 5 per cent. will enable the bodies to be recognised provided that a volume of fluid, at least twenty times the bulk of the piece, be used, but one cannot rely on good preparations with either of these fixatives.

A rapid diagnosis can generally be made by teasing out a fragment of a fixed hippocampus in water, when Negri bodies can be clearly made out in the isolated and unstained nerve cells. We have not relied on this performance for a positive diagnosis, much less for a negative one, but it has so far been supported by the finds in the stained sections.

To demonstrate Negri bodies for certain the best all-round stain seems to be Mann's watery eosin and methyl-blue mixture. The bodies show up fairly well after staining with any acid dye and differentiating, but for routine use Mann's stain has certain advantages over them all. It is not necessary to adhere rigidly to the instructions given by Mann, two hours' immersion in the stain with subsequent differentiation is ample, though a stay of twenty-four hours, if convenient, does no harm.

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[1] Pace, D. (April 7, 1908), "Parasiten und Pseudoparasiten der Nervenzelle, etc." *Zeit. f. Hyg. u. Infekt.*, Vol. LX.

[2] Negri, F. (1909), "Iodoresistenza del corpi di Negri e suo significato." *Ann. Ig. Sp.*, quoted in *Bull. de l'Inst. Past.*, 1909, p. 644.

[3] Cornwall, J. W., and Pai, M. K. (1908), *Bulletin of the Pasteur Institute of Southern India*, No. 1.

A more rapid stain is that of Unna, which gives beautiful pictures and more structural detail than Mann's, but it is not so reliable for mere diagnosis.

Rosanilin violet is at times a useful stain when no contrast colour is required. Half-an-hour in a saturated aqueous solution and differentiation in 90 per cent. alcohol depicts Negri bodies very clearly but without much detail. Some experience of it is desirable, otherwise errors may be fallen into.

The internal structure of the bodies is best brought out by various manipulations with alcoholic eosin and alkaline methylene blue followed by differentiation in acid and alkaline alcohols, which cannot be repeated with invariable success, far less described. Instead of paraffin sections the smear and dab methods described by several writers should be of value when dealing with fresh, unfixed brains. Teasing out fresh hippocampus in dilute acetic acid does not often display very much. The large nerve cells are so delicate and their processes are so interlaced that they can seldom be freed from their connections in the fresh state. Such a preparation shows little but cell nuclei, which are tougher than the cytoplasm, and myelin globules.

Dabs and smears—if whole, uninjured, isolated nerve cells can be rapidly fixed on the slide—ought to provide a means of studying the included Negri bodies something better than sections; but owing to the delicacy and entanglement of the cells alluded to above, it is exceedingly difficult to get preparations worth anything at all.

In their introductory note on these corpuscles they say :—

The presence of the bodies first described by Negri in 1903 in the cells of the nervous system of all animals, including man, which have died of naturally acquired rabies, seems now to have been established beyond dispute, and so invariable is their occurrence that in some institutes—*e.g.* Turin and Algiers—the microscope is exclusively relied upon to determine whether a suspected animal has died of rabies or not.

No similar appearances have ever been noticed in the nerve cells of animals dying from other causes, or in healthy brains, with the single exception of that of the cat, to which we shall recur.

Negri bodies are generally so numerous that an examination of a single section of the cortex, cerebellum or hippocampus major, brings dozens or even hundreds into view. It has been affirmed that they are occasionally absent from the hippocampus while present in the cerebellum, or *vice versâ*, but our experience has been that if they appear in the one they also appear in other parts. It has also been reported that they are occasionally so few and far between that a long search of many sections only reveals one or two. This has not yet occurred to us.

That they tend to occur in clumps there is no doubt; for, in sections of cortex, hippocampus and cerebellum some parts may be found practically free while others will be crowded with the bodies. The hippocampus major is usually regarded as the seat of election of these bodies, and it is the part of the brain one naturally turns to in making sections for the microscopic diagnosis, but this is more on account of the number of large ganglion cells found in that situation, which renders the recognition of the bodies easy, than because it is the seat of a specific lesion.

Nearly as many and nearly as large Negri bodies can be found in both the cortex and the cerebellum, but the size of the bodies depends on the size of the cell that contains them, and though they are easy to see in the large hippocampal ganglion cells, the oval cells of the cortex and Purkinje's cells in the cerebellum, they may be quite difficult to find in the small cell layer of the hippocampus and the small pyramidal cells of the cortex, and cannot be seen at all in the small cells of the cerebellum.

When we leave the brain and examine sections of the spinal cord, Negri bodies are not found with such ease, but a greater degree of degeneration of the nerve cells is met with than is common in the brain. The ganglia on the posterior nerve roots, however, with their large cells afford excellent pictures, and the degenerative changes induced by the Negri bodies can be studied here perhaps more easily than elsewhere.

It is by no means the case, as some authors would have it, that the presence of Negri bodies has no effect on the including cell or that the bodies are seen only in cells that are apparently quite uninjured.

Two or three bodies, it is true, may frequently be seen in apparently uninjured cells in which the cytoplasm, nucleus and nucleolus, are all as clearly defined as in a healthy brain, and it is in such cells that the clearest view of the inner structure of the bodies is obtained.

One may find, on the other hand, numerous cells, the nuclear structure of which has been entirely disintegrated, and the bodies, perhaps a dozen in number, which occupy the badly staining cytoplasm may be themselves in consequence ill defined. Other disorganised cells may be seen in which no bodies can be distinguished. A peculiar and most important difference between natural rabies and the rabies which has been passed through hundreds of rabbits subdurally, and is known as the fixed virus of antirabic institutes, is the fact that, whereas Negri bodies are abundant and easily recognised in the former, in the latter they are either absent or so small as to be seen with difficulty.

Finally, in speaking of human rabies, they say that typical Negri bodies are not always to be found in human brains even when the tissue is obtained in a fresh condition, and fixed and stained by methods which under ordinary circumstances never fail to give good results. They further note that there is a possibility of the existence of varieties of the rabies organism which do not furnish the same microscopical appearances as the Negri bodies. The latter, though not found in a human case, may reappear in the sub-passages in animals, though they may be of smaller size. We have quoted largely from this report, to which we may again have occasion to refer, for it is certainly the best article in English on the subject which we have so far encountered and cannot fail to be of value. Any one who has to work at rabies is recommended to obtain these excellent publications. Other papers on the differences in the occurrence of Negri bodies, as a result of the subcutaneous inoculation of rabic virus, derived (*a*) from the central nervous system, (*b*) from the salivary glands, and on certain changes in their size, will be found in the second of the reports.

Hydrophobia—*continued*

A most useful paper from the veterinary and laboratory standpoint is that by Raymond.[1] He gives special directions for the examination of the plexiform ganglion and an excellent coloured plate illustrating its dissection. He illustrates the histo-pathological changes in the plexiform ganglion, the medulla and the spinal cord of rabid dogs, as well as Negri bodies in the large nerve cells of the hippocampus. His notes on technique, staining, etc. will be found useful. Considerations of space prevent any quotation save that on the inoculation method. Here is the description of the procedure :—

> The brain pan of three rabbits is shaved, washed, and disinfected with absolute alcohol; the skin is incised under chloroform so as to permit a disc of bone to be removed with a very small trephine. A small quantity of an emulsion of the medulla of the suspected animal is injected; the skin is then closed with a stitch, treated with an antiseptic, dried and painted over with collodion. Another method is to cocainise the eye and to inject a small quantity of the emulsion into the anterior chamber. The emulsion is made by rubbing down some of the brain with the usual precautions and filtering the emulsion through sterilised butter muslin. The inoculation test is generally a reliable means of diagnosis; but a period of 13 to 18 days ensues on an average before the reaction shows itself; this is a very serious delay in cases where people who have been bitten want to know what they should do. The method is not infallible either; but failure is comparatively rare. Septicæmia is apt to cause trouble when the intracranial method is used with unfresh specimens. The results of the intra-ocular method take longer to appear, and may take a very long time, but the danger arising from septicæmia is not so great. When the brain is sent in putrid, or when it is preserved in antiseptics, inoculation fails.

Neri [2] has invented a new method of staining the Negri bodies which provides a quick means of diagnosis. Fix tissue in alcohol or acetone (Henke's or Teller's method), embed in paraffin and cut. After the usual treatment stain the sections for ten minutes in the following solution : Eosin 1 gramme, iodine 0·1 gramme, potassium iodide 2·2 grammes, distilled water 100 c.c. They are then carefully washed in distilled water, stained for five minutes in a watery solution of methylene blue (1 in 1000), and again rapidly washed in distilled water. Then the sections are differentiated in 95 per cent. alcohol, whereby their colour changes from a reddish-blue into a fine pink, and further dehydrated with absolute alcohol, dried, cleared up with xylol and mounted. In sections stained according to this method the Negri bodies adopt a bright reddish-violet colour, whilst the protoplasm of the cells shows a pale bluish, the nuclei and nucleoli a deeper blue colour.

Lentz [3] has given up Mann's stain owing to defects in it, and employs the following :—

(1) The section is fastened to the cover-glass, freed of paraffin, and stained in Hoehst extra B. eosin for one minute. The solution consists of eosin ·5, 60 per cent. alcohol, 100.

(2) Rinse in water.

(3) Counter stain for one minute in Lœffler's methylene blue.

(4) Rinse again.

(5) Differentiate by immersing in absolute alcohol, to every 30 c.c. of which five drops of a 1 per cent. solution of caustic soda in absolute alcohol has been added. The sections remain in this alcohol until they show only a slight reddish tint.

(6) Differentiate in absolute alcohol, to every 30 c.c. of which one drop of a 50 per cent. solution of acetic acid has been added, until the lines of ganglionic cells in the hippocampus are just visible as slightly blue streaks.

(7) Rinse in absolute alcohol and xylol, and mount in Canada balsam.

Indeed, there is no end to the methods for demonstrating Negri bodies. A paper by D'Amato and Flaggella [4] may be cited which also mentions the so-called Lentz bodies, and deals with the changes in the nerve centres in hydrophobia. It is illustrated by two coloured plates, which show rather more detail than usual. A well-illustrated and useful monograph which reviews the whole subject of rabies, and deals at some length with the question of Negri bodies, is that by Stimson.[5] It would take too long to give all the directions for technique in detail, but the following points are dealt with—

(1) Removal of the brain of animals for inoculation.

(2) Locating the hippocampus or cornu ammonis.

(3) Locating the plexiform ganglion.

(4) Staining Negri bodies.

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[1] Raymond, F. (1909), "Some Notes on Rabies." *Journal Tropical Veterinary Science*, Vol. IV., Part 3.

[2] Neri, F. (1909), "Le diagnostie rapide de la rage. Nouvelle méthode de coloration des corps de Negri." *Cent. f. Bakt.*, I. Orig., Vol. L., No. 3.

[3] Lentz, (May 6, 1909), "Bericht über die Tätigkeit der Wutschutzabteilung am K. Institut für Infektionskrankheiten zu Berlin, etc." *Berl. Tierärztl. Woch.*, No. 18.

[4] D'Amato, L., and Flaggella, V. (1910), "Negrische Körper, Lentische Körper und Veränderungen der nervösen Zentren in der Wutkrankheit." *Zeit. f. Hyg. u. Infekt.*, Vol. LXV.

[5] Stimson, A. M. (1910), "Facts and Problems of Rabies." *Hygienic Laboratory, Bull. No. 65, Public Health and Marine Hospital Service, U.S.A.*

This we give as a contrast to the others :—

Smears are made on slides or cover-glasses by crushing a small section of the brain matter between two of them, and drawing them out under gentle pressure to produce a fairly thin film.

(*a*) Fixation in Zenker's solution for fifteen minutes.

(*b*) Wash in tap-water.

(*c*) Ninety-five per cent. alcohol tinted with iodine.

(*d*) Absolute alcohol five minutes.

(*e*) Five to 10 per cent. watery solution of eosin (Grubler, W. g.) five minutes.

(*f*) Stain in Unna's polychrome methylene blue two to three minutes.

(*g*) Wash in water.

(*h*) Differentiate in 95 per cent. alcohol.

(*i*) Blot off, dry, and examine with oil immersion lens.

Sections.—Fix thin pieces in Zenker's solution for two and one-half to three hours. Wash well. Ninety-five per cent. alcohol, two changes, one hour each. Absolute alcohol, two changes, one hour each. In cedar oil until cleared. Cedar oil and paraffin equal parts, one hour. Paraffin, two changes, one hour each. Embed section and stain as above, but increase time somewhat, especially in iodine-alcohol, where the sections should remain until the mercury granules disappear.

Negri bodies stained in this way take a magenta colour, easily distinguished from the bright eosin tint of the red-blood corpuscles, and dark-bluish granules are distinguishable in their interior. The nerve cells and the nuclei of the glia and the endothelial cells are blue.

This method of staining is less successful following more rapid methods of fixation, but fairly good pictures are obtained with sections fixed in acetone.

The material is placed in acetone for forty-five minutes, then in several changes of paraffin ; embedded and sectioned. The iodine-alcohol step is omitted.

Following this comes a section on animal inoculations with a full description of Oshida's method for removal of the spinal cord. The monograph as a whole is an excellent review of our present knowledge of rabies, deals with pathology, symptoms, diagnosis, immunity, treatment, suppressive measures, sums up the whole situation tersely, and provides a good bibliography.

We have only space to deal very briefly with other papers.

Bain and Maloney [1] give an account of cases seen in Egypt. It deals specially with the clinical symptoms, is interesting as an account of the disease in natives, and gives information regarding the length of the incubation period and the results of anti-rabic treatment in Cairo. M'Fadyean [2] considers rabies in his papers on the ultravisible viruses. That of rabies is arrested by the ordinary Berkefeld and Chamberland filters, a fact which would lead one to think that it must be larger than the microbe of bovine pleuro-pneumonia, and therefore visible. The most porous or V (*viel*) variety of the Berkefeld candle, however, allows the virus to pass under certain conditions, and as most of the Negri bodies are much too large to do so, they would not appear to constitute the virus. They may, of course, contain it, for trituration has to be thorough for the virus to pass the V Berkefeld candle, and the granules or whatever form it may take, may be expressed from the corpuscles.

Personally, this fact makes one think that Babes may be correct, especially in view of the new facts accumulating regarding the rôle of infective granules in protozoal diseases.

Atypical, abortive, and atrophic forms of rabies are of interest. Those desirous of studying them may refer to papers in the *Indian Medical Gazette* for July, 1909, the *Zeitschrift für Hygiene*, etc. for November 26 of the same year, and No. 36 of the *Scientific Memoirs of the Government of India* respectively. Another paper on atypical rabies occurs in the above-mentioned *Zeitschrift* for October 28, 1910. Lignières [3] records some peculiar cases in animals, including one of spontaneous recovery of a dog from dumb rabies, the occurrence of an intermittent form in a cow, and a bovine case where the incubation period was three years. Rabies in oxen can be, and is, prevented in France by intravenous injection of an emulsion of medullary substance from the dog which has inflicted the bite. The *Lancet* of January 8, 1910, in an article entitled "Rabies in India," comments on the work of the Kasauli Pasteur Institute, and has the following notes :—

The wisest procedure to adopt in the case of dog bite is to cauterise the wound immediately, to secure the animal if possible, and keep it under observation segregated for ten days. If at the end of the tenth day after inflicting the bite the animal is alive and well, it is not suffering from rabies. If, however, the animal shows any

[1] Bain, A., and Maloney, W. J. (September 11, 1909), "Rabies, with Notes of Thirty Cases." *Lancet.*

[2] M'Fadyean, J. (September, 1908), "The Ultravisible Viruses: Rabies." *Journal Comparative Pathology and Therapeutics.*

[3] Lignières, J. (May 1, 1909). *Révue Vétérin.*

Hydrophobia—*continued*

symptoms of rabies the patient should proceed to a Pasteur Institute immediately, and bring with him portions of the dog's brain in bottles, preserved in glycerine or Zenker's fluid. He should be accompanied by all persons bitten or licked by the infected animal, and should further try to gather as much information as possible about the animal so as to discover whether other animals or persons have been infected. All such animals should be segregated for six months, and all infected persons should undergo Pasteur treatment at once.

Remlinger [1] contributes a paper on the latency of the rabic virus in the nerve centres. He says it is not necessary to exaggerate the importance of this latency, which is probably the exception, not the rule. There have been many recent papers on immunity in rabies, but these we must pass by and consider finally a few articles dealing with prevention and treatment. Before doing so, brief mention may be made of a paper by Zwick [2] on the curious condition known as false rabies, which affects domestic animals. It is readily distinguished from hydrophobia by its short incubation period, the rapid course of the illness, the absence of aggressive symptoms, the fact that the blood and various other organs, with the exception of the brain and spinal cord, are infectious, and that subcutaneous injection succeeds, a marked local reaction resulting. Bodies have been found in the brains of deceased animals which may be the cause of a disease characterised by an extraordinary restlessness, with incessant scratching, rubbing, biting, etc., of the body.

Smith [3] has suggested a very excellent set of rules for adoption in India with a view to preventing rabies in a country where the incidence of hydrophobia may safely be said to bear a simple relation to the number of dogs kept on a station. They are too long to quote here, but concern licensing, the issue of badges, the catching and destroying of ownerless dogs, etc. The penalties are advisably high. Scott [4] has recorded an Indian case where the violent spasms were relieved by the combined effect of scopalamine and morphine. Hyoscine hydrobromide was employed following injections of morphia.

In the case of animals, Remlinger [5] recommends vaccination by means of mixtures of virus and antirabic serum, the former being in excess.

Influenza. Some have thought that Pfeiffer's bacillus has played a part in certain cases of cerebro-spinal meningitis. Cohen [6] has studied the subject in three cases of septicæmic cerebro-spinal meningitis in children where he isolated an organism like the influenza bacillus morphologically and in culture, but differing from it in other respects. This bacillus is found in the blood, and, in addition to meningeal lesions, produces purulent effusions in serous cavities. The author regards it as distinct from *B. influenzæ*. Batten,[7] however, has recorded cases of meningitis in children which appear undoubtedly to have been due to Pfeiffer's bacillus. In such cases the diagnosis must rest entirely on the bacteriological examination, as, clinically, the condition cannot be distinguished from other forms of meningitis. Urotropine in large doses is considered worthy of a trial in such cases, because it is said to exercise an inhibitory effect on the growth of organisms in the cerebro-spinal fluid.

Allen [8] has a short paper on the symbiosis of other organisms, such as the pneumococcus or staphylococcus with the bacillus of influenza. He thinks they may weaken the tissues and pave the way for invasion by Pfeiffer's organism. He thinks that possibly vaccine treatment should be directed against them, as it is very hard to influence a chronic influenzal infection even when very large doses of the organism are employed. In a paper entitled "The Bacteriology of Influenza," the *Lancet* reviews a paper by Thursfield,[9] and deals with some interesting points, for views are changing about *B. influenzæ*. Organisms hitherto classed as such would appear to belong to a group, the various members of which possess very different pathogenic powers. What is clinically called influenza is not one disease, but a series caused by different microbes. The paper concludes :—

It will thus be seen that the presence of an organism conforming in every particular to Pfeiffer's bacillus does not necessarily indicate that there has been an influenzal infection. There would appear to be many "strains" of the bacillus, each possessing very different pathogenic powers, being in this particular somewhat similar to the characteristics exhibited by bacilli of the colon group. In some respects also a resemblance to the pneumococcus

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[1] Remlinger, P. (October 25, 1910), "Contribution à l'Étude de la Latence du Virus rabique dans les centre nerveux." *Ann. de l'Inst. Past.*

[2] Zwick, (October 4, 1910), "Über die sogenannte Pseudowut." *Cent. f. Bakt., Beilage zu* Abt. I., Vol. XLVII. *Referate.*

[3] Smith, F. A. (March, 1910), "The Prevention of Hydrophobia." *Indian Medical Gazette.*

[4] Scott, L. B. (January, 1910), "A Case of Hydrophobia." *Ibid.*

[5] Remlinger, P. (November 1, 1910), "Le traitement de la rage chez les animaux." *Revue Gen. Med. Vet.*

[6] Cohen, (April, 1909), "La Méningite cérébro-spinale septicémique." *Ann. de l'Inst. Past.*

[7] Batten, F. E. (June 18, 1910), "Influenzal Meningitis." *Lancet.*

[8] Allen, R. W. (May 7, 1910), "The *Bacillus influenzæ* and Symbiosis." *Ibid.*

[9] Thursfield, J. H. (October, 1910), "Influenzal Septicæmia, with a Short Review of the Present Status of *Bacillus influenzæ*." *Quarterly Journal of Medicine.*

Influenza —*continued*

and other organisms is shown, in that, although present in an apparently healthy body, or in a lesion, they do not produce their usual morbid effects. Further, the bacillus of Pfeiffer has been found in the secretions of the nose and throat for long periods after an attack of influenza has subsided, and it has been suggested that in this manner the interval between one epidemic and another may be bridged over. The question whether such cases may come under the category of germ carriers offers an interesting field for further research.

Ghedini [1] summarises no less than fifteen different groups of cutaneous affections described in association with influenza :—

(1) Morbilliform. (2) Scarlatiniform eruptions. (3) Urticarial. (4) Papular erythemata. (5) Polymorphous erythema. (6) Hæmorrhagica purpura. (7) Pemphigus. (8) Herpes. (9) Suppurative dermatitis. (10) Serous dermatitis. (11) Erysepilatous eruptions. (12) Œdematous infiltrations. (13) Pigmentary changes—for example, vitiligo. (14) Trophic changes—for example, sudden whitening of the hair ; alopecia. (15) Miliaria.

The question arises as to whether these numerous rashes are really influenzal or coincident rashes due to some other cause. The author adduces four cases observed by him where there appeared no doubt, from careful examination, that the cause in these cases was influenza. In his cases one assumed a scarlatiniform type, two a morbilliform, and the last showed as multiple cutaneous vasomotor œdema. In each of the cases the influenza bacillus was detected.

Jones [2] contends that influenza may be, and frequently is, a chronic intoxication, a belief worth remembering.

A paper of greater interest to tropical workers is that by Thayer.[3] He points out that there may be an intermittent fever in influenza simulating malaria, and gives two illustrative cases. In one the febrile paroxysms were very sharp, were associated with definite chills, and occurred regularly in the morning hours, as is common in malaria. When it is remembered that malarial cases are encountered which can only be diagnosed by splenic puncture or the therapeutic test, it will be apparent that it is well to bear influenza in mind, and also in cases where the latter is epidemic not to forget the possibility of malarial infection.

As regards treatment, Lipa [4] strongly advocates the use of quinine both by the mouth and by injection. He regards it as a specific and as preferable to salipyrin, a combination of salicylic acid and phenazone, which has been recommended in 10 to 15 grain doses, four times daily, along with the following draught :—

℞.	Spir. ammon. aromat.,	m $\bar{x}\bar{x}$
	Spir. ætheris. nitros.,	
	Glycerini,	āā $\bar{3}$ js
	Tinct. card. co.,	m $\bar{x}\bar{x}$
	Aquæ,	ad. $\bar{3}$ js

Thresh and Beale [5] speak highly of liquid Kolynos, which contains benzoic acid, eucalyptus oil, peppermint oil, and thymol, and which they found can kill *B. influenzæ* practically instantaneously in the strength (33 per cent.) recommended for use. It should be used as a fine spray for the throat and nostrils.

Insects. Apart from flies, mosquitoes and the insects producing myiasis in man, fleas are probably the most important of this great group of the animal world, so far as human pathology is concerned. Hence we find a considerable number of papers devoted to their consideration, chiefly of course with reference to the part they play in plague. It is possible that in kala-azar also their vogue as virus transmitters will be proved. Their probable rôle in enteric fever has already been mentioned.

A paper missed in our last Review is that by Jordan and Rothschild [6] wherein they revise the whole family *Sarcopsyllidæ*, enter fully into the literature, and provide numerous illustrations. The *Sarcopsyllidæ*, which constitute of course only one group of fleas, are, say the authors, plainly a development from the less specialised family *Pulicidæ ;* in fact, the gradation in the development of the organs from a generalised to a more specialised stage is strikingly illustrated in these insects. The family is of interest here in that it contains the genus *Dermatophilus*, *D. penetrans* being the Chigger or Chigoe. Another of this genus, *D. cæcata*, was found parasitic on *Mus rattus* in Brazil. McCoy and Mitzmain [7] conducted

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[1] Ghedini, G. (October 24, 1910), *Rif. Med.* quoted in Epitome, *British Medical Journal*, February 4, 1911.

[2] Jones, G. I. (February, 1911), "Chronic Influenza and its Relation to Neuropathy." *American Journal of Medical Sciences.*

[3] Thayer, W. S. (April, 1911), "Clinical Notes, Intermittent Fever in Influenza simulating Malarial Fever." *Bulletin of The Johns Hopkins Hospital.*

[4] Lipa Bey (1909), "Chininphytin bei Influenza." *Ärztl. Rundschau*, No. 16.

[5] Thresh, J. C., and Beale, J. F. (May 21, 1910), "The Action of Liquid Kolynos upon the Bacillus of Influenza." *Lancet.*

[6] Jordan, K., and Rothschild, N. C. (1906), "A Revision of the Sarcopsyllidæ." *Thompson, Yates and Johnston Laboratories Reports*, Vol. VII., Part 1.

[7] McCoy, G. W., and Mitzmain, M. B. (February 19, 1909), "An experimental investigation of the Biting of Man by Fleas taken from rats and squirrels." *Public Health Report, United States Public Health and Marine Hospital Service*, Vol. XXIV., No. 8.

Insects— *continued*

experiments in San Francisco to discover with what readiness and avidity fleas found on rats will bite man. As regards the two important species, *Lœmopsylla cheopis* and *Ceratophyllus fasciatus*, they found that a considerable percentage of both, with or without previous starvation, will attack man if given an opportunity to choose between a man and a rat. Moreover, they can be kept alive for long periods when fed only on human blood.

They also found that some other species will bite man at all times. This same subject has more recently been investigated by Chick and Martin.[1] They give a long table of references, and present the following list of fleas which, so far as is at present known, are those commonly infecting both *Mus rattus* and *Mus decumanus*.

(1) *Xenopsylla cheopis* (Rothschild).

Synon. *Pulex cheopis*, Rothschild, 1903.
Pulex pallidus, Tidswell, 1903.
Pulex brasiliensis, Baker, 1904.
Pulex murinus, Tiraboschi, 1904.
Pulex philippinensis, Herzog, 1904.
Lœmopsylla cheopis, (Rothsch.), Rothschild, 1908.

(2) *Ceratophyllus fasciatus* (Bosc.)

(3) *Ceratophyllus anisus*, Rothschild, 1907.

(4) *Ctenopsylla musculi* (Duges).

(5) *Ctenophthalmus agyrtes* (Heller).

The dog flea (*Ctenocephalus canis*), the cat flea (*Ctenocephalus felis*), the fowl flea (*Echidnophaga gallinacea*), and the human flea (*Pulex irritans*), are also sometimes found upon rats, but they appear to be only occasional visitors. In certain localities, however, they have formed quite a considerable proportion of the fleas captured.

They are of opinion that "the particular fleas found in greatest numbers upon rats seem to be determined by geographical position, including climate and the habitat of the rats examined." The influence of species of rat appears to be indirect and due to a general difference in mode of life and distribution. An account is given of the distribution of the different species, the views held regarding the readiness with which they will attack man, and the new experiments performed at the Lister Institute with *C. fasciatus*, *C. musculi*, and *C. agyrtes*. The following is the summary given :—

(1) As far as at present known, the great majority of the fleas infesting *Mus rattus* and *Mus decumanus* in different parts of the world, belong to either the species *Xenopsylla cheopis*, *Ceratophyllus fasciatus*, *Ceratophyllus anisus*, *Ctenopsylla musculi*, or *Ctenophthalmus agyrtes*, or are comprised of some admixture of these five species.

(2) *Xenopsylla cheopis* is the most prevalent in the Tropics and subtropical regions, and often occurs there to the almost complete exclusion of other species. It is common during summer and autumn in some of the warmer parts of the temperate zone, more especially in ports which have maritime intercourse with the Tropics.

(3) In the cooler regions *Ceratophyllus fasciatus* is the most universally distributed flea, and is associated with more or less of *Ctenopsylla musculi* and *Ctenophthalmus agyrtes* according to the locality and the habitat of the particular rats.

(4) In Japan *Ceratophyllus fasciatus* is replaced by *Ceratophyllus anisus*, a closely allied species.

(5) The numerous other fleas which have been captured off rats are only occasional visitors.

(6) *Ceratophyllus fasciatus*, like *Xenopsylla cheopis*, readily bites man. Out of 517 experiments 308 fed, or 59 per cent. were positive. In 101 experiments, under identical circumstances with a rat, 59 or 58·4 per cent. of the fleas fed.

(7) The experiments with *Ceratophyllus fasciatus* were made upon eight persons, and evidence was obtained of preference on the part of the insects for particular individuals.

(8) 111 experiments were made with 46 specimens of *Ctenopsylla musculi ;* only 4 fed = 3·6 per cent., whereas 9 out of 11 fed on a mouse.

(9) 68 specimens of *Ctenophthalmus agyrtes* were tried, in some cases upon three persons. None fed, whereas 11 out of 19 of the same fleas fed on a rat under identical conditions.

They conclude an interesting paper by saying that "*Xenopsylla cheopis* and *Ceratophyllus fasciatus* are the species of rat fleas which, when hungry, readily bite man. There is no reason to suppose that *Ceratophyllus fasciatus* would not be as efficient an agent in the transmission

[1] Chick, H., and Martin, C. J. (March, 1911), "The Fleas common on Rats in different parts of the world, and the readiness with which they bite Man." *Journal of Hygiene.*

Insects—*continued*

of plague from rat to man as *Xenopsylla cheopis* has been shown to be in India." Rothschild[1] deals with the fleas found on "domestic" rats and mice, *i.e.* the Norway rat, the black rat, and *Mus musculus*. He considers first the Chigoes (*Sarcopsyllidæ*), and gives the following key to the genera :—

(*a*) Hind coxa without a patch of spines on the inside.	
(*a* 1) Hind femur simple	1. *Dermatophilus.*
(*b* 1) Hind femur with a large tooth-like projection near the base . . .	2. *Hectopsylla.*
(*b*) Hind coxa with a patch of short spines on the *inside*	3. *Echidnophaga.*

Then he passes to the true fleas or *Pulicidæ*, and again supplies a key to the genera of Section 1, in which the club of antenna is distinctly segmented only on the hind side ("hind" side when lying in the groove). Here is the table :—

(*a*) No comb on head and thorax.	
(*a* 1) The internal incrassation, which extends from the insertion of the mid coxa into the thorax, joins the anterior edge of mesosternite . .	4. *Pulex.*
(*b* 1) This incrassation joins the upper edge of the mesosternite . . .	5. *Xenopsylla.*
(*b*) With a comb on the pronotum only	6. *Hyplopsyllus.*
(*c*) With a comb on the pronotum and at the lower edge of the head . . .	7. *Ctenocephalus.*

In Section 2 the club of the antenna is distinctly segmented all round, and the key to the genera is as follows :—

(*a*) Eye developed.	
(*a* 1) No comb on head.	
(*a* 2) Pygidium not projecting backwards ; frons with tubercle . . .	8. *Ceratophyllus.*
(*b* 2) Pygidium strongly convex, projecting backwards ; frons without tubercle	9. *Pygiopsylla.*
(*b* 1) Two spines at angle of gena	10. *Chiastopsylla.*
(*b*) Eye vestigial or absent.	
(*a* 1) Abdomen without comb.	
(*a* 2) Hind edge of tibiæ with about 8 short and several long bristles, which do not form a comb.	
(*a* 3) Fifth segment in fore and mid tarsi with 5, and in hind tarsus with 4 lateral bristles	11. *Neopsylla.*
(*b* 3) Fifth segment in fore and mid tarsi with 4 and in hind tarsus with 3 lateral bristles, there being an additional pair of bristles in all the tarsi on the ventral surface in between the first pair . . .	12. *Ctenophthalmus.*
(*b* 2) Hind edge of tibiæ with about 12 short and 3 long bristles, the short ones forming a kind of comb	13. *Ctenopsylla.*
(*b* 1) Abdomen with at least one comb	14. *Hystrichopsylla.*

For the differentiation of species, their geographical distribution, and for information regarding the species of rodent on which these fleas are found, reference must be made to the paper, which is illustrated. McCoy and Mitzmain[2] have worked at the regional distribution of fleas on rodents, and say :—

It would appear from the data presented that the favourite location for the common rat fleas of this vicinity, *Ceratophyllus fasciatus*, Bosc., and *Lœmopsylla cheopis*, Roth., is about the hind-quarters of the rat; while *Ctenopsylla musculi* (Duges), Wagner, prefers the region of the head and neck.

The same regional distribution of rat fleas was found in the case of the guinea-pigs.

Squirrel fleas are most numerous on the hind-quarters.

These observations, while they are not to be insisted upon as throwing any special light upon the regional distribution of buboes in naturally infected plague rats, are of particular interest in showing the very constant preference of *Ct. musculi* for the region of the head and neck.

In regard to the other species of fleas it should be borne in mind that the skin areas are not of equal dimensions ; that of the head and neck being smallest ; that of the hind-quarters being the largest ; and the skin area of the fore-quarters being between these in size.

Shipley[3] has a very useful paper on rat fleas. He points out that these insects, which

[1] Rothschild, N. C. (July, 1910), "A Synopsis of the Fleas found on *Mus norwegicus decumanus, Mus rattus alexandrinus*, and *Mus musculus*." *Bulletin of Entomological Research.*

[2] McCoy, G. W., and Mitzmain, M. B. (September, 1909), "The Regional Distribution of Fleas on Rodents." *Parasitology.*

[3] Shipley, A. E. (February 16, 1911), "Rat Fleas." *Journal of Economic Biology.*

Insects—*continued*

used to be classed under *Diptera*, have been raised to rank as the Order *Siphonaptera*. The article is illustrated, and drawings of egg, larva and pupa are shown, and the life history of the flea briefly described. The author notes that they are easily destroyed in the larval stage, which is found in floor sweepings, or where dust collects in the crevices and cracks between boards. Where fleas are a pest the adults can be trapped by draping the legs with sticky fly-papers and walking about. The fleas jumping at the ankles impinge on the papers, which of course have the sticky side outwards. The paper concludes with lists like those given by Rothschild. A parasitic and a predatory enemy of the flea has been described by Mitzmain [1] in California. This is a new tyroglyphid mite of the genus *Histiostoma*, which has been found on the adults of *Ceratophyllus acutus*, *C. fasciatus*, and *Xenopsylla cheopis*. It has not been proved that this mite feeds on the flea. A beetle (*Staphylinus sp.*), however, does, destroying squirrel and rat fleas. Five of these beetles rendered 97 adult fleas helpless in less than five minutes.

For those working with fleas Mitzmain's [2] notes on breeding them in the laboratory are likely to be useful. This can be done if a medium simulating the nest of the host be supplied them. Fleas reared from the cocoon kept without a host have never been observed to copulate or oviposit. The eggs are never laid on the host. Oviposition takes place within 36 hours after the female is removed from the host. . . . The larvæ can live on the bloody egg pellicles and the dejecta of the parent for a period of 5 to 6 days.

The question of flea destruction may be now considered. This has also been worked at by Mitzmain,[3] and it is noted that there are three ways of killing fleas :—

(*a*) *Chemically.*—A corroding of the tissue due to chemical action.
(*b*) *Physically.*—The stoppage of the spiracles, causing suffocation.
(*c*) *Physiologically.*—Effects on nervous system, such as produced by chloroform and ether. These latter agents are very active if the application is prolonged.

In the investigation the technique employed consisted in some cases in placing the fleas momentarily in the liquid, then returning them to a dry vial, or again by letting the insect float on the surface of the liquid. In the case of gaseous agents and insect powders special methods are used.

In the matter of the criterion of death the test applied was absence of movement for half-an-hour or more. In many instances the insect was at first apparently killed, but recovered sufficiently to perform its functions, including biting. It is often impossible to say that a flea is dead, unless the observation covers a considerable length of time. The fleas used were the ordinary *Pulex irritans*, *Ceratophyllus fasciatus*, *C. acutus*, and *Lœmopsylla cheopis*.

The practical result of the experiments may be summed up as follows: Water is of little value in the destruction of fleas, and glycerine is practically inert also. Alcohol in the strength of 70 per cent. and absolute alcohol are uncertain in action, and practically inefficient. Kerosine and "miscible oil" (potash soap, 40 per cent., made from whale oil, and mixed with kerosine, containing 60 per cent. of the latter) are extremely efficient as flea destroyers.

Formalin, phenol, mercuric chloride, and trikresol in the strengths used as disinfectants are of little value in killing fleas. Powdered sulphur proved of no value. Ordinary insect powder was only efficient when the fleas were shaken up in it and left in it. The *fumigants*, bisulphide of carbon, hydrocyanic acid gas, and sulphur dioxide are highly efficient in the usual strengths for flea destruction.

A very similar paper is that by Manaud,[4] whose classification of the action of insecticides on fleas is mechanical, corrosive and toxic, which corresponds very well to that of the American workers. He employed many substances, and found that those of an oily nature which adhere to the insects and kill them by penetrating the tracheal tubes, and producing asphyxia, act most rapidly. Petroleum residues, cresol, etc., come in this group. Of a group of solid and liquid substances which he tried, naphthalene proved itself the only one suitable for the disinfection of houses. As naphthalene is soluble in petroleum, he recommends the following formula :—

A.—1. Saturated solution of naphthalene in petroleum or oil of naphtha . .	*aa*
2. Black soap Water	*aa*
B.—Emulsion A	2 parts
Cresol	1 part

[1] Mitzmain, M. B. (1910), "A Parasitic and a Predatory Enemy of the Flea." *Public Health Reports, United States Public Health and Marine Hospital Service*, Vol. XXV., No. 13.

[2] *Idem* (July 29, 1910), "Some new facts on the Bionomics of the California rodent Fleas." *Annals Entomological Society of America.*

[3] Mitzmain, M. B. (July 29, 1910), "Notes on Agents used for Flea Destruction." *Public Health Reports, United States Public Health and Marine Hospital Service.* Quoted in *Journal Tropical Medicine and Hygiene*, October 1, 1910.

[4] Manaud, A. (April 12, 1911), "Prophylaxie de la peste par la désinfection pulicide." *Bull. Soc. Path. Exot.*

Two parts of water are added to one part of this mixture for house disinfection. Its unpleasant odour is a disadvantage. For personal protection he suggests oil of cherry laurel combined with eucalyptus or citronella in a liniment. Insects—*continued*

A letter in the *Lancet* for November 19, 1910, recommends, as a means of avoiding flea bites, the sprinkling of the parts apt to be attacked, and the drenching of infected mattresses with eucalyptus oil, a drop bottle of chloroform being kept for emergencies. Zupitza [1] affirms that a trace of iodoform on one's clothes is sufficient to keep all fleas at a distance. If this is so, the drug should have a wide use as a prophylactic in plague-stricken areas.

Cunningham [2] has shown that fleas can be destroyed by exposure to the sun in India :—

Various powders have been reputed to be effective, and were tried ; naphthaline acted well, but was too slow, requiring 6½ hours to kill fleas in a closed space and 9 hours in the open. It was then determined to ascertain the effect of the light and heat of the sun. In previous experiments it has been found that rags, spread on the ground in thin layers, were freed from fleas in three hours ; in the first part of the present investigation it was sought to determine the different ways in which fleas behave when clothes are spread out on different kinds of ground. Tin trays were made, 4 ft. by 4½ ft., with sides 4 in. high ; in these were placed *dhurries* (cotton carpets), spread over the surface ; and then 100 fleas were introduced, half above and half below the carpet. The tray was then drawn out into the sun, the temperature taken, and the behaviour of the fleas carefully watched : they were seen trying to escape from the glare, but after seven minutes all were killed that were on the surface, and at the end of half-an-hour all beneath the dhurrie were also found to be dead. When dhurries were spread on sand the effects were more marked, the sand absorbing the sun's heat faster than the tray surface ; the fleas made no attempt to burrow into the sand, but were almost immediately killed. When dhurries were spread on leaves and grass, the fleas dived under the grass and got protection from the sun. The time of exposure necessary to destroy all fleas was reckoned to be about 45 minutes when clothes were spread on hard ground, and somewhat less on sand, the temperature being 117° F., under, and 118° to 142° F. on the surface of, the carpets. The next point was to determine how far fleas could travel on sand under these temperature conditions without being destroyed. A " flea-park " was constructed of smooth soil, spread over with a 3-inch layer of dry sand, and enclosed in walls of tin, so constructed as to form a square which could be enlarged or diminished at will ; the pieces of tin were bent at right angles, so that adjoining the vertical 6-inch " wall " there was a horizontal surface 8 in. wide ; this was covered with white paint and resin just before any experiment was commenced. The flea-infested carpet was laid in the middle of the square ; at the end of an hour's exposure to the sun the paint-covered marginal surfaces were examined to see if any fleas had travelled as far ; if this was found to be the case, the " park " was enlarged, the walls being placed farther off from the carpet. In one set of experiments the sand was kept in the shade until the commencement of the observations, and only then exposed to the sun ; the distance from the carpet to which the fleas could travel was found to be 4 ft. In a second set the square was prepared in the same way as it would be in practice—viz., the carpet was not placed in position until thermometers on the sand registered 120° F. ; under these conditions no fleas were able to travel more than 2 ft. from the edge of the carpet—all were killed. Lastly, experiments were made with the padded cotton quilts (*resais*) ordinarily used by natives, to see if they protected the fleas from the sun's heat. In one or two cases the heat did not penetrate the whole thickness of the quilt, and some fleas survived, but on turning the quilt over no fleas were found alive after an hour's exposure to the sun ; the temperature inside the quilt was found to reach 143° F. As a result it is seen that the sun acts as a very efficient disinfectant for flea-infested clothing, simple to use, and free of expense. The rules drawn up are quite plain and easy of application. The ground must be fully exposed to the sun, flat, and devoid of anything that can shelter the fleas, and entirely covered with a 3-inch layer of fine sand. The surface temperature of the sand must be at least 120° F. before the clothing is spread upon it. The clothes must be spread evenly in a single layer and left for one hour in the sun, padded articles being turned once or twice ; no clothes to be placed within 3 ft. of the edge of the sand. The whole area should be fenced in to keep off animals.

Some further references to fleas will be found under " Plague," *page* 268, and under " Small-pox," *page* 323.

From fleas to lice is perhaps no great transition, and the latter are being found of importance in human pathology, as witness the rôle they play in certain forms of spirochætosis and in typhus fever. The loathsome louse, therefore, is worthy of attention. Recently I found it difficult to obtain information regarding the internal anatomy of lice, but happily came across a paper by Christophers and Newstead [3] previously missed, and to which reference is now made as it gives a very good account, unfortunately not illustrated, of the internal organs of a new pathogenic louse, *Hæmatopinus stephensi*. Workers called upon to dissect lice cannot do better than consult this article, for I find that the internal arrangements of human lice closely correspond to those of this louse of the Indian field rat. A useful entomological paper is furnished by Neumann,[4] who deals mainly with the genus *Hæmatopinus*, and gives some synoptic tables for differentiation, and drawings illustrating external anatomy.

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[1] Zupitza (1911), " Ein Mittel zur Abwehr von Pestflöhen." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XV., No. 6.

[2] Cunningham, J. (1911), " The Destruction of Fleas by Exposure to the Sun." *Scientific Memoirs, Government of India*, No. 40. Extract from *Lancet*, April 15, 1911.

[3] Christophers, S. R., and Newstead, R. (1906), " On a New Pathogenic Louse which acts as the Intermediary Host of a New Hæmogregarine in the Blood of the Indian Field Rat. (*Jerbellus indicus*)." *Thompson, Yates and Johnston Laboratories Reports*, Vol. VII., Part 1.

[4] Neumann, L. G. (April 20, 1910), " Notes sur les Pédiculidés." *Arch. de Parasit.*, Vol. XIII.

Insects— *continued*

Jakob [1] reports experiments that were made with two species of lice, namely, *H. macrocephalus* of the horse and *H. piliferus* of the dog, in order to determine the effect of water, air, and certain drugs used antiparasitically.

A submergence in water of from 20 to 28 hours was found to be necessary to kill them. When exposed in the sun's rays at a temperature exceeding 43° C. they were killed in two or three minutes. A watery solution of from 1 to 2 per cent. of *liquor cresoli saponatus* in the form of baths over the whole of the body was found to be sufficient to kill the parasites in 15 minutes.

It would seem that, as in the case of fleas, lice are very susceptible to the action of the sun. On the other hand it is worth noting that while the human flea (*P. irritans*) is apparently unknown in the Northern Sudan, or at least very rare, the lower class of natives harbour many head and clothes lice. The former are very dark coloured, and can, one would think, derive but little protection from the short crisp hair on the head of a Sudanese labourer.

Bed-bugs now claim attention. We may at once note that Dutton [2] in the United States appears to have proved that they can convey infection in enteric fever. He says :—

I had observed among Poles, Italians, and Russians, in filthy quarters, where the beds had been used by typhoid patients, that succeeding occupants were stricken with typhoid. I had noted that, after being bitten with bed-bugs, in from eight to fifteen days they were attacked with typhoid. This disease-carrying factor was suggested to an Italian tenant of one of a number of typhoid-infected houses, with the advice that the beds be destroyed by fire and the house fumigated. The advice was refused. To test the case, the man offered himself for experiment. I collected some bed-bugs, starved them for several days, then placed them on the abdomen of his eight-year-old daughter who had typhoid, incarcerating them under a square piece of a fleece-lined undershirt, fastened at the edges with zinc-oxide adhesive plaster. In six hours the bugs, satiated with blood, were imprisoned between soiled pieces of canvas and allowed to remain twenty-four hours. They were then transferred to the abdomen of the father, imprisoned in the same manner as on the child, and allowed to remain twelve hours. It was noted that only about one-third of the bugs had bitten the subject. After removal, the bugs were crushed between glass slides and cultures made. These cultures showed the Eberth bacilli. Unfortunately, a few of the bugs escaped, and fed on the blood of an eleven-year-old boy, with whom the subject was sleeping. The father developed typhoid of the most virulent type in fourteen days, and the boy in twelve days.

Girault [3] has commenced to study the biology of the bed-bug, *Cimex lectularius*. The first paper merely deals with the effect of quantitatively controlled food supply on development, and the mere reference to it must suffice. Future papers should be more valuable from the medical standpoint.

Sangiorgi [4] has tested bed-bugs (*C. lectularius*) as trypanosome carriers. We may note his conclusion that protozoal parasites can live and preserve their pathogenic activity in the tissues of the bug for about 4 days. He did not, however, find any evidence of multiplication of trypanosomes.

One may mention a couple of useful French works on insects and disease—one by Sergent [5] dealing with flies which bite and suck blood, the other by Blanchard [6] on the pathogenic rôle of the *Arthropoda*, of which only the volume on ticks has so far appeared. An excellent American work of a somewhat popular nature is Doane's *Insects and Disease*, which is very well illustrated.

Cockroaches are often a perfect nuisance in tropical countries; it has been suggested that they may convey the virus of plague. One has destroyed them in hundreds in the holds of Nile steamers by fumigating with sulphur. They can be poisoned by phosphorus paste or a mixture of chocolate and borax spread on bread, or taken in special traps. Gunn [7] gives the following instructions for destroying them by fumigation on a large scale :—

(1) Measure the cubical capacity of the room to be fumigated.

(2) Take 1 ounce of cyanide of potassium, 1 ounce of sulphuric acid, and 2 ounces of water to every 100 cubic feet of space.

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[1] Jakob, H. (1909). *Münch. Tierärztl. Woch.*, Vol. LIII., Nos. 11 and 12.

[2] Dutton, W. F. (October 16, 1909), "Present-day Problems and Progress in prevention of Typhoid Fever." *Journal American Medical Association.*

[3] Girault, A. A. (October 20, 1910), "Preliminary Studies on the Biology of the Bed-bug, *Cimex lectularius*, Linn." *Journal Economic Biology*, Vol. V., No. 3.

[4] Sangiorgi, G. (December 17, 1910), "Experimentelle Untersuchungen über die Übertragung der Protozoen-Blutparasiten durch 'Cimex lectularius.'" *Cent. f. Bakt.*, I. Orig., Vol. LVII., No. 1.

[5] Sergent, Ed. (1909), "Détermination des Insectes piqueurs et suceurs de sang." *Encyclopédie Scientifique Bibliothèque de Microbiologie et Parasitologie.*

[6] Blanchard, R. (1909), *L'Insecte et l'Infection, Histoire naturelle et médicale des Arthropodes pathogènes.* Paris.

[7] Gunn, D. (January, 1910), "Method of Fumigation for Cockroaches." *Transvaal Agricultural Journal*, Vol. VII., No. 26.

Insects—*continued*

(3) If the room is a large one, three or four enamelled dishes should be employed, and should be placed far apart in different parts of the room.

(4) Into these dishes first place the requisite amount of water, and pour slowly into it the requisite amount of sulphuric acid.

(5) Now place the proportionate amounts of cyanide of potassium into paper bags (thin paper bags similar to those used by a grocer).

(6) See that the room is now made air-tight, or as nearly so as possible, *and be very careful to remove all foodstuff and water or drinkables of any kind from the room.*

(7) Now take the cyanide of potassium (made up in paper bags as mentioned) and quickly drop each bag separately into each dish used, and leave the room at once, seeing that the door is shut and locked, so as to prevent children or others from entering.

(8) Allow the room to remain closed for at least four or five hours. It is better to carry out the fumigation at night time, and allow the room to remain closed during the night.

(9) On opening the room do not enter, but allow a free current of air to penetrate, and leave open for at least half-an-hour before you enter. For this purpose it is best to arrange the windows so that they can be opened from the outside.

When the paper bag containing the cyanide of potassium is thrown into the water containing sulphuric acid in solution, it generates hydrocyanic acid gas, and this gas is highly poisonous, and will destroy the cockroaches.

The reason for suggesting that the fumigation should take place over night is that the cockroaches are more likely to come out of the cracks and crevices in which they exist at night time than during the day, and thus are more readily subjected to the poisonous effects of the gas.

Jones has noted that in the Philippines a species of ant preys with avidity on fly larvæ, just as has been noted in India. In the Philippines, however, it seems to be very active and actually to keep flies in check. He describes its methods as follows :—

Upon watching these ants attack fly larvæ, it is interesting to note that they do so in a way which proves that they are no novices at the procedure. One will attack an extremity and apparently bite it, and as soon as the larva begins to coil and makes efforts to escape, numbers of others will immediately jump upon it, and in the course of a few moments the larva will be apparently dead. I believe that the ant introduces some venom in the act of biting, formic acid in character, which preserves the larva as food until such time as the ant needs it—eats it, in other words. As soon as the struggles of the larva have ceased, they haul it off to their nests and return for others. In many instances I have seen them carry away pupæ. It will be interesting for the reader to procure a few maggots and place them over an ant bed.

In Khartoum "zibla" heaps are always infested by fly larvæ, and small ants are very diligent in carrying these away. The extent of their depredations on the fly nurseries would form an interesting subject for research, and it is hoped to study the matter. A very useful paper is that by Howlett [1] on methods of collecting and preserving insects, especially in the Tropics. Speaking of the difficulties of obtaining good store-boxes, he says :—

The ideal box would be (1) light, strong, and easily handled, (2) made of impermeable non-conducting and non-hygroscopic material, (3) unaffected by any degree of moisture or drought in conjunction with any temperature between 30° and 120° F., (4) ant-proof and reasonably air-tight, (5) not expensive. It should not be difficult to make such a box, if not of wood or impregnated wood, then perhaps of metal covered with some non-conducting substance, or of one of the many patent materials and "substitutes" now available. Single boxes are preferable to double ones.

Apparently the best preservative is that of Lefroy, *i.e.* a mixture of white beech, creosote and saturated solution of naphthalene in chloroform, equal parts. There is now no need for poisoning boxes in order to kill mites, etc. What is done is to line a box with cork carpet, painted white, and run over this about a quarter of an inch of wax with 5 per cent. of naphthalene melted in with it. The melting-point of the wax should be about 20° F. above the maximum shade temperature. There are several other most useful hints for collectors. Merriman's method for closing tubes or bottles containing formalin specimens may be mentioned. A plug of plasticine (cheap and easily obtained) is pushed right down on to the surface of the liquid, until the latter spurts up through a pin-hole made in the plug, all the air in the tube having previously escaped through the same hole. The hole is then sealed by a wipe of the thumb, and the liquid remains, completely filling a permanently closed tube, preventing all damage from shaking.

While on the subject of technique one must not fail to direct attention to Hamerton's [2] introduction to methods of studying the morbid histology of disease-carrying insects. This deals with fixing, dehydrating, embedding, cutting, mounting, staining, etc., and will be found invaluable to those engaged in this class of work.

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[1] Howlett, F. M. (December, 1910), "On the Collection and Preservation of Insects." *Parasitology.*

[2] Hamerton, A. E. (September, 1908), "An Introduction to Methods of Studying the Morbid Histology of Disease-Carrying Insects." *Journal Royal Army Medical Corps.*

Insects— *continued*

A good remedy for the pain of insect bites is stated to be a mixture made by dissolving 30 or 40 grains of iodine crystals in one ounce of saponated petroleum (Moloney). It is said to remove the pain of wasp or mosquito bite "like magic."

Additional Notes

Wellman [1] has an interesting lecture on insects and human disease in the Tropics. Although it chiefly refers to conditions met with in Angola it forms a good contribution to the literature. He says that craw-craw is really due to scabies. Myriapods are mentioned, both centipedes and millipedes. The former bite severely, the latter excrete a poisonous secretion, probably from the *Foramina repugnatoria* at the sides of their segments. He has something to say about the *Orthoptera*, mentioning especially *Dacnodes wellmani*, a new giant earwig, which can draw a large drop of blood with its pincers, and may introduce septic matter into the wound it produces. He also notes that possibly a tape-worm (*Davainea*) may be disseminated by cockroaches. He again describes *Phonergates bicoloripes*, the bug that preys upon *O. moubata*, and mentions other groups of bugs, notably species from South America, which are said to suck human blood. The remarks on flies and fleas do not call for notice here, but the author deals also with beetles. The larvæ of *Blaps mortisaga* are often found as pseudo-parasites in man, and Daniels found a coleopterous larva in an abscess case in Demerara. Other beetles are said to be intermediate hosts of tape-worms. There are beetles with poisoned spines (*Drilus and Tetralobus*), and bushmen prepare a deadly arrow poison from the grubs of a chrysomelid beetle (*Diamphidia locusta*). Some large African carabidæ eject with great force a strong-smelling liquid from the posterior part of the abdomen, which, if it reaches the eye, gives rise to a severe irritative conjunctivitis. Urticaria due to Lepidoptera claims attention; moths are mentioned as the secondary hosts of cestodes, and as parasites on mammals; and, following Williamson, the rôle of ants as possibly spreading anthrax receives consideration.

Maxwell-Lefroy [2] supplements Howlett's note (*loc. cit.*). He says :—

> We use teak boxes of a standard size well varnished within; when the varnish is dry, a piece of cork carpet cut to fit the box and previously enamelled white above, is laid ready to hand, a mixture of paraffin wax (melting point 136° F.) 80 per cent. and flake naphthalene 20 per cent. is kept melted and a small quantity is run into the box, the cork carpet is at once put in and rolled down on the melted mixture which sets and holds it; more of the liquid is then run in, sufficient to cover the cork completely: this sets with an even smooth surface (the box being on a perfectly horizontal surface), and the box is ready when cold. This method has not only been tried, but we have nearly 2000 boxes in use, and are replacing all our papered boxes.

Such boxes are too heavy if one is moving about, and for that a lighter paraffined box is recommended. The paraffined cork requires no poisoning, keeps white and does not harbour insects.

Stevenson [3] mentions a method for killing bed-bugs which has been successfully used in sleeping carriages at the Cape of Good Hope. It consists in the use of potassium cyanide 1 ounce to 100 cubic feet, with an exposure time of two hours. It not only kills the majority of the bugs present, but prevents eggs from hatching out.

Leishmaniasis. Under this heading oriental sore is not included. We consider only infantile kala-azar, and the ordinary disease of that name. The most notable discovery regarding both these forms, if indeed they are separate forms of the disease, is the recognition of their wide distribution. Already well-nigh every country of the Mediterranean littoral has been found to harbour cases of the infantile form, while, in not a few, Leishmania have also been found in adults. Other countries also, such as Portugal, not hitherto known to be infected, have been proved to be so, at least to some extent. Hence at the present time there is no more interesting and important disease than that which gives this section its title. In the first place we consider a paper dealing with the infantile form. Nicolle's work was cited in our first Review. In a paper [4] which escaped attention he describes the successful cultivation of Leishman bodies obtained from the spleens of three infantile cases. He employed blood-salt-agar, and gives its formula and the technique for its preparation. At 22° C. culture forms did not appear till about the seventh day, but were abundant by the twelfth. The parasites

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[1] Wellman, C. (1910), "Diseases in the Tropics.—Lecture I. Insects and Human Disease in the Tropics." *Collected Papers American Society of Tropical Medicine.*

[2] Maxwell-Lefroy, H. (June, 1911), "Note on Entomological Boxes." *Parasitology.*

[3] Stevenson, W. W. H. (June, 1911), "Bugs in Railway Carriages." *Indian Medical Gazette.*

[4] Nicolle, C. (1908), "Culture des corps de Leishman isolés de la rate dans trois cas d'anémie splénique infantile." *Bull. Soc. Path. Exot.*

were still living and motile after three months, and presented all the familiar cultural forms of *Leishmania donovani*. Subculture was easy. He gives a method for staining these cultural forms by Giemsa. In a later paper [1] the same author signalises the discovery of *L. infantum* in the peripheral blood where, however, it is not easy to find. In the infant he does not think liver puncture can replace splenic puncture, as the results are inconstant. It is, however, excellent for following out the development of the parasite and the progress of the infection in experimental animals such as the dog and the monkey. In this paper he mentions the spontaneous leishmaniasis of dogs in Tunis, and reaffirms his belief as to the canine origin of infantile kala-azar. One need not cite all the scattered earlier papers on the subject, for Nicolle [2] has gathered all the facts collected down to the middle of 1909 into a couple of excellent papers illustrated by temperature charts and coloured plates. He gives a full bibliography, and summarises in twelve conclusions, some of which we note :— Leishmaniasis— *continued*

(1) The malady is confined to young children, and usually makes its appearance in the course of the second year of life, but it may develop earlier or later.

(2) The symptoms are characteristic, and are extreme pallor, marasmus, considerable splenomegaly, a somewhat less enlargement of the liver, fleeting and painless œdemas, a very irregular temperature capable of exhibiting several "maxima" on the same day, a notable quickening of the pulse rate, digestive troubles and an increase of the mononuclear elements of the blood. Hæmophilia, gingivitis and purpura are frequently complications. The duration of the illness is very long. Death is the rule, but spontaneous cure may apparently occur.

(3) Quinine has no effect upon the fever.

(5) Post mortem, in addition to the splenic and hepatic hypertrophies, the bone-marrow is found to be red in colour.

(6) The condition only differs from true kala-azar in the age of the patients.

(7) It is allied to the splenic anæmias of infancy, and is apt to be confounded with them.

(8) On blood-salt-agar the cultural forms take the herpetomonas type.

(9) Dogs and monkeys can be infected. Other animals seem to be refractory. In the dog the disease is often benign so far as symptoms go, but terminates fatally. The monkey infection is more like the human. The dog infection is not transferable from mother to fœtus.

(10) Small doses of cultures are innocuous to the dog, but large and repeated doses, as in Novy's kala-azar experiments, produce infection.

(11) The disease is a natural infection of the dog transmissible to the child. The absence of clinical symptoms in the animal makes it difficult of recognition.

(12) The transmitting agent requires discovery.

With this valuable list as a basis let us explore further developments. Novy [3] has succeeded in inoculating dogs with smaller doses of cultures, and recommends blood culture as a means of diagnosis in doubtful cases. In addition to the nucleus and blepharoplast, he finds the parasite possesses a rhizoplast which he illustrates rather feebly by photographs. This proves the parasite to be a flagellate. The rhizoplast is always perpendicular to the blepharoplast, and is a spherical body, the root, indeed, of a flagellum.

A considerable number of papers will be found in the *Archives of the Tunisian Pasteur Institute* for 1909, but as their contents are repeated in later papers, or as they deal with unsuccessful attempts at treatment with arsenophenylglycin, etc., the mere reference must suffice. One paper only will be mentioned, *i.e.* that wherein Nicolle and Manceaux [4] show that the virus diminishes in activity by passage through the monkey. The indefatigable Nicolle [5] again summarises some of the later work published in the above-mentioned *Archives*. A dog inoculated experimentally 18 months before succumbed to the disease, which was entirely latent, the temperature being normal for 16 months. The parasite was found in blister serum taken from this dog, a fact indicating a possible means of diagnosis in the human subject. The mononuclear leucocytes were infected. The above-mentioned monkeys recovered after injection with the weakened virus. Dogs, on the contrary, died after severe attacks.

Inoculation with *L. tropica* appears to protect monkeys, wholly or partly, against infection with *L. infantum*. Subcutaneous inoculation with a weakened virus in a monkey produced a local lesion, but no general infection. The local lesion did not resemble oriental sore. Comte

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[1] Nicolle, C. (1908), "Quelques faits nouveaux relatifs au Kala-azar Infantile." *Bull. Soc. Path. Exot.*

[2] *Idem* (May 25, and June 25, 1909), "Le Kala-azar Infantile." *Ann. de l'Inst. Past.*

[3] Novy, F. G. (1909), "Sur Leishmania infantum." *Bull. Soc. Path. Exot.*

[4] Nicolle, C., and Manceaux, L. (1909), "Résistance du singe au virus du kala-azar après passage de ce virus par le singe." *Archiv. de l'Inst. Past. de Tunis*, No. IV., p. 188.

[5] Nicolle, C. (1909), "Quelques données nouvelles relatives au Kala-azar Infantile." *Bull. Soc. Path. Exot.*

Leishmaniasis— *continued*

and Manceaux assisted Nicolle in this work. Laveran and Pettit [1] found that both in dogs and monkeys the infection might be either very slight or latent, and only recognisable by cultural methods, for both liver puncture and the examination of the bone-marrow during life might give negative results. Aspland [2] has found infantile kala-azar common in Peking, and believes it may exist throughout North China. In Peking the features of the disease are—

(1) Age rarely under two years, and never over ten.

(2) The spleen is always much enlarged, in later stages filling the pelvis.

(3) Diarrhœa in the later stages, constant and severe.

(4) Great debility generally, but not pronounced until the cancrum oris has set in.

(5) "Cancrum oris." The condition does not really affect the cheek, but begins at the root of the upper or lower central incisors, the teeth dropping out in a week or so, leaving a black slough. The author favours a syphilitic origin of the disease.

(6) The disease is always fatal.

(7) As regards fever, no data were obtainable.

He mentions that in one case in Tientsin, Leishman bodies were found in the peripheral blood.

Cannata [3] has examined the blood in seven cases of the disease. The formula varies very much, not only in different cases, but in the same case at different times. It is therefore unlikely to be of value for diagnosis. The presence of myelocytes was noted. Once more we find Nicolle [4] presenting new discoveries regarding the disease in Tunis. Amongst other points we note a case apparently cured, one successful case of diagnosis from blister fluid, no evidence of a lessening in virulence of the virus by passage through dogs, a great variation in its action for different animals of any one batch even when the same doses and the same method of administration are employed. It is specially noteworthy that the injection of a large number of parasites does not necessarily mean a severe infection. A first attack of the experimental disease can, as shown in cases apparently cured for some time, confer complete immunity on dog and monkey. In an animal incompletely cured or only recently recovered, however, a second inoculation proves fatal.

Removal of the spleen in an infected dog does not influence the course of the disease. Subcutaneous injection in the dog and monkey may be followed by a local reaction as well as a general infection. The former is not like that which follows subcutaneous inoculation with *L. tropica*. The site of selection for liver puncture in the dog is the tenth right intercostal space one or two fingers-breadth from the costo-vertebral joints. A steel needle, free from all rust and slightly longer and stronger than that used in the case of children, is indicated. These are the results of work performed by Nicolle and his colleagues, *i.e.* Cortese, Lévy, Triolo, Conor, Comte and Manceaux, and the details of which will be found in the three numbers of the *Archives of the Tunis Pasteur Institute* for 1909.

A number of Italian and other papers will be found reviewed in the *Bulletin of the Pasteur Institute* for August 15, 1910. We note the following: Basile [5] has, in Sicily, confirmed Nicolle's work as regards the presence of spontaneous Leishmaniasis in the dog. One of the villages where the discovery was made was where Gabbi [6] found infantile cases. The work of Jemma [7] and other observers is also cited. They succeeded in inoculating dogs both intraperitoneally and intravenously. The cases found by Alvarez [8] and his colleagues at Lisbon also receive mention. So does the work of Critien [9] in Malta. He found ten cases there. We only give here a selection from the numerous papers reviewed, but some of these

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[1] Laveran, A., and Pettit, A. (1909), "Infections expérimentales légères au latentes du singe et du chien par le Kala-azar tunisien." *Bull. Soc. Path. Exot.*

[2] Aspland, W. H. G. (January 15, 1910), "Is Ponos Kala-azar?" *British Medical Journal.*

[3] Cannata, S. (May, 1910), "Recherche ematologiche nell' anemia splenien infantile de' parassiti di Leishmann." *La Pediatria.*

[4] Nicolle, C. (July 13, 1910), "Quelques données nouvelles relatives au Kala-azar Infantile." *Bull. Soc. Path. Exot.*

[5] Basile, C. (1910), "Alcune osservazioni sulla presenza di Leishmania nei cani." *Rend. d. Accad. dei Lincei,* Vol. XIX., No. 3.

[6] Gabbi, U. (1909), "Facolai endemia della varietà febrile l'anemia splenica infetiva dei bambini." *Policlino.*

[7] Jemma, R., Cristina, G., and Cannata, S. (1910), "Infezione sperimentale da 'Leishmania infantum' nei cani." *La Pediatria.* See also *Cent. f. Bakt.,* I. Orig., December 17, 1910, Vol. LVII., No. 1.

[8] Alvarez, D. (March 20, 1910), "Um caso de Kala-azar infantil em Lisboa." *Med. contemp.*

[9] Critien, A. (1910), "Kala-azar infantile à Malte." *Archiv. de l'Inst. Past. Tunis,* No. 2.

Leishmaniasis—*continued*

authors have carried out later work of interest and value which we now proceed to discuss. Thus Basile [1] describes two different forms of natural infection in dogs, the acute and the chronic. He thinks that the former, which affects young dogs and lasts from 3 to 4 months, plays the more important part in the spread of the disease. This author was able to infect three young dogs by keeping them beside cases of infantile kala-azar, and believes that the flea (*Pulex serraticeps*, and possibly also *P. irritans*) is the most likely vector. Quite recently Critien,[2] in the case of a child aged 3 years, found the parasites in smears from mucous flakes excreted with the fæces. It is evident that if this observation is confirmed in other cases it may possess much significance.

Cristina and Cannata [3] have a paper on the morphology and cultural characteristics of *L. infantum*, in which they describe involution and other forms. A few illustrations would have been helpful. The Sergents [4] announce the presence of the parasite in dogs in Algiers. Commenting on their figures, Nicolle [5] points out that protozoal infections are more common in the summer, when they made their examinations, than in the spring, when he made his researches on dogs. The disease has recently been found in Tripoli, and Jérusalemy [6] has now confirmed Aspland's view (*loc. cit.*) as to its occurrence in China.

Ponos has been mentioned in the references, and there has been some discussion as to whether this disease of the Greek Archipelago is, or is not, kala-azar. Williamson [7] was the first to advance the former view, and it appears to be correct, to judge by Galle's [8] recent discovery of *Leishmania* in a case of "ponos" at Spetsai. Leaving aside for the present papers on the efforts at treatment in the infantile form, we turn to kala-azar proper, the disease affecting both adults and children, and due to *L. donovani*. Patton [9] believes that it should be named *Herpetomonas donovani*, regards it as allied to *H. muscæ domesticæ*, and even more closely to *H. lygæi*. (*See also* paper by Archibald in the Fourth Report of these Laboratories, Vol. A.) He suggests the term herpetomoniases for the group of diseases now classed under leishmaniases. He was unable to transmit the disease to dogs. In a previous paper [10] he had given an account of his few experiments with dogs, and had stated that in Madras there was no evidence that dogs play any part in the spread of kala-azar. Speaking of the genus *Herpetomonas*, he says :—

> In their pre-flagellate stages they are round or oval bodies of varying size, and contain two characteristic chromatic bodies, the nucleus and blepharoplast. In this stage they multiply by simple longitudinal fission or by multiple segmentation, and are found in the midguts of their insect hosts, except in the case of the three human parasites. I have been able to show that this stage in a known species occurring in *Culex* mosquitoes is exactly similar to that of the human parasites. The flagellate stage is characterised by the formation of a *single* flagellum, and the multiplication of the resulting flagellates by equal or unequal longitudinal division. The adult forms are long, spindle-shaped organisms, with a single flagellum, but no undulating membrane. This stage occurs in the mid- and hind-gut of their hosts, but in the case of *Herpetomonas donovani* it takes place naturally in *Cimex rotundatus*. The post-flagellate stage is characterised by the massing together of the flagellates in the midgut, their shortening and rounding up; the resulting cysts are passed out in the fæces and are accidentally sucked up by fresh hosts. It is not known yet whether *H. donovani* undergoes this stage in the bed-bug.
>
> It is important to remember that many of these *Herpetomonads* are indistinguishable in their *pre-flagellate stages*, and therefore if this stage alone is studied two distinct species may be classed as one. Further, I wish to point out here that a partial study of the stages of these flagellates is very apt to lead to confusion, so that what are true *Herpetomonads* may quite easily be mistaken for *Crithidia* or young *Trypanosomes*. A reference to recent literature will show that this has actually occurred in more than one instance.

Donovan [11] expressed himself as dissatisfied with Patton's bed-bug theory, and suggested

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[1] Basile, C. (1910), "Sulla Leishmaniosi del cane e sull'ospite intermedio del Kala-azar infantile." *Rend. d. Accad. dei Lincei*, Vol. XIX., No. 5.

[2] Critien, A. (January 28, 1911), "Kala-azar in Malta." *British Medical Journal.*

[3] Cristina, G., and Cannata, S. (September 6, 1910), "Über die morphologischen und kulturellen Eigenschaften des Parasiten der infantilen Milzanämie." *Cent. f. Bakt.*, I. Orig., Vol. LV., No. 6.

[4] Sergent, Ed. and Et. (October 12, 1910), "Existence de la leishmaniose chez les chiens d'Alger." *Bull. Soc. Path. Exot.*

[5] Nicolle, C. (January 11, 1911), "A propos de la leishmaniose canine en Afrique Mineure." *Ibid.*

[6] Jérusalemy (May, 1910), "Kala-azar infantile en Chine." *Rev. de Méd. et d'Hyg. Trop.*

[7] Williamson, G. A. (August 16, 1909), "Is Ponos Kala-azar?" *Journal of Tropical Medicine and Hygiene.*

[8] Galle, (January 2, 1911), "Is Ponos Kala-azar?" Professor Galle's Discovery, Article in *Journal of Tropical Medicine and Hygiene.*

[9] Patton, W. S. (January 30, 1909), "The Parasite of Kala-azar and Allied Organisms." *Lancet.*

[10] *Idem* (December, 1908), "Inoculation of Dogs with the Parasite of Kala-azar (*Herpetomonas* [Leishmania] *donovani*), with some Remarks on the Genus Herpetomonas." *Parasitology*, Vol. I.

[11] Donovan, C. (1909), "Kala-azar in Madras." *Transactions Bombay Medical Congress.*

Leishmaniasis— *continued*

a reduviid bug, *Connorrhinus rubrofasciatus*, as a possible carrier. No experimental proof has been advanced that this is the case, but it is interesting to note that the human *Trypanosoma cruzi* of Chagas undergoes development in a bug of this genus. Of more importance are some other notes by Donovan. He has abandoned splenic puncture as a means of diagnosis, and relies on the examination of films of peripheral blood prepared in a special manner. Here is the technique :—

> A finger of the patient is taken, the tip washed with water and then dried with a towel, the finger is compressed below the pulp for half a minute so as to allow as many leucocytes as possible to exude in the drop of blood obtained by the prick of a new pin, one not used before. A needle's prick does not give enough blood, and the employment of a surgical needle is barbarous. A small drop of blood, about the size of a large pin's head, is taken up by a slide near its end and a smear made of it by another slide passed slantwise over it.
>
> The main object is to have the smear end in a straight edge at the finish. All that is necessary is to examine, of course after fixing and staining the film, this edge ; here everything of importance in the smear is located, the leucocytes and any Leishmania that may be present in them ; in ten minutes the whole of the contents of the drop of blood are ascertained. Some training is necessary to procure perfect slides of this nature. The slide with which the smear is made should have a perfectly smooth-ground edge to obviate " tailing " at the finished margin. It is by neglect of making smears of this kind that success does not attend the endeavours of other observers in detecting Leishmania in the peripheral blood.

In a later paper [1] this author mentions that the *Connorrhinus* sucks human blood, and describes negative experiments in dog inoculation.

He has tried quinine, fuchsine, and other methods of treatment, but change of air appeared to be the only curative agent known so far.

Treatment with hetol, 0·1 c.c. of a 1 per cent. solution by intravenous injection, the dosage being gradually increased, was carried out by Harrison [2] in an Indian case, and was followed by some improvement, especially as regards the temperature and the blood condition. Soamin and exposure of the spleen to X-rays produced no benefit. McKaig [3] reported a case of apparent cure after atoxyl, in doses varying from 6 to 12 grains daily. Laveran and Pettit [4] inoculated mice and a guinea-pig intraperitoneally, and some rats in the liver, with emulsions of organs rich in *L. donovani*. (As the strain was Tunisian it would seem to have been *L. infantum*, unless one is agreed that the species are identical.) The animals remained perfectly well, but intra-cellular parasites were found for some time in the peritoneal exudate which also yielded cultures of flagellates on the Novy-Nicolle medium. In one instance a mouse inoculated subcutaneously showed five days afterwards a very few Leishmania in its peritoneal cavity. Otherwise the parasites did not appear capable of traversing the peritoneum. Nicolle [5] has a short paper on the technique of spleen puncture. He advises a fine needle, and points out that one does not wish to see any blood appear in the barrel of the attached syringe. There is usually enough fluid in the lumen of the needle to make all the smears required. Moreover, if cultures are required, it is to be remembered that any blood will have an inhibitive effect on growth.

Platinum-iridium needles and old needles, especially if the least rusty, should never be used. In short, new steel needles of fine calibre are indicated. The syringe must be dry, and for this purpose may be passed through a Bunsen flame or put in a hot oven. Day and Ferguson[6] have described a form of splenomegaly with hepatic cirrhosis which is endemic in Egypt. They have never found Leishmania present, but have noted marked changes in the bone-marrow. The cause of this curious condition is unknown, but they compare it with kala-azar, saying :—

> Kala-azar, while closely resembling the condition which we have described in certain respects, differs from it in others. Thus the febrile onset, chronic course, presence of intestinal symptoms, the aspect of the patient in the advanced stages, the condition of the blood, bone-marrow and spleen, are very closely similar in both affections. Kala-azar, however, in the following particulars, apart from certain clinical features, differs from the condition to which we have called attention.
>
> (1) The presence of a crusted papular eruption or of ulcers on the limbs, containing the parasite.
>
> (2) The presence of intestinal ulcers, chiefly in the colon, also containing the parasite in small numbers.
>
> (3) The tendency to noma and local areas of gangrene, as well as to internal hæmorrhages.

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[1] Donovan, C. (November 20, 1909), " Kala-azar in Madras, especially with regard to its connection with the dog and the bug (connorrhinus)." *Lancet.*

[2] Harrison, L. W. (January, 1909), " A Case of Kala-azar." *Journal Royal Army Medical Corps.*

[3] McKaig, A. (December, 1908), " Atoxyl in the Treatment of Kala-azar." *Edinburgh Medical Journal.*

[4] Laveran, A., and Pettit, A. (July 3, 1909), " Infections légères du rat et de la souris par la Leishmania Donovani. Idem du cobaye." *C. R. Soc. Biol.*

[5] Nicolle, C. (1909), " Sur la technique de la ponction de la rate." *Bull. Soc. Path. Exot.*

[6] Day, H. B., and Ferguson, A. R. (1909), " An Account of a form of Splenomegaly, with Hepatic Cirrhosis Endemic in Egypt." *Annals of Tropical Medicine and Parasitology*, Vol. III., No. 3.

Leishmaniasis—*continued*

(4) The condition of the liver. In sporadic kala-azar, according to Rogers' observations, the liver showed marked cirrhotic changes in four out of forty-eight cases examined post mortem, while slight degrees of fibrosis were observed in a certain additional number. In the condition we are describing, however, hepatic changes in various degrees form an integral part of the malady at different stages, and are constantly met with. Again, the type of cirrhosis met with is portal in character and not intralobular, as described by Rogers for kala-azar. And lastly, "the persistence of the parasites in the advanced cirrhotic stage of the organ," as noted by Rogers in kala-azar, is a feature which stamps a distinctive character on the liver in this affection.

As already noted, Gabbi (*loc. cit.*) found the disease in Sicily. He has discovered it in adults as well as in children, and true kala-azar has also been found to exist in China, as reported by Bassett-Smith.[1] The upper part of the Yangtse Valley is evidently an endemic centre.

Harrison and Cumming[2] reported two cases in which treatment by arylarsonates failed to avert fatal issues. Atoxyl, soamin and arsacetin were all used without benefit. Archibald[3] investigated the alkalinity of the blood serum of four cases in the Sudan, and concluded that—

It is evident that the alkalinity of the blood in these four cases of undoubted kala-azar was diminished, and it is worth remembering that Rogers, Leishman, Statham, and other observers found that the ideal culture media for successful cultivation of the Leishman body is an acid one.

If, then, the alkalinity of the blood serum in cases of kala-azar be diminished, it is conceivable that the blood and tissues present a more favourable medium for the Leishman parasite than is usually the case; and, in order to obviate this, it would not seem unreasonable, whatever specific line of treatment be adopted, that drugs should be administered which tend to increase the alkalinity of the blood.

Of the above cases, only one was subjected to an alkaline treatment by calcium lactate, and unfortunately the disease was so far advanced in this instance that the drug had scarcely a fair trial.

A specific drug for the successful treatment of Leishmaniosis has not yet been found. Quinine and various arsenical preparations have not given satisfactory results up to the present, and hence the record of these four cases points to the advisability of employing such remedies as would increase the alkalinity of the blood.

Further, the alkaline reaction obtained in testing the serum of kala-azar cases may be of service in assisting the diagnosis in early cases where splenic enlargement is not marked.

Laveran and Pettit[4] recommend the use of a fluid medium for cultivating *L. donovani*, especially when a large growth is required for the purposes of experimental inoculation. The following is the formula they employ :—

Peptone (chapoteau)	2 grammes	1 Volume
Sod. chlorid.	6 grammes	
Water	900 grammes	
Defibrinated rabbit's blood		1 Volume

The peptone-salt solution is prepared separately and then the blood is added to it. Cubical flasks or Roux's bottles laid flat are used, so that the liquid may have as large a surface area as possible, because the parasites do not develop in the depths of the medium. The medium must be fluid, not sticky, and should present the aspect of laked blood. In such a medium the Leishmania agglomerations show as numerous white particles plainly visible to the naked eye. An important and well illustrated paper on kala-azar in the Sudan is that by Bousfield,[5] a résumé of which appears in the Fourth Report of these Laboratories, together with later papers by Douglas Thomson and Marshall.[6] Bousfield did not find the parasite in two dogs which he examined, and his paper is more of local than general interest. At the same time he gives a good clinical account of the disease as met with in certain parts of the Anglo-Egyptian Sudan, and deals with preventive measures, such as the avoidance of native bedsteads. Thomson extended Bousfield's clinical studies, while Marshall has worked at the pathological aspects of the disease in the Sudan. Their joint conclusions are as follows :—

(1) Kala-azar in Sennar Province affects, for the most part, children whose average age is about 12 years. This does not appear to hold in the neighbouring Province of Kassala, where adults are commonly affected.

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[1] Bassett-Smith, P. W. (December 4, 1909), "Kala-azar in the Far East." *British Medical Journal.*

[2] Harrison, W. S., and Cumming, C. C. (February, 1910), "Two cases of Kala-azar treated by the Arylarsonates." *Journal Royal Army Medical Corps.*

[3] Archibald, R. G. (June, 1909), "The Alkalinity of the Blood Serum in Kala-azar." *Ibid.* See also *Fourth Report, Wellcome Tropical Research Laboratories,* Vol. A.

[4] Laveran, A., and Pettit, A. (April 13, 1910), "Sur les cultures de 'Leishmania donovani' en milieu liquide." *Bull. Soc. Path. Exot.*

[5] Bousfield, L. (August and September, 1910), "A Tour of Investigation as to the prevalence of Kala-azar in Kassala and Blue Nile Districts, Sudan, from January 12 to May 16, 1909." *Journal Royal Army Medical Corps.*

[6] Thomson, D. S. B., and Marshall, W. E. (1911), "Kala-azar Commission to investigate the prevalence and cause of the disease in the Eastern Sudan." General and Pathological Reports. *Fourth Report, Wellcome Tropical Research Laboratories,* Vol. A.

Leishmaniasis—*continued*

(2) The disease runs an acute course, and chronic cases were not met with.

(3) The disease is not invariably fatal, cases of recovery having been met with.

(4) The Leishman-Donovan parasite was found in the peripheral blood in 86·6 per cent. of the cases.

(5) The ordinary grey monkey of the Sudan (*Cercopithecus sabœus*) can be infected with kala-azar.

(6) It can be infected by intraperitoneal inoculation and by subcutaneous inoculation.

(7) Natural infection, from an infected to a healthy animal, can occur provided the animals are kept in close contact.

(8) The Leishman-Donovan parasite is present in the peripheral blood of infected monkeys.

(9) So far we have found that the best method of infecting the monkey is by injecting into the peritoneal cavity the contents of a spleen puncture taken during life.

(10) So far we have not succeeded in infecting dogs, nor have we found spontaneous Leishmaniasis in the dog.

(11) The parasite can be cultivated readily on artificial media, development into flagellate forms being obtained in 10 per cent. citrate, on Novy and MacNeal's medium and on Nicolle's modification of that medium.

(12) The parasite appears to degenerate quickly after the death of the host. Post mortem examinations and post mortem spleen punctures for diagnostic purposes should be done immediately after death.

A paper by Visentini [1] is of special interest, because in it he traces and illustrates by a good coloured plate two modes of development of the parasite. In one there is a process of fission, two *Leishmania* being produced from one by division of the nucleus in the first instance and then of the blepharoplast. In the other, one finds a regular rosette formation. Balfour and Archibald [2] found similar appearances in splenic smears from a severe case treated by injections of "606." The drug appeared to cause some degeneration of the parasites, as evidenced by chromatolysis of their nuclei. Nicolle and Conor,[3] however, have succeeded in banishing the parasite from the blood and organs of infected monkeys by the use of the Ehrlich-Hata preparation, but unfortunatcly Nicolle, Cortesi, and Lévy [4] were not successful in the case of infantile kala-azar in children, albeit the salvarsan appeared in one case to cause degeneration of the *Leishmania*. It is difficult to make sure of the precise action of a drug in this disease, for most cases improve naturally every now and then, while a certain percentage undoubtedly recover. Recently Nicolle and Lévy [5] record a case of the infantile form in Tunis in a Jewish infant which terminated in complete recovery, the only one of twenty-five cases in which this has occurred. They do not think the benzoate of soda and anilin salt of antimony employed had anything to do with this fortunate termination. The amelioration of the symptoms and the return of the spleen to its normal size preceded the disappearance of the parasites.

The use of senega, advocated by Ensor,[6] undoubtedly seems to benefit certain cases of splenomegaly, and though one cannot definitely say it has ever cured a case of undoubted kala-azar, it seems worthy of a trial. Its virtues are supposed to depend on the saponin it contains, and as more of the latter is found in *Quillaia saponaria* (soap bark) of the U. S. P., Ensor suggests its use in preference to senega. The latter appears capable of producing a leucocytosis on which, possibly, some of its beneficial action depends. Quinine has long been used in the treatment of kala-azar, and finds a strong advocate in Muir,[7] who has had large experience in India, and believes if it is given hypodermically, and if cases are treatcd with it, early recovery is the rulc.

The treatment consists of the injection of the following solution :—

Quin. sulphat.	Grains 32
Acid. sulph. dilut.	Drachm 1
Aqua distil.	Drachms 4

From 20 to 90 minims of this solution are injected into the latissimus dorsi muscle in adults, or into the gluteal region in children.

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[1] Visentini, A. (July, 1910), "Über die Morphologie und den Entwicklungskreis der bei Kranken Kalabriens und Siziliens beobachteten Leishmania." *Arch. f. Schiffs-u. Tropen-Hyg.*, Beiheft, Vol. XIV., No. 4.

[2] Balfour, A., and Archibald, R. G. (1911), "A case of Kala-azar treated by 606." *Fourth Report, Wellcome Tropical Research Laboratories*, Vol. A.

[3] Nicolle, C., and Conor, A. (December 14, 1910), "Application du 606 au traitement du Kala-azar." *Bull. Soc. Path. Exot.*

[4] Nicolle, C., Cortesi, A., and Lévy, E. (April 12, 1911), "Application de l'arséno-benzol au traitement du Kala-azar de l'enfant." *Ibid.*

[5] Nicolle, C., and Lévy, E. (March 8, 1911), "Un cas de Kala-azar terminé par la guérison." *Ibid.*

[6] Ensor, H. (December, 1909), "The treatment of Kala-azar by the usc of Senega." *Journal Royal Army Medical Corps.*

[7] Muir, E. (February, 1911), "Treatment of Kala-azar by the Hypodermic Injection of a solution of Quinine Sulphate." *Indian Medical Gazette.*

Leishmaniasis—*continued*

The injection of such a solution is necessarily very painful, and where, as is generally the case, it has to be given repeatedly the patient naturally objects to it. The injection may be given absolutely painlessly, however, by a very simple expedient. Five minims of a 2 per cent. solution of cocaine is first injected; the needle is left inserted; the syringe withdrawn from it; the solution drawn up into it and injected after a couple of minutes into exactly the same place where the cocaine solution was injected.

The result of the injection, if given in the right dose, is to produce a certain amount of painless effusion, which lasts for a greater or less time depending on the dose and on the individual. If the blood be examined and a differential leucocyte count taken, a marked increase of the polymorphonuclear leucocytes will be noticed. In one case in which I had failed after searching three slides to find a single polymorph, I found 47 per cent. a week after such an injection. At the same time there is a very marked reduction in the size of the spleen and, if it is enlarged, in the size of the liver. As a rule, if the case is not very far advanced, the temperature becomes normal and, what is even more important, the patient begins to put on weight.

Injections have to be repeated as soon as, or rather before, the effusion from the first injection has disappeared, until the spleen and liver have entirely disappeared (*sic*). If too large a dose be given a certain amount of pain may accompany the effusion; but there will be a still greater leucocytosis, a still more rapid diminution in the size of the liver and spleen, and, although there may first be a few days' rise in temperature before it becomes normal, the appetite, weight and general health of the patient increase more rapidly.

He evidently regards the local irritation of the tissues at the site of injection as having a good deal to do with the result, for benefit is likewise obtained by turpentine injections which, however, are more painful. This, however, cannot be the only action, as he believes in giving cinchona by the mouth at the same time, finding it more effective than quinine. As a rule he administers a mixture of cinchona, arsenic, iron and magnesium sulphate while giving the injections, the amount of quinine administered being regulated by the effusion produced. He points out that kala-azar may be cured by the occurrence of cancrum oris, and cites the following interesting case :—

A patient was admitted to hospital with a large spleen extending to beyond the umbilicus and suffering from gangrene of the lung. He was coughing up large quantities of putrid matter by the mouth. The chest was drained by removing a part of a rib. The boy made a rapid recovery, but as long as there was any pus in his chest his spleen continued to diminish in size and the temperature remained normal. When, however, the wound in his chest had healed up there was a return of temperature accompanied by enlargement of the spleen. It was not till after three or four quinine sulphate injections that his temperature became normal and his spleen finally impalpable under the costal margin.

Muir's method is interesting when one recalls successful results in typhus fever by turpentine injections (*page* 389). This quinine or irritation therapy evidently demands a more extended use.

Additional Note

A useful recent paper on infantile Leishmaniasis,[1] illustrated by a coloured plate and giving prominence to the occurrence of chromatin granules in the tissues, is that by Jemma and Di Christina. It is in the main a review of recent work, and is furnished with a lengthy bibliography which will be found valuable by all interested in the subject.

Leprosy. Papers of bacteriological interest first claim attention. Smith and Bisset[2] deal with the subject chiefly from an historical aspect. They mention that Babes found leprosy bacilli to be slightly motile, and claimed to have seen branching forms in culture. They also quote Lehmann and Neumann as to the difference between tubercle and leprosy bacilli, the latter being more abundant, and appearing in heaps like a cigar in form, while the former are less numerous, and occur either singly or in irregular bunches. After staining, the granules in bacilli lepræ are coarse and widely separated, and in tubercle bacilli fine and close together. One point may be quoted as follows :—

They (leprosy bacilli) resist decoloration by acids, but to a less extent, according to Muir, Ritchie, and Woodhead, than do tubercle. Macé, however, states that they resist acids better than tubercle. Our own observations upon this point show that while tubercle bacilli appear red after 24 hours' immersion in 25 per cent. sulphuric acid, leprosy bacilli, which at the end of each hour up to 16 hours remain well stained, lose their stain after 18 hours' treatment; they are thus, according to Coles' table, more resistant to acids than all acid-fast bacilli except tubercle in sputum. The method we adopted was to place on the same slides smears of both bacilli, to ensure that in each case they received the same treatment.

The two bacilli were also similarly compared by Honsell's method, namely, after staining, washing and drying, by immersing for certain periods in a 3 per cent. solution of hydrochloric acid in alcohol, and then counterstaining in a saturated alcoholic solution of methylene blue. Up to 12 hours the tubercle bacilli retain their stain; after 2 hours the lepra bacilli remained well stained; after 3 hours very few could be distinguished, and after 6 hours

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[1] Jemma, R., and Di Christina, G. (June 24, 1911) "Über die Leishmania-Anämie der Kinder." *Cent. f. Bakt.*, I. Orig., Vol. LIX., No. 2.

[2] Smith, F. A., and Bisset, E. (1909), "The Bacteriology and Treatment of Leprosy." *Transactions Bombay Medical Congress.*

Leprosy— *continued*

only one or two very faintly reddish bacilli were seen. These results again place the bacilli in the same position as to their power of resistance relative to other acid-fast bacilli.

We venture to suggest that in these staining reactions lies the best method of clinically differentiating leprosy and tubercle in cases where either doubt exists or there is a question of a mixed infection.

Unna [1] describes a method of double staining for differentiating living and dead leprosy bacilli in tissue. It is too complicated for detailed description here, but the reference is likely to be useful, and the paper is illustrated by coloured drawings. Victoria blue, nitric acid and saffranin are employed; and normal bacilli stain blue, dead bacilli, yellow. This and other staining methods are mentioned by MacLeod [2] in a general survey of the leprosy question from the pathological aspect. He points out that recent work tends to class the leprosy bacillus under the streptothriceæ, and not with the schizomycetes. There is, so far, no evidence of true spores, though small spheres have been demonstrated in the bacilli. Many of the other points he mentions are now no longer correct, owing to the rapid advance of our knowledge as regards leprosy and improvements in technique. This, for example, applies to his remarks on cultivation of the bacillus, for more recently Clegg,[3] by first of all making use of symbiosis, has succeeded in obtaining the leprosy bacillus in pure culture. In summarising his work he says :—

(1) The leprosy bacillus was first cultivated from leprosy material in symbiosis with other unidentified bacteria and amœbæ, and later from other cases in symbiosis with amœbæ and the cholera vibrio.

(2) By heating a symbiotic culture of amœbæ, cholera and leprosy for a half-hour at 60° C. and incubating, the leprosy bacillus was obtained in pure culture.

(3) The leprosy bacillus isolated in this manner grows readily on the ordinary laboratory culture media.

(4) The bacillus is pathogenic for guinea-pigs, subcutaneous inoculations having caused lesions which macroscopically and microscopically resemble the leprous lesions of human subjects.

A full description of cultural characteristics on different media is given.

Still more recently Duval [4] has confirmed Clegg's work, has obtained pure cultures upon special media, and has succeeded in inoculating the Japanese dancing mouse and producing in it typical leprous lesions. This is a very important matter, as it may be the first step in the preparation of an artificial immune serum for use in human cases.

Russell [5] has reported an interesting case of infection by inoculation in South Africa. A white boy cut his foot when bathing. The wound bled freely. A native offered him a piece of tobacco, which he had been chewing, as a styptic. This was applied under a bandage and kept in contact with the wound for three days. The wound healed, but eventually broke down and became unhealthy. General leprosy, not at first recognised, set in, and death occurred about eleven years after inoculation. On inquiry the native who furnished the tobacco was found to have been a leper, who had died about four years after his act of mistaken charity. There was no other possible source of infection, and the case appears to have been a clear example of bacillary inoculation. Boeck [6] has met with three cases of advanced leprosy in which the leprosy bacillus was recovered from the fæces. He refers to the possibility of contracting leprosy both by inoculation of bare feet and by way of uncooked vegetables from land fertilised by infected human excrement. Gerber [7] discusses certain points in connection with the disease. Many believe that the primary lesion is to be found in the nasal mucosa. Gerber admits that leprosy of the head and face begins in the nose, but these cases only represent 78 per cent. of all the cases. After adducing the evidence of his experience of leprosy in Königsberg, the author comes to the following conclusions :—

(1) No bacilli are, as a rule, found in the healthy air passages of lepers.

(2) Bacilli are not found in the air passages of healthy persons living with lepers.

(3) Typically affected upper air passages secrete bacilli continuously in enormous numbers.

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[1] Unna, P. G. (1909), "The Differentiation of Living and Dead Bacilli of Leprosy in Tissue by Double Staining." *Transactions Bombay Medical Congress.*

[2] MacLeod, J. M. H. (August 21, 1909), "The Present State of our Knowledge of the Bacteriology and Pathological Anatomy of Leprosy." *Lancet.*

[3] Clegg, M. T. (December, 1909), "The Cultivation of the Leprosy Bacillus." *Philippine Journal of Science*, B.

[4] Duval, C. W. (September, 1910), "The Cultivation of the Leprosy Bacillus and the Experimental Production of Leprosy in the Japanese Dancing Mouse." *Journal of Experimental Medicine.*

[5] Russell, W. (September 10, 1910), "A Case of Leprosy by Inoculation." *South African Medical Record.*

[6] Boeck, (October, 1910), *Norsk Magazine for Lægevidenskaben*, quoted in *Journal Tropical Medicine and Hygiene*, January 2, 1911.

[7] Gerber, P. (September 15, 1910), "Über Lepra." *Deut. Med. Woch*, quoted in Epitome, *British Medical Journal*, January 7, 1911.

Leprosy—*continued*

(4) The greatest number of bacilli are derived from the nose.

(5) The secretion becomes the poorer in bacilli the farther down its source is placed

(6) Bacilli can be detected in fluid or dried secretion after months or even one year.

(7) Bacilli are sprayed most freely by sneezing, and next most freely by coughing and spitting.

(8) Pocket-handkerchiefs act as the chief carriers of bacilli, and give off bacilli to the washing water. Next to them, other linen and clothing carry bacilli, after these have come into contact with secretions.

(9) The author failed to find bacilli on the walls, in the beds, and on the floors of the rooms in which the lepers live. These rooms, however, were very well kept.

(10) No bacilli can be found in the secretion of the trachea below the tracheotomy wound. The bacilli are situated both intracellularly and extracellularly. He has gained the impression that the latter were more common. Lastly, he points out that although Ebstein believes that it is not possible to distinguish between leprosy bacilli and tubercle bacilli, the very enormous numbers in which the former are met with serves to distinguish them from the latter.

These conclusions may, of course, not be applicable to the coloured races and to leprosy in tropical countries.

Campana [1] has a paper on cultural methods, and gives a drawing showing the appearance of the bacillary culture under anærobic conditions, but more important recent work is that by Duval and Gurd [2] of New Orleans, who state :—

That the *Bacillus leprœ* may be cultivated on a variety of artificial media, and is capable of living and retaining its infectibility for months under adverse conditions outside of the animal body. Further, they claim that the bacilli can also be cultivated from contaminated leprous tissue and from the nasal discharge that has been kept at room temperature for more than a year. Contaminating organisms apparently have no appreciable effect on the viability and infectivity of some strains of the lepra bacilli. Pure cultures can be obtained directly from the infected leprous tissue on a variety of special media, including tryptophane and glycerinated blood agar, without first growing them in the presence of amœbas and their symbiotics. The authors cultivated in pure growth the specific organism directly from two cases of leprosy on Novy-MacNeal rabbit blood agar to which 1 per cent. glycerin had been added. Multiplication takes place slowly on artificial media, but once the growth has started it can be readily accelerated by frequent transplantations. That the cultures are leprosy bacilli, and not some other acid-fast species, they state, has been definitely proved by cultural and animal tests. White and Japanese dancing mice have been successfully infected, and lesions have also been produced in monkeys by the authors. As regards the spread of the disease from man to man they believe direct inoculation may occur, but it is the exception. Indirect transmission is more likely they think, and their investigations also confirm the belief that the mucous membrane of the naso-pharynx is the port through which the bacilli gain entrance to the body, as well as the chief source from which infection spreads.

Marchoux [3] also believes he has succeeded in cultivating the bacillus from nasal mucus, but only in impure culture. He speaks of a resting stage of the bacillus in which it is surrounded by a membrane resistant alike to acids and alkalis, and only very slowly digested by trypsin.

Duval,[4] who seems to have become the main exponent of the method, has continued his researches, and finds that unless amino-acids are present in the medium the initial multiplication outside the body cannot be obtained. The products of tryptic digestion must be present. This explains why symbiosis with putrefactive and other bacteria which split up nucleo-proteids into their end acid products is of value in isolating and cultivating the lepra bacillus. Amœbæ are not necessary, and indeed are detrimental, as they feed upon the organisms. Duval employs two methods of cultivation from the tissues. In one (the direct) tryptophane or a mixture of albumen and trypsin are employed with a culture medium ; in the other (indirect) bacterial species capable of digesting the albumen constituent of the culture medium are introduced into the medium. In both, the end result is identical, since they both provide for the presence of the amino-acids in the medium, without which the primary multiplication of the leprosy bacilli cannot be secured.

Nicolle and Blaizot,[5] by using lepra material rich in young bacilli, have succeeded in producing in inoculated monkeys local lesions similar to human lepromata. They cite the earlier work of Marchoux and Bourret, which, though doubtful, tended to show that the chimpanzee was susceptible. Their own experiments were conducted on the lower monkeys.

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[1] Campana, R. (December 31, 1910), "Über die Kultur des Leprabacillus und die Übertragung der Lepra auf Tiere." *Zeit. f. Hyg. u. Infekt.*, Vol. LXVII., No. 3.

[2] Duval, C. W., and Gurd, F. B. (February, 1911), "The Cultivation of the Lepra Bacillus." *Archives of Internal Medicine*, quoted in *Journal Tropical Medicine and Hygiene*, March 15, 1911.

[3] Marchoux, C. (February 8, 1911), "Culture d'un bacille acido-résistant provenant du mucus nasal des lépreux." *Bull. Soc. Path. Exot.*

[4] Duval, C. W. (March 1, 1911), "The Cultivation of the Leprosy Bacillus." *Journal of Experimental Medicine.*

[5] Nicolle, C., and Blaizot, L. (July 30, 1910), "Reproduction expérimentale de la lèpre chez les singes inférieurs." *C. R. Soc. Biol.*

Leprosy— *continued*

A general review of the subject is given in German by Bertarelli,[1] who appends a copious bibliography, but, as is all too common, largely ignores British and American work on the subject.

Closely allied to questions of bacteriology are those concerned with the diagnostic skin reactions in leprosy, the Wassermann test, other methods of diagnosis, the condition of the blood, and the possible rôle of insects as transmitters of the bacilli. To these various subjects we would now direct attention.

Brinckerhoff [2] records the reaction of lepers to Moro's "percutaneous" test for tubercle. He finds that—

(1) The "percutaneous" tuberculin test of Moro is of no value in the differential diagnosis of leprosy and tuberculosis.

(2) A certain number of cases of leprosy, in which there is no clinical evidence of tuberculous infection, give a reaction to Moro's test.

(3) The fact that lepers react to cutaneous inunction of a tuberculin salve may be taken as additional evidence of the chemical nearness of the product of the lepra and tubercle bacilli, and support the suggestion already made that tuberculin be given another trial in the therapeutics of leprosy.

Teague, in a preliminary report, states that he obtained negative results by the cutaneous method which, however, had not a fair trial. He promises more information on the subject. Slatineau and Danielopolu [3] tried both the cutaneous and ophthalmo reaction in lepers, obtaining thirteen positive out of twenty as regards the former, and fifteen out of twenty-five as regards the latter. They considered these to be due to an associated tuberculosis, but this is not the view of Babes,[4] who believes the reaction to be specific and different from that obtained in tuberculosis by being later in appearance, lasting longer, and sometimes only appearing after several injections. There have been numerous papers on the Wassermann reaction in leprosy. Deviation of the complement occurs, but the exact significance and nature of the test do not appear to have been settled. This and the fact that the reaction appears to vary, without apparent reason from time to time in the same patient, is brought out in an article by Ehlers and Bourret,[5] who also give full references to previous work on the subject.

Eliasberg [6] found that in a good many cases the serum of lepers caused complement deviation in the presence of syphilitic antigen, an observation of considerable value and significance, as the differential diagnosis between these two diseases is by no means always easy, and mercurial injections may cause marked improvement in leprosy, as noted by White and Richardson.[7] Serra [8] has carried out very complete researches :—

He followed Wassermann's technique as closely as possible ; each experiment was conducted in triplicate, and further, each patient's serum was tested six times over, using antigen from six different sources—leprous nodules, syphilitic nodules, normal liver and spleen from the guinea-pig, 0·3 per cent. lecithin solution, syphilitic liver, and normal guinea-pig's heart. Serra examined the serum of seventeen patients with leprosy, using the leproma antigen ; thirteen gave a positive, two a partially positive, two a negative reaction. Using the lecithin antigen, only one gave a positive reaction, ten a partially positive, and six a negative reaction. The other antigens gave intermediate results ; with syphilitic antigen seven were positive, with syphilitic liver eight, with normal organs four, with guinea-pig's heart five. Two patients with smooth or nerve-leprosy of twenty-six and thirty years' standing, gave uniformly negative results with the six varieties of antigen ; one with nodular leprosy gave uniformly positive reactions. Eight of the patients had mixed, smooth, and nodular leprosy, and seven of these gave a positive, one a partially positive reaction, with leprous antigen ; six had nodular leprosy, and all gave positive reactions with leprous antigen ; three had smooth or anæsthetic leprosy, and one of them gave a partial Wassermann reaction, two a negative result. The more florid and recent the infection is, the greater is the probability that the patient will give a positive reaction.

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[1] Bertarelli, E. (March 28, 1911), "Die neueren Ergebnisse der Forschungen über die Kultivierbarkeit des Hausenschen Bazillus und die Übertragung der Lepra." *Cent. f. Bakt.*, I. *Ref.*, Vol. XLIX., No. 3.

[2] Brinckerhoff, W. R. (1908), "The Reaction of Lepers to Moro's 'Percutaneous' Test." *Report to Treasury Department, Public Health and Marine Hospital Service, U.S.A.*

[3] Slatineau, A., and Danielopolu, D. (November 17, 1908), "Réaction des lépreux à la Tuberculine." *C. R. Soc. Biol.*

[4] Babes, V. (March 18, 1909), "Sur la signification de la réaction des lépreux à la tuberculine." *Ibid.*

[5] Ehlers, E., and Bourret, G. (November 10, 1909), "Réaction de Wassermann dans la lèpre." *Bull. Soc. Path. Exot.*

[6] Eliasberg, J. (November 4, 1909), "Komplementablenkung bei Lepra mit syphilitischem Antigen." *Deut. Med. Woch.*

[7] White, C. J., and Richardson, O. (January 2, 1909), "A Deceptive Case of Leprosy." *Journal American Medical Association.*

[8] Serra, A. (1909), "La seriodiagnosi di Wassermann nella lepra." *Il Polyclin.*, quoted in Epitome, *British Medical Journal*, November 5, 1910.

Fox [1] used both the Wassermann and Noguchi (human blood corpuscles) tests, and obtained somewhat similar results, the most positive findings occurring in cases of the tubercular and mixed types. Leprosy—*continued*

Ehlers, Bourret and With [2] recommend other methods for bacteriological diagnosis, *i.e.* the examination of blood-stained fluid obtained by needle prick of the skin lesions, and the examination of the serous fluid obtained from the same lesions by means of a sharp pointed Pasteur pipette introduced through the skin. The latter gave on the whole better results than the former, and was also superior to examination of the nasal mucus. Both procedures are fully described. They failed to find the bacilli by direct examination of pus from an abscess produced by the application of turpentine, although Hansen has shown that the bacillus is present in the circulating blood, and in the pus of suppurating comedones in tuberculous leprosy. The Legers [3] have studied the blood in leprosy cases in Madagascar, more especially as regards the differential leucocyte count. They find this to be different in nerve leprosy to what is found in the tuberculous form. In the former there is an increase, sometimes considerable, of the large mononuclears, in the latter there is an inconstant eosinophilia. Bourret, [4] from a study of the literature, finds that views vary greatly on this subject, all kinds of counts being recorded. He carried out observations which showed that the count varied greatly from day to day, a fact which robs it of all diagnostic value.

We have mentioned Hansen's discovery, that the bacilli are to be found in the circulating blood. At the Second International Congress on Leprosy in 1909, it was shown by a mixed French and Danish Commission which studied the disease in the West Indies, that the bacilli are not found at all times in the circulating blood, but only where there is an aggravation of the disease, hence insects are unlikely to acquire bacilli by sucking blood. It is possible that shortly before death the tissues become charged with bacilli, and that then insect bites may play an important part in infection. As both the urine and fæces are often crowded with bacilli it is possible flies and other insects may pick up the organisms from these sources (A.B.). This leads us to the consideration of methods of infection, and to the consideration of papers dealing with the rôle of insects, a subject which every year is attracting more attention, but which is yet far from being definitely settled. We cannot do better than begin by quoting the resolution of the British and Colonial Delegates at the above-mentioned conference which was held at Bergen. They stated that :—

(1) Leprosy is spread by direct and indirect contagion from persons suffering from the disease. The possibility that indirect contagion may be effected by fleas, bugs, lice, the itch parasite, etc. has to be borne in mind. Leprosy is most prevalent under conditions of personal and domestic uncleanliness and overcrowding, especially where there is close and protracted association between the leprous and non-leprous.

(2) Leprosy is not due to the eating of any particular food, such as fish.

(3) There is no evidence that leprosy is hereditary; the occurrence of several cases in a single family is due to contagion.

(4) In leprosy an interval of years may elapse between infection and the first recognised appearance of disease. It is a disease of long duration, though some of its symptoms may be quiescent for a considerable period and then recur.

(5) The danger of infection from leprous persons is greater when there is discharge from mucous membranes or from ulcerated surfaces.

(6) Compulsory notification of every case of leprosy should be enforced.

(7) The most important administrative measure is to separate the leprous from the non-leprous by segregation in settlements or asylums.

(8) In settlements, home life may be permitted under regulation by the responsible authorities.

(9) The preceding recommendations, if carried out, will provide the most efficient means of mitigating the leper's suffering and of assisting in his recovery, and at the same time will produce a reduction and ultimate extinction of the disease.

It will be seen that the fish theory of Hutchinson has apparently received its quietus, but Sticker,[5] at the Congress, mentioned having found an acid-fast bacillus in fish suffering from various affections. It is not unlike the leprosy bacillus in some respects. Sticker thinks

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[1] Fox, H. (May, 1910), "The Wassermann and Noguchi complement fixation test in leprosy." *American Journal of Medical Science.*

[2] Ehlers, E., Bourret, G., and With (April 12, 1911), "Recherches sur le mode de propagation et les procédés de diagnostic bactériologique de la lèpre." *Bull. Soc. Path. Exot.*

[3] Leger, A. and M. (October 14, 1908), "Contribution à l'hématologie de la lèpre." *Ibid.*

[4] Bourret, G. (January 13, 1909), "Sur la valeur séméiologique de la formule leucocytaire dans la lèpre." *Ibid.*

[5] Sticker, G. (1909), "Fragen zur Ätiologie der Lepra." *Report of Second International Leprosy Conference.*

Leprosy— *continued*

this observation may be useful, though he regards Hutchinson's complete theory as untenable. This and several other papers read at the Congress will be found reviewed in the *Bulletin of the Pasteur Institute* for September 15, 1910. To return to the insect question, which is intimately associated with that of leproid diseases amongst animals such as rats, Wherry,[1] who had already dealt with leprosy, carried out some further work upon it, more especially as regards the part flies might play in its transmission.

He also extended his observations to human leprosy, and concluded :—

(1) Flies (*C. vomitoria, L. Cæsar, M. domestica*) take up enormous numbers of lepra bacilli from the carcass of a leper rat and deposit them with their fæces ; but the bacilli apparently do not multiply in the flies, as the latter are clear of bacilli in less than 48 hours.

(2) The larvæ of *C. vomitoria,* hatched out in the carcass of a leper rat, become heavily infested with lepra bacilli.

(*a*) If such larvæ be removed and fed on uninfected meat they soon pass out most of the lepra bacilli. Such larvæ pupate and the flies hatching therefrom are generally uninfected. Occasionally a fly may deposit a few lepra bacilli after emerging from its pupal case—but is apparently not infested in the real sense of the term.

(*b*) If the larvæ of *C. vomitoria* be fed almost continuously on the carcass of a leper rat they remain heavily infested with lepra bacilli. When they pupate, the heavily infested pupæ seem to be incapable of undergoing further development.

(3) A fly (*M. domestica*) caught on the face of a human leper was found to be infested with lepra-like bacilli. These were few in number at the beginning of the observation, but on the third day more than 1,115 lepra-like bacilli were present in each speck deposited. However, only one bacillus was found in the specks deposited between the third and sixth days. The acid-proof bacilli in this fly were not infective when injected into the subcutaneous tissue of a guinea-pig.

(4) The agglutinating action of blood serum from three human lepers was tested on washed suspensions of rat lepra bacilli with practically negative results.

At a later date the same author [2] found acid-fast bacilli resembling those of rat leprosy in what appeared to be the intestinal contents of rat lice (*Hæmatopinus spinulosus*) taken from a Norway rat suffering from the disease, and which was covered with louse eggs. Borrel,[3] in a paper illustrated by several coloured plates, seeks to prove that *Demodex folliculorum* and allied skin parasites can transmit leprosy from the sick to the sound. His ideas, like those in relation to malignant disease, are ingenious, but so far are not founded on exact experimental work. Lefebvre [4] has recently taken up the matter in the Philippines, and has decided against Borrel's theory, both in the case of *Demodex folliculorum* and in that of *Sarcoptes scabiei.* Apart from anything else the sedentary habits of the *Demodex* preclude its being an active transmitter of leprosy. Both papers are, however, full of interest. A most important recent article is that by Currie,[5] who carried out work at Honolulu with mosquitoes and flies. The paper is a long one and requires careful study, but the conclusions are well worth quoting, for they appear to settle the question, at least so far as mosquitoes are concerned. He finds that mosquitoes, feeding under natural conditions upon cases of leprosy, do not imbibe the lepra bacillus. This is because when these insects feed they insert their proboscis directly into a blood-vessel, and thus obtain bacilli-free blood unmixed with lymph. He states that the above-mentioned habit alone accounts for the absence of lepra bacilli in mosquitoes that have fed on lepers ; the insect neither avoids biting a leprous nodule, nor is its digestive tract or the contained fluids capable of altering the morphology of this bacillus in a reasonable length of time.

The species of mosquito employed in the experiments was *Culex cubensis,* but it is to be expected that the above finding would apply to other species as well. The flies used were *Musca domestica, Sarcophaga pallinervis* (Thomson), *Sarcophaga barbata* (Thomson), *Volucella obesa* (Fabr.), and an undetermined species of *Lucilia,* and the conclusions arrived at were :—

(1) That the above-named flies, when given an opportunity to feed upon leprous fluids, will contain the bacilli in their intestinal tracts and fæces for several days after such feeding.

(2) That the above fact, together with the well-known habits of these flies, makes it certain that, given an exposed leprous ulcer, these insects will frequently convey immense numbers of lepra bacilli, directly or indirectly to the skins, nasal mucosa, and digestive tracts of healthy persons.

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[1] Wherry, W. B. (December 18, 1908), " Further Notes on Rat Leprosy and on the Fate of Human and Rat Lepra Bacilli in Flies." *Journal Infectious Diseases.*

[2] *Idem* (November 5, 1909), " Rat Lepra Bacilli in the Rat Louse." *Ibid.*

[3] Borrel, A. (February 25, 1909), " Acariens et Lèpre." *Ann. de l'Inst. Past.*

[4] Lefebvre, M. (November, 1910), " Researches on Acarids among Lepers." *Philippine Journal of Science,* A.

[5] Currie, D. H. (1910), " Mosquitoes and Flies in Relation to the Transmission of Leprosy." *Public Health Bulletin,* No. 39 ; *Public Health and Marine Hospital Service, U.S.A., Treasury Department.*

Leprosy—*continued*

(3) That our present state of knowledge does not permit us to determine whether such insect-borne bacilli are or are not capable of infecting persons whose skin and mucosa are thus contaminated; but until we have more accurate knowledge on this point we are justified in regarding these insects with grave suspicion as being one of the means of disseminating leprous infection.

Ehlers, Bourret and With [1] conducted similar experiments with *Stegomyia fasciata*, *Acanthia* (*Cimex*) *lectularius*, *Pulex irritans*, *Pediculus capitis*, and *Argas persicus*, and found that the first four of these at least so rarely absorb the bacilli that it is scarcely possible that they can act as carriers. In the case of the tick the experiments were too meagre to permit any conclusions to be drawn.

There now remain some other questions regarding transmission, the consideration of certain general and clinical papers and reports, and the unsatisfactory subject of treatment. Nicholas [2] thought it probable that the disease could be transmitted by coitus, and advanced some bacteriological arguments in favour of this view, to which, however, Jeanselme would not subscribe, pointing out that acid-fast bacilli are found in the normal vagina, and stating that the hypothesis was very difficult to establish owing to the long period of incubation, which often extended to several years. Marchoux agreed with this view. Atcherley [3] advances a new theory as to the origin of leprosy :—

Briefly stated, it is that leprosy is a chronic, diathetic disease, with a gradual onset and irregular course, characterised by an inflammatory fibroid degeneration of the nerve tissue generally, which precedes the deposit of the lepra bacillus. This nerve degeneration is the result of defective food pabulum supplied by the blood, from the ingestion of improper food. This theory is based on the fact that the pathological changes in leprosy bear a striking analogy to those of scurvy. The position of the lepra bacillus is explained by that of the micrococcus of scurvy, which is found along the track of the degenerated arteries. There are several diseases that have their origin in improper foods; these are pellagra, podagra, leprosy, scurvy and urticaria. Were leprosy contagious, ports of entry should be full of lepers. No cases are definitely known to have been caused by direct contact, but many are known to have occurred without it. Infants never have leprosy or develop it before five years of age, and many remain entirely immune from it although born of leprous mothers. Segregation is of little value, because many cases having the lesions concealed remain at large. The improper food is such as is found far removed from centres of industry, in inaccessible, barren places, such as a seashore, where shell-fish are eaten raw with spoiled vegetable food. The scurvy theory explains cases of spontaneous cure of leprosy; it explains why the same remedy will succeed in one case and fail in another, how cases may be found at great distances from the sea, and why a leper improves when removed from his home to another climate.

Of great importance and interest, though unfortunately too voluminous for insertion here, are the reports and recommendations of the special French Commission appointed to inquire into the whole question of leprosy in the French colonies. One must rest content with referring the reader to the *Bulletin de la Société de Pathologie Exotique* for February 10, and March 14, 1909. In the latter the discussion of the report and the various amendments proposed will be found fully detailed, while it is clearly shown that a grave view is taken of the spread of the disease in some of the French colonies. Wherever possible the establishment of leper colonies on islands in rivers is advocated. A general account of the measures in force in Madagascar is given by Lamoreux.[4] One specially mentions his papers, as the question of leper settlements will sooner or later have to be seriously faced in the Sudan, and it is helpful to be able to study well-devised schemes elsewhere. It is specially interesting to note that Jeanselme [5] has recently brought to light that there are between 160 and 200 lepers in Paris. An inquiry showed several unsuspected cases, some in schools and institutions, one a valet, and one actually a child's nurse. As a result of his representations [6] a commission was formed which reported on the prophylactic measures to be taken in France. Brinckerhoff and Moore [7] have investigated the question as to the nose being the site of the primary lesion. They detail the technique employed, give numerous references to the literature, and conclude :—

(1) The routine examination of the nasal septum and the nasal secretions of individuals of a race with a high incidence of leprous infection did not reveal as many cases of leprosy as would be expected from statistical data, had the method been an efficient one for establishing a diagnosis of the disease in the incipient stage.

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[1] *Loc. cit.*

[2] Nicholas, C. (April 14, 1909), "Contagion possible de la Lèpre par le coit." *Bull. Soc. Path. Exot.*

[3] Atcherley, J. (August 6, 1910), "A Theory as to the Origin of Leprosy." *Medical Record*, quoted in Epitome, *British Medical Journal*, September 3, 1910.

[4] Lamoreux, A. (March 3, and April 13, 1910), "Les conditions d'isolement des lépreux dans la région du plateau central à Madagascar (province de Tananarive)." *Bull. Soc. Path. Exot.*

[5] Jeanselme, E. (December 14, 1910), "L'afflux des lépreux étrangers à Paris." *Ibid.*

[6] *Idem* (January 11, 1911), "Rapports au nom de la Commission de Prophylaxie de la Lèpre en France." *Ibid.*

[7] Brinckerhoff, W. R., and Moore, W. L. (1909), "Upon the Utility of the Examination of the Nose and the Nasal Secretions for the Detection of Incipient Cases of Leprosy." *Public Health Report*, "Studies upon Leprosy." *Public Health and Marine Hospital Service, U.S.A., Treasury Department.*

Leprosy—*continued*

(2) The examination of the nasal septum and the nasal secretions is not of dominant value in confirming a diagnosis of leprosy in the early stages of the disease.

(3) The conditions found in the noses of non-leprous children of leprous parents do not differ in important respects from those found in the descendants of non-lepers.

(4) When it is not practicable to make a complete physical examination of all individuals of a class suspected of leprosy, the examination of the nasal septum and the bacteriological examination of the nasal secretions will prove of value by permitting the recognition of the most dangerous type of the disease, and is therefore worth while even if it does not reveal all cases of the discase in those who come under observation.

The general view is that leprosy is not hereditarily transmitted. A paper on this subject and dealing with infection by contagion is that by Le Dentu,[1] who cites some experiences of Noël in the leper settlement on Guadeloupe. The discussion on this paper was interesting. In Madagascar the infants of leprous parents are separated from their mothers and reared by hand in an orphanage. Jeanselme [2] also discusses these questions. He says hereditary transmission has never been proved, and he failed to find any lesion in the placenta and umbilical cord from a case of maculo-anæsthetic leprosy. He thinks that in countries where leprosy is endemic children born of a leprous mother should not be wet-nursed, as it is possible that the infant might have acquired infection during labour. He notes that in countries where the disease is not endemic the leper is very slightly contagious.

Gurd [3] describes a case where there was suppuration in leprosy tubercles accompanied by fever and constitutional disturbance, and yet in which organisms of suppuration could be found. The attack benefited the general condition just as a bout of the so-called lepra-fever does. Legendre [4] records a curious case which exhibited a tuberculous eruption from the very beginning. This remained confined to the face, and there was a rapid development of the affection, which terminated sharply by granulating. The diagnosis was confirmed microscopically, and lepra bacilli were found in the nasal mucus.

Jeanselme [5] has recently reported an example of pulmonary leprosy chiefly characterised by a raised temperature, an area over the middle part of the right lung where moist râles could be heard, and a development of intra-dermic nodules. In the nasal mucus and the discharge from the skin tubercles the characteristic "*globi*" or clumps of bacilli were numerous. The pulmonary condition is very difficult to distinguish from tuberculosis, and it is to be noted that both diseases may occur simultaneously.

Ashburton Thompson [6] in his reports gives many interesting clinical notes. In that for 1909 he says: "Direct epidemiological evidence on the means by which leprosy is maintained and diffused has been adduced very seldom. Now inference is relied upon to support the hypothesis of contagion, drawn from records which (as it seems to me) admit of other interpretations."

In support of this statement he quotes the *Report of the Indian Leprosy Commission* for 1893, in which the commissioners stated that:—

Although they consider leprosy an infective disease, caused by a specific bacillus, and, moreover, also a contagious disease, they are of opinion that there is not sufficient evidence that leprosy is maintained or diffused by contagion; indeed, under the ordinary human surroundings the amount of contagion which exists is so small that it may be disregarded, and no legislation is called for on the lines either of segregation or of interdiction of marriage with lepers.

His remarks are interesting, but he does not put forward any alternative explanation, and, as has been shown in this Review, the main body of observers are now in favour of contagion as at least one method of spread. Thompson's reports, however, deal chiefly with questions of treatment, and more especially with the nastin method. One has reference to many papers on this subject, but they do not call for special notice, as, though nastin has been of benefit now and then, it has unhappily fallen short of expectations. The Second International Congress on leprosy decided that a clinical study of the disease leads to the conclusion that it is not incurable, but no certain remedy has yet been discovered. Some favourable results both with nastin and its modification nastin B. were, however, reported, and the leproline of

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[1] Le Dentu, A. (June 8, 1910), "L'hérédité et la contagion à la léproserie de la Désérade." *Bull. Soc. Path. Exot.*

[2] Jeanselme, E. (May 11, 1910), "L'enfant issu d'une lépreuse peut-il être allaité par une nourrice?" *Ibid.*

[3] Gurd, F. B. (January 3, 1911), "Upon the Presence of Suppuration in the Tubercles of Leprosy." *Journal Infectious Diseases.*

[4] Legendre, J. (January 11, 1911), "Sur un cas de lèpre à forme anormale." *Bull. Soc. Path. Exot.*

[5] Jeanselme, J. (February 8, 1911), "Sur la lèpre pulmonaire." *Ibid.*

[6] Thompson, J. A. (1909), *Nineteenth Report of the Board of Health on Leprosy in New South Wales.*

Rost has been found useful. So has antileprol, a special form of chaulmoogra oil, and one more easily tolerated than the ordinary preparation. Leprosy—*continued*

Nastin B. is a solution of nastin in benzoylchloride of about 1-30, and with it Jackson [1] in nine cases has reported encouraging results after 14 weeks of treatment. Messum [2] in South Africa treated twenty cases without benefit, using both nastin B_1 and B_2. Brinckerhoff and Wayson [3] tried the drug on six cases in Hawaii, and reported as follows :—

(1) In our hands the administration of nastin to six cases of leprosy gave slightly encouraging results in two cases. In one of these the lesions decreased in extent and took on a focal character. In the other case a tubercle disappeared during the treatment.

(2) Four cases seemed unaffected by the treatment, even when persisted in for over a year.

(3) Constitutional reactions were only seen when the dosage was large. No local reaction or puriform softening of tubercles was observed.

Peiper [4] also records benefit in two cases, using B_1 and B_2, and other papers testify to its partial efficacy in India and elsewhere, but on the whole the drug has proved disappointing, and the evidence is conflicting. One may perhaps quote the most recent expression of opinion available, that of Ranaday [5] in India, who says :—

I have great pleasure in reporting a case of anæsthetic leprosy which has improved a great deal under nastin treatment. The patient had noticed patches on the cheek, lips, and back thirteen years ago without suspecting it to be leprosy. The hands had lost sensation, and were wasted, having assumed the peculiar leprous character. The patient's fingers constantly got hurt, and it was to get one of these hurts dressed that the patient came under observation. The patches when noticed were distinctly anæsthetic, with raised and red margins.

The patient was given twelve injections of nastin BO and twelve Bl, one every week. The margins of the patches after this treatment have altogether disappeared, and the sensation has returned. The patches have faded away; the general health of the patient has greatly improved.

In several of the other papers quoted in this section accounts of the nastin treatment will be found, notably, perhaps, in the article by Smith and Bisset.

Turning to other methods, we find Whitmore and Clegg dealing with what they call the specific treatment of leprosy, and summarising as follows :—

(1) We have prepared a vaccine, a glycerine extract and a soap solution, from an acid-fast bacillus which Clegg cultivated from leprous tissue. We have used these preparations in the treatment of cases of leprosy for twelve and one-half months without noting any improvement in the condition of any of the patients. In some of the cases we have noted reactions after the injections, but we are not prepared to say whether or not these reactions are specific.

(2) Our glycerine extract of this organism does not produce a skin reaction on leprous or tuberculous patients, nor on normal persons.

(3) We have treated these same leprous patients for two and one-half months with a soap solution of leprous spleen, rich in leprosy bacilli, without noting any improvement in the condition of the patients.

(4) We have treated cases of leprosy for eight months with injections of atoxyl and also with injections of a mixture of sodium cinnamate and mercury cinnamate, without noting any improvement in the patients.

(5) We have treated cases of leprosy for eight months with injections of Nastin B. These patients already had been treated with injections of Nastin B. for nine months by Dr. Teague. At the end of the seventeen months no improvement was noted.

Montel [6] has revived the method of Diesing, *i.e.* the hypodermic injection into the lesions of a suspension of iodoform in olive oil. The preparation ought to be freshly prepared, the oil brought to the boil in a porcelain capsule, and then, the flame being removed, the iodoform added. He has also given potassium iodide combined with chaulmoogra oil, and has administered the latter by injection. He finds that :—

(1) The local injections of a suspension of iodoform in olive oil (10 to 20 per cent.) are followed by a disappearance of the localised leprous skin lesions, of the anæsthesia and of the pain.

(2) Iodide of potassium has clearly a favourable action on the symptoms in leprosy.

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[1] Jackson, T. (December 15, 1909). *Therapist.*

[2] Messum, G. (May, 1910), "Twenty cases of Leprosy treated simultaneously with Deycke's Nastin." *Transvaal Medical Journal.*

[3] Brinckerhoff, W. R., and Wayson, J. T. (1909), "A Report upon the Treatment of Six Cases of Leprosy with Nastin (Deycke)." *Public Health Report,* "Studies upon Leprosy." *Public Health and Marine Hospital Service, U.S.A., Treasury Department.*

[4] Peiper (1910), "Zweiter Bericht über die Behandlung von Leprakranken mit Nastin B_1 and B_2." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIV., No. 9.

[5] Ranaday, S. G. (April 29, 1911), "Nastin in Leprosy." *British Medical Journal.*

[6] Montel, M. L. R. (January 11, 1911), "Notes de thérapeutique sur la lèpre." *Bull. Soc. Path. Exot.*

Leprosy—*continued*

(3) Oil of chaulmoogra is best given hypodermically.

(4) All substances capable of producing a leucocytosis appear to have a favourable action on the course of the disease in leprosy.

As regards the last conclusion, Marchoux pointed out that leprosy is a "malady of phagocytosis" in itself, and thought that *à priori* a substance causing leucocytosis would do harm. He looked upon the results obtained as most interesting. Lukis [1] treated five cases with X-rays. They assisted in healing up superficial ulcerations, but otherwise did not help greatly. The treatment, however, was not prolonged. Heiser [2] has reported a case of apparent cure by this means. The bacilli disappeared from the lesions. The face was the part affected, and the patient was under observation for a period of nearly two years.

Treatment was begun on November 5, 1906, by exposing the lesions on the patient's head every three days to X-rays for ten minutes at a sitting at a distance of 26 cm. from the tube. The intensity of the light employed was just sufficient to give a distinct outline of the bones of the hand. The regular Gundlach tube and a 45 cm. spark induction coil and a mercury turbine interrupter were used. From November 21 to January 21 the treatment was the same, with the exception that his head was placed within 18 cm. of the tube. During this period he commenced to show considerable improvement, in that the lesions, most noticeable in the right ear, were rapidly growing smaller. From January 21 to February 8, 1907, he was exposed at a distance of 12 cm. from the tube. From February 8 to February 26 he was exposed every two days at a distance of 12 cm. From February 26, 1907, to July 1, 1908, every two days at a distance of 25 cm. for ten minutes.

During June, 1907, the affected parts presented almost a normal appearance. The lepra bacillus was difficult to demonstrate, and many specimens were often necessary in order to find it. During January, 1908, the case was apparently cured, from a general clinical standpoint; the infiltrations had entirely disappeared, there were no anæsthetic areas, the ears were normal in size, and the cosmetic effect was practically perfect, so far as the leprosy was concerned. No lepra bacilli could be demonstrated at the site of the leprous lesions at which they had heretofore been found, but they could be found in scrapings made from the nasal septum. Shortly before this period yaws made its appearance among the inmates of the Leper Hospital, and he also contracted this disease soon afterwards.

Between January and June, 1901, repeated microscopic examinations were made, and lepra bacilli could be found only in specimens taken from the septum of the nose, and during the latter part of this period it became more and more difficult to find them even there. From June 15, 1908, to August 1, 1908, the date of the last observation, it has been impossible to find lepra bacilli in specimens taken from any portion of his body, and he presents practically a normal appearance.

Hollmann [3] believes in eucalyptus, and thinks it would cure if used at the beginning of the disease. His cases, 275 in number, had been leprous for from 5 to 20 years, and apparently they all improved. The treatment consists of two stages :—

(1) The compound eucalyptus treatment for medicated baths. Formula : Take of thoroughly cut eucalyptus leaves ¼ lb., of ohia leaves (mountain apple, *Jambos malaccensis*) ¼ lb., ground hæmatoxylon bark, and ground hemlock bark, each 1 oz. These are tied in a small muslin bag. Directions : To make the bath, place the bag in 5 gallons of water, boil for 1 hour, of this take 2½ gallons and add to the daily bath.

(2) Eucalyptus distillate treatment, for internal use. Formula : Take eucalyptus leaves, cut up thoroughly and place in still, cover with water and place on fire. From a 5-gallon still there result 3 gallons of distilled eucalyptus. Directions : Take ½ teaspoonful in a glass of water three times a day. Gradually increase the dose until the patient is taking a tablespoonful three times a day.

It is, however, worthy of note that the patients who showed the most marked improvement used after the bath an inunction of equal parts of eucalyptus oil and chaulmoogra oil. The latest attempts at therapy have been by means of salvarsan. Montesanto [4] has tried it in several cases. Given subcutaneously in small doses it does not affect the lepra bacilli. Larger doses, especially if given intravenously, have a destructive action on the organisms, and superficial lesions tend to heal. The drug does not affect the granulomata in development. He thinks it should be given both in the early and late stages. Other observers like Gioseffi have not seen any benefit from its use, and in any case it is too early for any definite or permanent results to have been obtained. It does not seem likely that it will cure leprosy, which still unfortunately in the great majority of cases baffles the therapist.

Additional Notes

A paper which would appear to be of great importance has recently appeared. It is that by Williams,[5] who adopts a new view of the bacteriology and treatment of the disease. This is put forward in a special paper illustrated by coloured plates, some of the work having been

[1] Lukis, C. P. (July, 1908), "Cases from the Medical College Hospital, Calcutta." *Indian Medical Gazette.*

[2] Heiser, V. G. (October 31, 1908), "A case of Leprosy apparently cured by X-rays." *Medical Record.*

[3] Hollmann, H. T. (March 27, 1909), "Eucalyptus in Leprosy." *New York Medical Journal.*

[4] Montesanto, D. E. (March 7, 1911), "Der Einfluss des Salvarsan auf die Leprabazillen." *Münch. Med. Woch.*

[5] Williams, T. S. B. (May, 1911), "Leprosy: A new View of its Bacteriology and Treatment." *Supplement Indian Medical Gazette.*

accomplished by Rost. Here we can only give the résumé, but the paper must be studied by all concerned with the leprosy question, as indeed will be seen from the following :— Leprosy—*continued*

I have shown in the preceding parts of the paper that we have cultivated, primarily, a non-acid fast streptothrix, which may be a definite streptothrix or a diphtheroid bacillus, according to the media on which it originates. There is no essential morphological difference between these two, and both, at some period, produce acid fast bacilli, identical with the bacillus lepræ. Also this non-acid fast diphtheroid bacillus always grows acid fast in the bodies of amœbæ, and old cultures also show a disappearance of the non-acid fast portions and the presence of swollen acid fast elements. This diphtheroid bacillus has been grown frequently by many people. Further, by continuing to subculture the organism in Rost's medium, instead of on solid media, a definite acid fast streptothrix has been obtained, remarkably similar to the organisms of Rost and Deycke. This acid fast streptothrix produces in guinea-pigs lesions somewhat resembling those of leprosy, and in leper patients it causes severe general and local reactions, which would appear to be specific, as judged by its negative action on healthy people. I believe that it is possible to miss out the non-acid fast diphtheroid bacillus stage, and to grow the acid fast streptothrix stage direct, as has been done by Rost and Deycke, and lately by ourselves in this laboratory. What obtains in a culture would seem to depend on hitting off some special medium, and some special phase of the streptothrix. Even if one succeeds in getting the acid fast form directly, it tends to lose this property very easily, but we are now learning that, by putting it back into certain media, it can be made to regain its acid fastness.

It will now, I hope, be admitted that there are certain grounds for the view which I put forward earlier in this paper, to the effect that we must consider the organism of leprosy, not as an acid fast bacillus only, but as a pleomorphic streptothrix, which in addition to changes in form may also show great changes in its staining properties. It follows obviously from the foregoing that, if our views are correct, the question of the mode of spread of the disease should be approached in a much broader spirit. In the past, all attention has been concentrated on the acid fast bacillus, and no attention was paid to results which did not show this acid fast bacillus.

In the future we must approach the question with a full knowledge of the streptothriceæ, and be prepared to weigh carefully results which may seem, at the moment, hopelessly incongruous.

The treatment is by a vaccine prepared from a six weeks' growth of the streptothrix in broth. It has been found to produce a marked reaction, and further details will be awaited with interest. In the light of this paper one need merely mention that Twort [1] has introduced a new culture method for the lepra bacillus. It is based on the property which the glucoside ericolin possesses of destroying all organisms which are not acid fast.

Liver Abscess. At the British Medical Association Meeting in 1908 the subject of Tropical Abscess of the Liver was fully discussed. An account of the proceedings will be found in the *Journal of Tropical Medicine and Hygiene* for August 15, 1908. Havelock Charles pointed out that in India the native soldier is seventeen times less liable to hepatitis and twenty-five times less liable to hepatic abscess than the European soldier. Other statistics also show the much greater incidence of this liver disease in Europeans. He believes this is accounted for by the facts that—

(1) The liver of the European is handicapped by tropical conditions of life.

(2) It is the induced vulnerability that causes it to fall a more facile victim on its invasion by micro-organisms, and suppurative processes are more easily set up therein.

(3) The condition of hepatic congestion and irritation is the prime predisposing cause, whether the direct cause be protozoal or bacterial. That is, the necessary antecedent of abscess must be an inadequacy of the liver to cope with the work thrown on it. Amongst the conditions adversely affecting the physiological balance of liver action were heat, food, alcohol, malaria, abuse of exercise, congestion and inflammation. He maintained that there was a tropical liver with its special etiology as a definite disease, distinct from the congestive liver trouble of temperate climes.

He discussed the relationship of dysentery to liver abscess, and pointed out that there are countries where the former is rare, the latter common, and vice versa. His method of treatment in patients threatened with liver abscess was—

(1) Rest in bed, absolute.

(2) External applications, oleate of iodine under hot fomentations.

(3) The use of sod. salicylat., ammon. chloride, sod. sulph., pot. iod., ipecac. According to the case, calomel, soda and phenalgin, not forgetting the old blue pill, followed by a saline purge, which with him had often cured the fouled tongue, the painful enlarged liver, in which pus was of a certainty thought to exist or about to form.

Rogers referred to his ipecacuanha treatment for pre-suppurative hepatitis, a method long ago introduced by Maclean, discussed in our first Review, and the value of which has received ample confirmation both in India and elsewhere. Bose, like Havelock Charles, thought the amœba was not the sole cause of liver abscess. There were cases which could not be traced to dysentery. He mentioned having seen two cases in infants a few months old.

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[1] Twort, F. W. (November 17, 1910), "A Method for Isolating and Growing the Lepra Bacillus of Man." *Proceedings Royal Society*, B., Vol. LXXXIII.

Liver Abscess—*continued*

Manson spoke to the importance of always examining the blood before exploring a liver abscess, as an unrecognised leucocythemia might lead to fatal hæmorrhage. These appear to be the main points in an interesting discussion.

We have mentioned the ipecacuanha treatment. Rogers [1] returns to it in a later paper. He again refers to the peculiar and characteristic type of leucocytosis, *i.e.* one without any marked increase of the polynuclears, which run from 70 to 80 per cent. He now gives the drug in 20–30 grain doses, four to six 5-grain keratinised capsules being given at one time. This greatly lessens nausea, for the ipecacuanha is not set free till it reaches the intestines. Pills coated with melted salol also serve the purpose. He gives one full dose in the twenty-four hours, preferably late at night, on an empty stomach. In this paper he also again advocates aspiration and the injection of quinine in cases of liver abscess. The *Indian Medical Gazette* for September, 1910, is a special number largely devoted to the consideration of hepatitis and liver abscess, in which Pilgrim, Drury, Calvert and Nott all testify to the value of the ipecacuanha treatment of hepatitis. The method adopted by Pilgrim [2] is given in careful detail, and may perhaps be quoted in full as a guide.

> When not associated with loose stools and the bowels are on the contrary inclined to be costive, a mild mercurial purge is first given; otherwise the ipecacuanha treatment is begun on the evening of admission or diagnosis of the disease. It is necessary that the patient should have nothing to eat or drink for at least two hours before and after the giving of ipecacuanha. Twenty minutes before taking the ipecacuanha I give 20 grs. of chloral, and then in average cases I give 25 grs. of ipecacuanha; in severe cases in which the full influence of the drug is immediately required, I give 30 grs. for the first three or four nights, after that reducing it to 25 and 20 grs. gradually. I have occasionally given 40 grs., but I believe this is seldom necessary, and the cases treated in this hospital have responded very favourably to 30 gr. doses and less. As a rule I find one dose daily suffices, but in severe cases I do not hesitate to give it night and morning, and also in cases apparently severe, but in which the leucocytosis does not rapidly reduce. The ipecacuanha is given in keratine capsules, 5 grs. in each, and I am quite sure that given in this way the ipecacuanha treatment is robbed of half its horrors; given in capsules, both the nausea and vomiting are very greatly reduced. Many patients do not vomit at all, but only suffer for a short time from nausea, while some few are absolutely free from any unpleasant or abnormal sensation; it is all a question of whether the capsule breaks or comes undone before it has passed through the pylorus. I have at the present time a gentleman under my treatment who for three nights in succession took 40 grs. of ipecacuanha (prescribed outside the hospital) in keratine capsules without any unpleasant results, while three or four days later when taking only 20 gr. doses he was sick and had nausea on one occasion, in all probability due to one of the capsules breaking, or in some way prematurely releasing its contents. After swallowing the ipecacuanha the patient is enjoined to lie absolutely still in bed; when under the influence of chloral he usually soon drops to sleep, and if he wakes up two or three hours later feeling uncomfortable, the drug will at all events have largely exerted its influence. I think it a mistake to put on mustard plasters or other local applications to the stomach, which only attract attention to that organ, and interfere with the drowsy feeling which begins to steal over the patient, ending soon in sleep.
>
> The daily dose of ipecacuanha is continued till the leucocytosis falls to 10,000 or less, and the temperature has become normal, and the pain or discomfort in the region of the liver has gone, this latter being amongst the first symptoms that disappear under this treatment. I then continue the ipecacuanha for another week in daily doses of 20 grs., for by this time, even in cases where the drug has proved obnoxious, toleration is usually established, and the patient, seeing the result obtained, is seldom refractory. Other important accessories such as diet and rest are, of course, very carefully arranged for, but need not be detailed here.

One has seen a case in Khartoum clear up quickly under this treatment, as mentioned under "Fevers in the Sudan" in the Fourth Report of these Laboratories.

Greig [3] writes upon the effect of the ipecacuanha on the leucocyte curve in which it causes a fall. He also points out that in ordinary mild cases of amœbic dysentery the temperature and total leucocyte count remain about normal. If a rise of both occurs it usually signifies that the infection has extended to the liver. Muir [4] maintains that the drug is also very useful even when an abscess has formed. He cites one case where it appeared actually to cure the condition, no operation being required. He thinks that it should very rarely be necessary to operate on liver abscess at all, and recommends a powder of Pulv. ipecac. gr. xx., tannic acid gr. x., and calomel gr. i., twice a day as long as required. Rogers,[5] in a recent paper, gives the following as the reasons which induce him to advocate aspiration and quinine injection :—

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[1] Rogers, L. (August, 1910), "Liver Abscess as an Important and Easily Preventable Cause of Death in the British Army." *Journal Royal Army Medical Corps.*

[2] Pilgrim, H. W. (September, 1910), "The Ipecacuanha Treatment of Acute Hepatitis." *Indian Medical Gazette.*

[3] Greig, E. D. W. (September, 1910), "Effect of Ipecacuanha on the Leucocyte Curve in Amœbic Hepatitis." *Ibid.*

[4] Muir, E. (January, 1911), "The Ipecacuanha Treatment in Liver Abscess." *Ibid.*

[5] Rogers, L. (December, 1910), "The Treatment of Amœbic Abscess of the Liver by Aspiration and Injection of Quinine without Drainage; with some remarks on Major Stevens' Series of Cases." *Ibid.*

Liver Abscess—*continued*

(1) The amœba is always present in the walls of recent tropical liver abscesses, being the only constant organism present, and is doubtless its cause.

(2) The very large majority of such liver abscesses are sterile as regards bacteria before being opened; 86 per cent. of my last 87 cases having been so.

(3) The open operation in the warm, damp climate of Calcutta is almost invariably followed by infection of the wound by staphylococci and bacteria within three days. In a series published in 1908, 80 per cent. were found to have become infected, but I am now convinced that even this is an underestimate, probably due to the pus for examination having sometimes been taken immediately after irrigation with an antiseptic. Since this source of fallacy has been guarded against not a single one of several records of cases examined at the time of operation and at subsequent periods have remained sterile after the open operation.

(4) The almost inevitable septic infections of amœbic liver abscess are a serious cause of the high mortality of the disease in the case of large, deep-seated cavities, and even when not fatal it greatly retards the healing of the wounds.

He gives an account of a series of cases treated by his method with very gratifying results. As much pus as possible is removed with the aspirator, and through the cannula from two to four ounces of a solution of the soluble bihydrochlorate of quinine of the strength of ten grains to the ounce is injected, the cannula withdrawn and a collodion dressing and a bandage applied. If the abscess contains less than a pint of pus a single injection often suffices, but in larger abscesses it is necessary to repeat the process at intervals of a week or ten days. A return of fever and pain or of the local swelling will be an indication for another aspiration. A rise in the leucocyte curve is also a guide. Lane [1] asks if the injection is likely to force pus or the quinine solution into the hepatic veins, and Rogers [2] replies in the negative, and also points out that in cases where bacterial infection does occur, daily irrigation with a 1 per cent. solution of potassium permanganate is indicated. The flexible sheathed trocar invented by Rogers for his aspiration method is mentioned in an earlier paper along with an account of a case which bears out his contention that this operation is most efficient in abscesses of large size.

Hull,[3] in a well illustrated paper, advises the employment of Rogers' method supplemented by the use of a Bier's bottle, in order to subject the abscess cavity to negative pressure. He gives the advantages as follows :—

(1) The method of treatment by aspiration of pus and the injection of quinine has given such good results that any other mode of treatment may appear unnecessary. Many cases, however, are quite unsuited to this treatment, and some form of drainage is essential. The patient upon whom the procedure here described is performed is submitted to no more severe operation and runs no more risk of secondary infection than the patient who is merely aspirated, and in addition is placed in a more secure position.

(2) The negative pressure within the abscess cavity promotes rapid obliteration of the cavity.

(3) If the abscesses be multiple, adjacent abscesses will open into the abscess cavity subjected to negative pressure.

(4) Secondary infection is almost impossible.

(5) Convalescence is greatly accelerated; in the last case operated upon by this method the patient was earning his living as a blacksmith within six weeks of the operation.

While on the subject of treatment we may note Brock's [4] account of a remarkable case where an hepatic abscess had burst into the right lung, and where recovery occurred after administration of a streptococcal vaccine. It is a most interesting history, which must be read in the original.

Thompson [5] records a case where breaking-down gummata of the liver closely simulated tropical abscess, the discharge being exactly like what is found in the latter condition. Such a possibility should be kept in mind, and potassium iodide tried in any suspicious case.

A paper of surgical interest is one by Cantlie,[6] which is chiefly concerned with operative

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[1] Lane, C. (March, 1911), "Liver Abscess Aspiration and Injection of Quinine." *Indian Medical Gazette*, and "Reply" by L. Rogers.

[2] Rogers, L. (October 31, 1908), "A Case of Tropical Abscess of the Liver rapidly cured by means of the Flexible Sheathed Trocar." *British Medical Journal.*

[3] Hull, A. J. (July, 1909), "The Operation for Liver Abscess." *Journal Royal Army Medical Corps.*

[4] Brock, J. H. E. (February 27, 1909), "A Case of Hepatic Abscess (?) treated by a Vaccine; Recovery." *Lancet.*

[5] Thompson, G. S. (November 12, 1910), "Breaking-down Gummata of Liver Simulating Tropical Abscess." *Ibid.*

[6] Cantlie, J. (June 15, 1910), "Photographs of Chests in which Liver Pus was coughed up in one case through the Right and in another through the Left Lung." *Journal Tropical Medicine and Hygiene.*

Liver Abscess—*continued*

methods in cases where liver pus has found its way into the lungs. One useful medical note may be quoted. He says that :—

> A congestion of the right lung is a common feature of practice in the Tropics, and the practitioner will do well to examine the liver when a patient suffering from this condition of lung presents himself for treatment. It is the liver that requires treatment, and when this is successfully dealt with the lung congestion will disappear.

Couteaud [1] has described a case of liver abscess where dilatation of the right pupil has led him to ask if inequality of the pupils may not be amongst the diagnostic signs in cases of hepatic suppuration. Another clinical sign which may possibly have some diagnostic importance is an inversion of the daily urinary rhythm in cases of liver abscess where in any case the total urine of the twenty-four hours is frequently diminished. Leger [2] finds that most urine is excreted during the earlier part of the day, a reversal of the normal condition.

This section began with Havelock Charles [3] and his views, and as we are on the subject of diagnosis we may again quote from one who has had very large experience. He enters into great detail, so one must be content to give the very useful extract in the *Medical Annual* for 1910, which says :—

> The most important conditions to differentiate are :—
>
> (1) *Malaria :* chronic malaria with hepatitis may closely simulate liver abscess, but the spleen is enlarged.
>
> (2) *Febrile congestion of the liver,* due to malaria, alcohol, dietetic errors.
>
> (3) "Hepatitis," with diarrhœa, fever, pain, appears and disappears.
>
> (4) *Chronic intermittent fever,* with indigestion.
>
> (5) *Intermittent hepatic fever due to infective cholangitis.*—There is a history of cholelithiasis, grave symptoms, tender enlargement downwards, acute course with intervals of fair health. If there is suppuration the temperature is continuously raised.
>
> (6) *Syphilis,* gummata of the liver.
>
> As regards the signs of liver abscess, we may consider the following :—
>
> (1) *Fever.*—It is one of the most constant signs, but its character is variable.
>
> (2) *Sweating.*—It is generally profuse, especially at night.
>
> (3) *Irregularity of the bowels* may be complained of, or there may be a history of dysentery or diarrhœa.
>
> (4) *Indigestion,* anorexia, dyspepsia, alternating constipation and diarrhœa, are common.
>
> (5) *Sudden pain* over the liver.
>
> (6) *Breathing* is defective on the right side, the movement at the base of the chest is markedly less.
>
> (7) *Temperature.*—A normal or subnormal temperature is possible, or either of these conditions, with an evening rise. Hectic cases present no difficulty.
>
> (8) *Blood count.*—Hyperleucocytosis, with an increase of polynuclears, provided the clinical signs coincide, is diagnostic. (*Note.*—Rogers states that the proportion of polynuclears is but little if at all increased in amœbic abscess in its pre-suppurative stage.)
>
> (9) *Palpation.*—A zone of maximum sensibility may be located.
>
> (10) *Percussion.*—There may be dullness to the fourth or third rib in front, behind possibly to the angle of the scapula.
>
> (11) *Position of abscess.*—In the right lobe in 85 per cent. of cases, at the posterior and upper aspect. When the abscess is on the under side of the right lobe the colon may be displaced forward, giving resonance to percussion.

Malaria. Considering that forty-six pages of the new edition of Scheube's work on Tropical Diseases are wholly devoted to lists of references on malaria, it almost seems presumptuous to attempt to deal with the papers on this huge subject in a few pages. However, one can pick and choose, for such new monographs as those of Craig, Deaderick and Ross, and the fact that certain periodicals such as *Malaria* and *Paludism,* deal solely with the disease obviate the necessity for a very complete consideration of the subject here. Our object is rather to carry the reader up-to-date as far as possible, than to make him conversant with the majority of articles which have appeared since our first Review was issued. As before, we begin with papers which deal with the parasite and with blood changes in malaria.

Külz [4] has a paper on malaria without the finding of parasites in the blood, and on the finding of parasites in the blood without malaria. He limits his remarks to the malignant

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[1] Couteaud (July 8, 1908), "L'inégalité pupillaire signe possible de l'abcès du foie." *Bull. Soc. Path. Exot.*

[2] Leger, M. (April 8, 1908), "Hépatite suppurée : modifications du rythmie urinaire." *Ibid.*

[3] Charles, R. H. (October 24, 1908), "Tropical Abscess of the Liver." *British Medical Journal.*

[4] Külz (1908), "Malaria ohne Parasitenbefund und Parasitenbefund ohne Malaria." *Arch. f. Schiffs-u. Tropen-Hyg.,* Vol. XII., No. 8.

Malaria—*continued*

tertian form, and points out that malaria may be present even when no parasites can be detected in the spleen. In this group of cases which is the more numerous come those seen in adult natives of the country. The relative immunity, or rather the tolerance, seen amongst negroes, is limited to their country of origin. If expatriated they are liable to malarial attacks, and then in a minority of cases parasites are found in the peripheral blood. In the same group come the larval and chronic paludisms most commonly seen in adult natives, while a third class consists of Europeans who practise quinine prophylaxis, and a fourth of cases of blackwater fever. A fifth and modified class is that in which the parasites are at first present in the peripheral blood, are banished from it by a dose of quinine, but in which the malarial attack still persists. The last type he illustrates by an experimental case in which a person newly arrived from Europe and free from fever was inoculated with blood serum from a primary case which had been treated by quinine, and whose peripheral blood was free of parasites. So far as possible other sources of infection were excluded, and yet the inoculated person showed signs of illness after seven days, and on the eleventh day after the injection parasites appeared in the peripheral blood. The second group of cases constitutes the malaria carriers, and these are chiefly represented by native children. Occasionally, also, isolated parasites without accompanying fever are found in the blood of those practising quinine prophylaxis, the treatment preventing multiplication of the parasites. The author issues a warning against relying solely on the microscope for diagnosis, as in this way some other disorder superimposed on an old malaria may easily be overlooked.

Karrewij [1] states that parthenogenesis of the macrogametes (female crescents) has often been described in the malignant tertian form, but that Schaudinn alone has described it in the benign tertian variety. Hence he records a case seen in the Dutch East Indies. The parthenogenetic stages were encountered at the height of the fever. A portion of the nucleus of the macrogamete took on an intense staining, the other portion became paler and paler. The two portions eventually separated. Then the pale moiety travelled to one end of the cell and remained undivided, while the chromatic portion divided successively into a great number of small nuclei which remained situated at the other pole of the cell. The protoplasm massed itself around these little nuclei in the form of spheres, and these ultimately formed merozoites.

Nocht,[2] in a paper on treatment, cites Schaudinn's work on the persistence of the macrogametes, their resistance to quinine, the casting off of their envelopes, and their formation of schizonts from which the young parasites which penetrate the red cells are derived. Like Schaudinn he regards these specialised macrogametes as the long-sought-for latent forms of the malarial parasite which bridge the space between the primary infection and the relapses. As macrogametes form early, usually after the second or third attack, and at times even after the first, the necessity for early treatment becomes apparent. Harrison [3] gives a brief account of the changes seen by Schaudinn in the female gamete, and, after mentioning that Anschutz [4] has described an almost identical cycle * occurring in the spleen of paddy birds (*Spermestes orizivoræ*) infected with a hæmoproteus (*H. orizivoræ*), he states that specimens which illustrate only the last stages of the process are unconvincing, as they might just as well be interpreted as due to a simultaneous infection of a red cell by a gamete and a schizont. There is no such difficulty in the early stages, and the author describes two cases in infection by *Plasmodium vivax*, one of which is illustrated by a coloured plate showing the parthenogenetic cycle. He did not, however, observe all the phases described by Schaudinn, and asks why, if this process is the cause of relapse in malaria, it is not more frequently seen. This objection he himself answers by suggesting that perhaps it is only accidentally that the gameto-schizonts appear in the peripheral blood, and that possibly the normal place for their production is in the deeper organs, like the spleen. The process may go on there quietly without any symptoms until there are a sufficient number of parasites to set up a paroxysm of fever. A full description of the process, with extracts from Schaudinn's paper, was given also by Blüml

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[1] Karrewij, H. (1907), "Parthenogenesis der Makrogameten bij recidief van Malaria Tertiana." *Geneesk. Tijdschr. voor Nederl. Indie*, quoted in *Bull. de l'Inst. Past.*, December 15, 1908.

[2] Nocht, B. (1909), "Die Therapie der Malaria." *Deut. Med. Woch.*, Vol. XXXV.

[3] Harrison, W. S. (December, 1909), "On the Cause of Relapse in Malaria." *Journal Royal Army Medical Corps.*

[4] Anschutz, G. (1909), "Über den Entwicklungsgang des 'Haemoproteus orizivorae' nov. spec." *Cent. f. Bakt.*, I. Orig., Vol. LI., No. 6.

* Very well illustrated by coloured plates—A. B.

Malaria—*continued*

and Metz,[1] and a translation of their paper will be found in the *Indian Medical Gazette* for March, 1909. Amongst other things they say :—

> Instead of looking upon the sexual forms as being adaptation-forms of the schizonts, we are inclined to look upon them as being specific forms, of which the schizonts are an adaptation, which has been needed, and is fitted to render the body of the new human host so weak, by pathological action, that it can present a good breeding-ground for the sexual forms of the *Plasmodium vivax*.

Craig [2] has returned to the subject of intra-corpuscular conjugation, and believes that at least some of the forms described by Schaudinn were really the large pigmented forms which result from this process. His paper will be considered a little later, but some of his remarks on parthenogenesis may well be quoted here. He says :—

> Schaudinn claimed that parthenogenesis was complete in from nine to twelve days, and authorities, such as Ziemann and Mariotti-Bianchi, call attention to the occurrence of relapses most frequently at this period of time. While relapses often do occur at intervals of nine to twelve days, it has not been my experience that the majority do, and it is very difficult, upon Schaudinn's assumption, to explain the occurrence of relapses occurring all the way from nine to eighty days after the initial attack, and the occurrence of latent infections, in which for weeks a few plasmodia may be demonstrated in the peripheral blood at intervals. I have observed relapses occurring at intervals of from two to four weeks very frequently, and several cases in which two to three months intervened between the malarial attacks. Taking these facts into consideration, I believe that it is much more rational to consider that the cause of relapse is some form of the parasite which is resistent to quinine, and which remains latent in the spleen or bone-marrow until conditions are favourable for development, when it undergoes multiplication, and eventually develops into the forms which are familiar to us as schizonts; and I believe that it is the function of intra-corpuscular conjugation to produce such forms of the plasmodia.
>
> The discontinuance of quinine in malarial patients is often followed by recurrences, even in patients who have been under treatment for a long time, and it is evident that during this time the forms of the plasmodia present in the body must have been resistent to the drug. Now, as a matter of fact, the only forms of the malarial plasmodia which resist quinine are the fully-developed gametes and the forms concerned in intra-corpuscular conjugation, and while the parthenogenesis of the macrogamete might explain the occurrence of such relapses, *if macrogametes were always present*, it is a fact that relapses occur in many patients in whom the initial infection has not resulted in the development of any form of gamete. Thus, in a very large proportion of estivo-autumnal patients, *relapses occurred repeatedly, but the gametes* (crescents) *were never observed in either the peripheral blood or in blood obtained by splenic puncture*. In such cases, which were numerous, how can parthenogenesis of the macrogametes explain the occurrence of the relapses ? Intra-corpuscular conjugation is observed very frequently in patients in whom no gametes can be demonstrated, and these facts are sufficient proof, to my mind, that latency and recurrence in the malarial fevers cannot be explained by the parthenogenesis of the macrogamete, and that in intra-corpuscular conjugation we probably possess the true explanation of these phenomena.

Neeb [3] is one of the latest to describe parthenogenesis of the female crescent body, and his paper, which is illustrated, is useful as showing the difficulties in coming to a conclusion as regards some of the peculiar or less common forms of the malaria parasite. At Hamburg he had an opportunity of contrasting his parthenogenetic forms with a long series of schizogenetic forms, and he gives the following useful comparative table, the heading of which one has slightly altered :—

SUPPOSED PARTHENOGENESIS OF THE FEMALE CRESCENT Figs. 1 and 2 (Neeb)	SCHIZOGENESIS OF THE TROPICAL PARASITE
(a) *Size*	
The segmenting form fills up almost the whole normal-sized red blood-cell.	Segmenting forms reach a maximum of two-thirds of the size of the cell.
(b) *Shape*	
Fig. 1.—Elongated oval shaped, with a slightly indented margin on the right, and terminating in an obtuse and slightly bent point. Fig. 2.—Oval, with its centre lying slightly beyond the real centre of the blood-cell.	Mostly circular and generally centrally, or almost centrally, situated in the red blood-cell.
(c) *Chromosomes*	
Large, coarse, purple-brown coloured, peculiarly imbedded and arranged in a red-violet basic substance which is band-like, and runs like a curve parallel to the margin of the parasite.	Small, fine, purple, separated from one another, and distributed in a circular form round the pigment which lies in the centre.

[1] Blüml, M., and Metz, G. F. (1908), "Schizogonie der Makrogameten." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XII.

[2] Craig, C. F. (March 1, 1910), "Studies in the Morphology of Malarial Plasmodia after the Administration of Quinine, and in Intra-corpuscular Conjugation." *Journal Infectious Diseases.*

[3] Neeb, H. M. (April 1, 1910), "The Parthenogenesis of the Female Crescent Body." *Journal Tropical Medicine and Hygiene.*

(d) *Protoplasm*

Light-blue violet stained, and quite identical with that of the crescent bodies.	Light azure-blue and including more or less the small chromosomes.

(e) *Pigment*

Coarse, yellow-brown, distributed, eccentrically situated, quite similar to the pigment of the crescent bodies.	Fine, dark-brown or black, mostly concentrated in one clump, generally situated in the centre and surrounded by the merozoites.

Although of course the paper only refers to an individual case it is worthy of study, and the table may be of help to those who encounter parthenogenesis and are in doubt as to its true nature. The same paper, illustrated by a coloured plate, occurs in the *Philippine Journal of Science*, B, for July, 1910. Deaderick [1] reviews the subject well. He points out the three chief views which have been advanced to explain latency and relapse, and tabulates them as follows :—

(1) Feeble schizogonic reproduction in the spleen and elsewbere, too feeble to produce active symptoms, but sufficiently vigorous to prevent complete annihilation of the parasites which reproduce actively when circumstances are favourable.

(2) Intra-corpuscular conjugation of young parasites resulting in a zygote stage or resting body.

(3) Parthenogenesis, or reproduction by unfertilised macrogametes.

As regards the first he says that—

While it is probable that brief periods of latency may be thus explained, especially in persons possessing a relative immunity, it is evident that this is not the common mode, particularly of relapses at long intervals, since the asexual cycle is known to wear out spontaneously after certain periods.

He considers intra-corpuscular conjugation at some length, summarising Craig's views as follows :—

(1) Intra-corpuscular conjugation is the principal cause of the maintenance of malarial infection in man, and its absence the cause of spontaneous recovery.

(2) It maintains malarial infection by producing a "resting" or zygote stage of the plasmodia, which is resistent to quinine and other injurious influences.

(3) It is the cause of latent and recurrent malarial infections, the zygote stage remaining dormant or "latent" until conditions are favourable, when it gives birth to several young plasmodia which, penetrating the red blood corpuscles by their growth and sporulation, cause a recurrence of the infection.

He himself states that while it is probable that intra-corpuscular conjugation occurs in malaria, its importance in the etiology of relapses at long intervals is probably minimal. He announces himself a believer in Schaudinn's view, saying :—

It appears to me that parthenogenesis, first observed and construed by the most eminent protozoologist the world has ever produced, and whose observations have been repeatedly confirmed, must be accepted as the true explanation of chronic malaria.

and adding :—

Secondary etiological influences play a much more prominent *rôle* in relapses than in primary infections. Of these the most important are changes of residence, fatigue, abuse of alcohol, exposure, and gastro-intestinal disturbances. All are familiar with the frequency with which a change of residence "brings the malaria out." These influences are much commoner factors in the relapses at long intervals than in those at shorter intervals.

The prevention of relapses may be summed up in a few words, though its accomplishment is sometimes far from easy.

The prime requisite is the radical cure of the acute attack. After treating the attack by quinine in the usual manner I employ a modification of Koch's methods, and give fifteen grains of quinine in three-grain doses every sixth and seventh days for not less than twelve weeks. This has rarely failed where reasonable hygienic restrictions can be instituted. The secondary etiological factors mentioned above are more influential in chronic even than in acute malaria, and unless guarded against constitute a serious obstacle to the radical cure. A tonic of iron, arsenic and strychnine is a valuable aid in the treatment, and occasionally a temporary change of residence is advisable.

James,[2] in a recent paper on quartan malaria, as met with at Panama, states that if there be a special form of the malarial parasite responsible for relapses it should be most readily

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[1] Deaderick, W. H. (October 12, 1910), "Recurrences in Malaria: Their Cause and Prevention." *Bull. Soc. Path. Exot.*

[2] James, W. M. (1910), "Quartan Malaria and its Parasite." *Proceedings Canal Zone Medical Society*, Vol. III.

Malaria— *continued*

demonstrated in quartan infections. He further says that there is some evidence to show that such a form exists and can be well seen in these infections.

Ross, however, believes that the ordinary sporulation of asexual forms which persist in small numbers is quite sufficient to keep infection alive indefinitely, and adequately explains the phenomenon of relapse (*see page* 176). Recently, Rowley-Lawson [1] has described a new sexual cycle for the sub-tertian parasite in the circulating blood, for she maintains that fertilisation and sporulation occur there in the crescents, and that the spores so derived enter the red cells as the small ring forms. This is something different from parthenogenesis, and though her paper is copiously illustrated, it is evident that the work will require confirmation before a view of this kind can be adopted.

Craig [2] is a believer in the quotidian parasite as one cause of æstivo-autumnal fever. He finds that both pigmented and unpigmented quotidian plasmodia are met with in the peripheral blood. The diagnosis of this form, which he proposes to name *Plasmodium falciparum quotidianum*, is most easily made by splenic puncture. The same author's paper on intra-corpuscular conjugation has already been mentioned, and perhaps enough has been said on this subject, for Craig has so far failed to convince the highest authorities of the importance of the phenomena he describes, but he has some useful notes on morphology, and on the action of quinine on the different forms of malarial parasite. The paper must be consulted for the detailed and most interesting observations, but his "practical deductions" may be quoted with advantage. He remarks :—

> It is evident from the observations noted that quinine, whenever given, is effective in destroying the plasmodia, but it is also evident that the drug is most effective if given in divided doses at regular intervals, thus keeping the blood charged with it. Given in this manner the plasmodia are continually exposed to the action of the drug, and the morphological changes observed in the plasmodia prove that the drug is capable of destroying them at every stage in their life-cycle in man, with the possible exception of the sporulating stage, but even in this stage it produced an atypical division of the parasite, resulting in a lessened number of merozoites and sterility of many of the latter.
>
> If the drug be administered in one large dose just before sporulation, very many of the merozoites are at once destroyed, but those which are able to survive for a few hours develop and sporulate in a normal manner, the drug having been excreted before the cycle of development has been completed, some stages escaping entirely from the effect of the drug. If, on the other hand, after a moderate-sized initial dose, the drug be continued at intervals of three or four hours, those parasites which have escaped the first dose are not free to develop normally, but are continually exposed to the action of the drug, which is always present in the blood.
>
> My observations show that the plasmodia under such conditions are injured during every stage of their growth, many perishing before sporulation, while those that sporulate do so in an atypical manner. The conclusions drawn regarding the time of the administration of quinine, as the result of the study of the morphological changes produced by the drug, are not only justified theoretically, but have the confirmation of actual clinical experience.

Brumpt,[3] in an illustrated memoir, describes some of the changes found in red cells in malaria and malarial cachexia. After mentioning Schüffner's dots found in benign tertian infection, and Maurer's granules seen in malignant tertian cases, he states that they are found in monkey malaria, and are probably due to the action of a toxin. The other most important changes described by him and by Billet are the ring forms, the half-moon red cells, and the *corps en pessaire*. Further information regarding these will be found in the Fourth Report of these Laboratories, Volume A, 1911.

Brown [4] has worked at the nature and mode of production of malarial pigment. He finds that it consists of hæmatin, and believes that it is probably due to the action of a proteolytic enzyme of the malarial parasite upon the hæmoglobin of the red blood corpuscle. Passing now to other aspects of the question, and more especially the epidemiological and clinical, it is interesting to find Easton [5] recording a case of benign tertian infection contracted at Aldershot, in England, by a soldier who had never been abroad. There seemed little doubt that he had been bitten by an infected anopheline, as anophelines are found at Aldershot, and there are a considerable number of malarial subjects in that command. The patient remembered being bitten by a gnat about a fortnight before his admission to hospital. For some time it was not easy to

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[1] Rowley-Lawson, M. (February 1, 1911), "Æstivo-autumnal Parasite: Its Sexual Cycle in the Circulating Blood." *Journal of Experimental Medicine.*

[2] Craig, C. F. (May 27, 1909), "The Classification of the Malarial Plasmodia." *Boston Medical and Surgical Journal.*

[3] Brumpt, E. (April 8, 1908), "Globules géants ou 'corps en demi-lune' du paludisme—autres altérations globulaires au cours de cette maladie infectieuse." *Bull. Soc. Path. Exot.*

[4] Brown, W. H. (February 1, 1911). *Journal of Experimental Medicine.*

[5] Easton, P. G. (November, 1909), "A Case of Malarial Fever contracted at Aldershot." *Journal Royal Army Medical Corps.*

Malaria—*continued*

obtain definite information regarding the prevalence of malaria in Egypt, but this has now been remedied by a special chapter in Ross's *Prevention of Malaria*, and also in a paper by Dreyer,[1] who states that it occurs throughout the whole delta and also in Upper Egypt. Christophers [2] has an article on the epidemic malaria of the Punjab, with a note on a method of predicting epidemic years. In the Punjab an epidemic frequently appears when a year of heavy rainfall follows one of deficient rainfall. As the author says :—

A comparison of charts of rainfall and of fever deaths shows how true this observation is, and I found that if a coefficient be obtained as above it picks out in an extraordinary way epidemic years, and not only assists by giving an indication of the probability of epidemic conditions occurring in any given year, but even helps to indicate the intensity of these epidemics.

He gives a formula for working out the problem, and states that it answers well, but his paper must be consulted for details. Gioseffi [3] had an opportunity of fixing accurately the incubation period in an outbreak of mild tertian infection on board ship. The maximum was 22 days, the minimum 10 days, and the average for the series of cases 16 days. This is somewhat longer than was at one time supposed, but it appears to be the correct figure. Taking now some clinical papers we find Watson [4] describing a case with epileptiform attacks, and in which there appeared to be a very localised interference with a nerve centre in the brain by presumably malignant parasites. There was diplopia, which passed off after treatment, but which Watson thinks was the first symptom of the general brain paralysis so commonly seen in coma. Deaderick [5] deals with the literature of malaria as a cause of purpura hæmorrhagica, a very rare condition, and describes a case which came under his own notice in the United States, and which was benefited by the exhibition of calcium chloride, 5 grains every four hours, and of an anti-malarial tonic. It is important to differentiate these cases from acute leukæmia. Letulle and Nattan-Larrier [6] record a case of apical pulmonary cirrhosis due to malaria. The naked-eye appearance of the indurated area was of a peculiar yellowish-brown "chamois" colour, quite different from the usual slaty-grey or greenish-black hue found in ordinary pulmonary sclerosis. They give a very careful account of the histo-pathology of the lesion, which was superimposed on an old cured focus of tuberculosis.

Marchoux [7] deals with malarial attacks simulating pneumonia and dysentery. In the pneumonic form the physical signs were typical of a double pneumonia at an early stage, and there was rust-coloured sputum. In this, pigmented malignant tertian parasites were much more common than in the peripheral blood, though they were not rare in the latter. The condition rapidly cleared up under quinine. In the dysenteric form parasites both free and intra-corpuscular were found in the blood passed per rectum. Cardamatis [8] has a paper on phagocytosis in malaria, and states that he has seen the polymorphs as well as the mononuclears participate in the process. Cases of mixed infection are not uncommonly encountered. Hoffmann [9] records an instance in a sailor where benign tertian and sub-tertian co-existed, and where the facts obtained did not point to any transformation of one form into the other, but to two separate and distinct infections, thus negativing Laveran's view as to the unity of the malarial parasite, a view supported by Thiroux, as mentioned in our first Review. The *Journal of Tropical Medicine and Hygiene* for July 1, 1909, has the following note on a case described by Donovan in India :—

Major Donovan also records an exceptionally instructive case of a patient, a wandering mendicant, from the West Coast; he was admitted for fever, and all the three species of the malarial parasites were present. *Plasmodium malariæ* (quartan) predominated in numbers, *Laverania malariæ* (malignant) next in frequency, with a few of *Plasmodium vivax* (benign tertian). A single dose of sulphate of quinine in solution was given by the mouth, and the temperature came to normal and remained so till nineteen days afterwards, when a rise in temperature took place, accompanied this time by a crowd of schizonts of *Plasmodium vivax*, but no *Plasmodium malariæ* or

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[1] Dreyer, W. (1910), "Über durch Protozoen im Blut hervorgerufene Erkrankungen bei Menschen und Tieren in Ägypten." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIV., No. 2.

[2] Christophers, S. R. (January, 1911), "Epidemic Malaria of the Punjab, with a Note on a Method of Predicting Epidemic Years." *Paludism*, No. 2.

[3] Gioseffi, M. (1911), quoted in *Wien. Klin. Woch.*, p. 292.

[4] Watson, M. (October 31, 1908), "Rare Nervous Symptoms produced by Malaria." *British Medical Journal.*

[5] Deaderick, W. H. (October 14, 1908), "Malaria as a cause of Purpura Hæmorrhagica." *Bull. Soc. Path. Exot.*

[6] Letulle, M., and Nattan-Larrier, L. (November 11, 1908), "Sclérose paludéene du sommet du poumon." *Ibid.*

[7] Marchoux, E. (April 8, 1908), "Accès paludéens à formes pneumonique et dysentérique." *Ibid.*

[8] Cardamatis, J. (1908), "Die Phagocytose bei Malaria." *Cent. f. Bakt.*, I. Orig., Vol. XLVIII., No. 5.

[9] Hoffmann, G. (1909), "Tertianarezidiv nach Malaria tropica." *Deut. Med. Woch.*, No. 11.

Malaria—*continued*

Laverania malariæ. Another dose of quinine of 30 grains was administered, and after thirty-six days of apyrexia a second relapse took place; on this occasion *Plasmodium malariæ* turned up, but no *Plasmodium vivax* or *Laverania malariæ*. This would favour in a way Laveran's view that the parasite of malaria constitutes a single species with three varieties. However, obvious objections are forthcoming that militate against the acceptance of this theory; for instance, to be brief, a mixed infection or an unaccountable alternation in the recrudescence of the latent forms. In half-a-dozen other instances patients have been admitted twice into hospital for paludal fever; in the first instance infected by *Laverania malariæ:* after quinine treatment and discharge they have come again in about a month or longer interval with *Plasmodium vivax*. Has there been a change in type or variety, a second infection by a different species of parasite, or was mixed infection in the first admission latent or missed?

Graham [1] gives records of three cases, one cerebral, one with symptoms like peritonitis, and one dysenteric, in none of which were any parasites found in the blood, nor did quinine given by the mouth have any effect. As they came from a highly malarial region, quinine treatment was persisted in and the drug given by injection—intravenously in the cerebral case, and with the happiest results. Trincas [2] states that there may be no rise of temperature in malaria. Apyretic forms occur characterised by such symptoms as renal colic, sciatica, facial paralysis, aphasia, and even hemiplegia. The blood examination and the therapeutic test alone serve for diagnosis. Fink [3] has a paper on peripheral neuritis of malarial origin, and believes the blood count helpful in distinguishing it from the same condition due to beri-beri. Murray [4] mentions a dark blush or red coloration of the hypothenar eminence of the hand as a sign of chronic malarial poisoning. It is not a deposit of pigment, as it disappears on pressure, quickly reappearing when the latter is removed. It is only visible in Europeans who have had repeated attacks, and is not present in Malta fever or in the Low fever of European immigrants (Rogers). Bentley has confirmed the observation, finding it in 75 per cent. of Europeans in the Duars, an intensely malarious region of India. Low,[5] in dealing with the duration of infection of malaria, refers to the case of a person

infected artificially in England with malaria, well treated with quinine in the usual manner over a prolonged period of time, with no possibility of reinfection, and yet having a relapse, with parasites demonstrable in his blood, two years and three months afterwards. The duration of infection in a badly treated or untreated case might therefore conceivably last even longer than this, and might approach the record of four years mentioned by Professor Ross.

Baker [6] has recorded his own case, in which apparently a relapse occurred after thirteen years without any fresh reinfection. Mousséos [7] has written specially of "larval" forms of malaria, a term used to denote "different affections of a periodic character, having a course more or less obscure, presenting some analogy with intermittent fever, and yielding to similar treatment." The author divides malaria into (1) intermittent fever, (2) "fièvre larvée," and (3) malarial cachexia.

Ross and Thomson [8] have recently applied more exact methods to the study of malaria. They give an account of their special "detective" and "enumerative" methods, and summarise their results in 33 cases studied, the majority of which showed *P. falciparum*. These results are specially interesting as regards the question of relapse already fully discussed, and are as follows:—

(1) There would seem to be a very decided correlation between the number of asexual *Plasmodia* found in the peripheral blood and the fever.

(2) As a rule, no fever exists unless the asexual forms exceed some hundreds per c.mm.

(3) The asexual forms do not always disappear between relapses (as often thought), but tend to persist in small numbers per c.mm., and often increase again for some days before the actual febrile relapse occurs.

(4) These observations give a coherent theory of the malarial invasion, according to which the infection is kept alive indefinitely by the ordinary sporulation of the asexual forms, and not by parthenogenesis or by resistant forms; and fever recurs only when the parasites are numerous enough to produce it.

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[1] Graham, E. N. (May 15, 1909), "Unusual Manifestations of Malaria." *Journal Tropical Medicine and Hygiene.*

[2] Trincas, G. (August 31, 1909), "Gli equivalenti termici dell' infezione malarica." *Gazz. d. Osp. ed. Clin. Milan.*

[3] Fink, G. H. (December 1, 1909), "Peripheral Neuritis of Malarial Origin." *Journal Tropical Medicine and Hygiene.*

[4] Murray, W. A. (June, 1910), "Note on a Sign of Chronic Malarial Poisoning." *Indian Medical Gazette.*

[5] Low, G. C. (November 15, 1910), "The Duration of Infection of Malaria." *Journal Tropical Medicine and Hygiene.*

[6] Baker, O. (April, 1910), "The Duration of Latency of Malarial Infection." *Transactions Society Tropical Medicine and Hygiene.*

[7] Mousséos, B. (1910), *Les Formes Larvées du Paludisme: Diagnostic et Traitement*, Paris. Reviewed in *Lancet* November 19, 1910.

[8] Ross, R., and Thomson, D. (December 20, 1910), "Some Enumerative Studies on Malarial Fever." *Annals Tropical Medicine and Parasitology*, Vol. IV., No. 3.

(5) We estimate from our cases that considerable continued doses of quinine reduced the asexual forms by 50 to 80 per cent.

(6) There are strong reasons for supposing that the sexual forms require eight to ten days for development; that the often noticed long persistence of crescents is not due to their long life (as generally thought) but to constant replenishments of the stock by fresh broods; that they sometimes show a distinct tertian periodicity, and that quinine does not affect them when once generated, but ultimately reduces their numbers by destroying the generating cells. The sexual forms were never seen to produce fever.

(7) The leucocytes are below normal during febrile periods and above normal afterwards. The percentage of mononuclears rises after paroxysms, and is always in excess of the normal.

(8) Methylene blue, soamin, X-rays, and faradic and galvanic currents had no results in a few experiments.

(9) The hæmoglobin falls markedly with fever, but rises rapidly with convalescence.

(10) The fæcal urobilin shows marked correlation with the occurrence of fever.

Surveyor [1] has reported a type of malaria in Bombay due to *P. falciparum*, and where patients even in a moribund state and whose blood showed typical ring forms and crescents were absolutely free of fever and exhibited no splenic enlargement. He was able to show that crescents can remain in the blood for more than two months. This paper will again come under notice when we consider treatment.

Smallman [2] draws attention to the prevalence of the malaria carrier amongst British troops in India. The paper is chiefly concerned with prophylaxis, but as the result of some experimental work he puts forward two practical deductions :—

(1) That a malignant case is infective, as a rule, for a fortnight or three weeks from the time that crescents first appear in the finger blood, which time it may be noted is usually about a week after the cessation of the fever.

(2) That a patient may be highly infective when even only one crescent can be found after a good search.

Tate [3] deals with the occurrence of fever in old malarial cases chiefly with a view of pointing out the frequent inadequacy of quinine treatment in such conditions and the value of iron and arsenic, the former given as one of the "scale" preparations which are better tolerated. A most valuable contribution is that by Darling. Most of his work will fall for consideration under mosquitoes, but some notes as regards the value of the splenic index in determining the amount of malaria in a community may be quoted here with advantage. He says :—

The degree of splenic enlargement in a malarial region seems to depend on the following factors :—

(*a*) Amount of blood destruction or loss.

(*b*) Duration of the blood destruction.

(*c*) Ability of the hemopoietic organs to regenerate red-blood cells.

(*d*) Degree of reaction to the infection as in such infections as relapsing fever, where there is at first not a high degree of blood destruction or, at any rate, the splenic enlargement is so rapid and the red count so little decreased, perhaps, that the splenic enlargement is a measure of toxæmia rather than blood destruction. When there is much blood destruction or depletion and the blood-forming organs are not passive, then the splenic enlargement will be considerable.

In this region there is a source of splenic enlargement which is confused with that of malaria. I refer to uncinariasis. Some of the largest spleens encountered here are undoubtedly those secondary to uncinariasis anæmia.

The presence of eosinophilia in the latter aids the diagnosis, but it is to be remembered that in a region infected with uncinariasis, as well as malaria, the splenic index is an index of the former as well as the latter.

This brings us to questions of diagnosis. Plehn [4] deals with that of latent malaria. He believes that the presence of urobilinuria is a valuable diagnostic sign, except in what he terms the primary period of latency, *i.e.* the time between the moment of infection to the first attack of fever. Hepatic disturbance has much to do with urobilinuria, which is not found in healthy persons, or occurs in them only to a very slight degree. He gives the new method of Schlesinger for its detection by which the least traces can be demonstrated.

To the unfiltered urine one adds an equal quantity of a solution of 10 parts of zincum aceticum in absolute alcohol in a test tube. You shake it well and add a few drops of lugol solution, stirring it again. Afterwards the filtered mixture shows fluorescence more or less intensively according to its content of urobilin.

Urobilinuria is, however, not a specific sign of malaria. It is only a symptom of liver disturbance, and as such may be absent in malaria, for that disease may occasionally spare

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[1] Surveyor, N. F. (December 20, 1910), "Some Observations on Malaria in Relation to Splenic Enlargement." *Annals Tropical Medicine and Parasitology*, Vol. IV., No. 3.

[2] Smallman, A. B. (May, 1911), "Some Points in the Prevention of Malaria among British Troops in India." *Journal Royal Army Medical Corps.*

[3] Tate, R. G. H. (May, 1911), "Fever of Malarial Origin." *Ibid.*

[4] Plehn, A. (October 31, 1908), "The Diagnosis of Latent Malaria." *British Medical Journal.*

Malaria— *continued*

the liver. It must, therefore, be considered in connection with the history of the case. Plehn says, however, that a strong urobilinuria after malarial infection proves that the organs have not yet recovered, and is a contra-indication for return to the Tropics. Surveyor (*loc. cit.*) was not able to confirm Plehn's findings in his Indian cases showing crescents. Recently Urriola [1] has described a new urinary test which he regards as pathognomonic. It is the discovery of malarial pigment in the urine. The urine is centrifuged and the deposit examined under a high magnification. Four types of pigment granules may be found in malarial cases. (1) Very fine granules massed together. (2) Larger grains arranged in similar groups. (3) Large masses varying in form. (4) Granules included within leucocytes or hyaline casts. The colour is usually an intense black of the Chinese ink type, but blue granules may be seen, rarely some which are yellow-ochre. This malarial pigment cannot be confused with the granules found in other febrile disorders; for one thing it is much more abundant. Even so more than one drop of the deposit should be examined, and half-an-hour may have to be devoted to the search.

Kirkovic [2] deals with the diagnosis of malarial splenomegaly. What he terms the para-malarial forms are distinguished from this condition by the constant absence of malarial parasites from the peripheral blood, and by the presence of a leucopenia with a relative lymphocytosis. He considers the question of pseudo-leukæmia, *i.e.* Banti's disease, but the paper must be consulted in the original.

Thayer [3] states that certain infections may give rise to paroxysms which intrinsically, and in the character of their periodicity, may closely simulate malaria. The paroxysms of streptococcus, pneumococcus and gonococcus septicæmia are usually distinguishable by the irregularity, often the great frequency of the paroxysms and the short duration of the individual access. The paroxysms occurring in tuberculosis may often suggest malaria, but are usually readily distinguishable. According to Thayer, influenza is the malady which gives rise to those forms of intermittent fever which most closely simulate malarial parasites. He gives illustrative cases. The *Lancet* of April 17, 1909, has an article on congenital malaria in which is mentioned Hitte's observation of malarial parasites in the blood of the umbilical cord in two cases and Thayer's pronouncement that the evidence for its occurrence is unconvincing. It then gives an account of a case reported by Dumolard and Viallet, which seems to put beyond doubt the possibility of congenital infection. One need not give the details of the case, which the French authors consider

proves the possibility of the transmission of the malarial parasite across the placenta to the fœtus, for there was no uterine hæmorrhage by which the infection could have been conveyed. The question of the frequency of such transmission remains to be determined. As in other infcctions, the health of the mother, the virulence of the infection, the age of the fœtus, and alterations in the placenta, no doubt are factors. Many cases have been published to show that even in severe malaria the fœtus is not infected, but its health is often impaired. Probably when it escapes the hæmatozoon itself the toxins filter across the placenta. Another question is the relation of malaria to abortion. Malaria must be regarded as a powerful cause of abortion, which is more likely to occur when, as in the present case, the fœtus is infected. But apart from fœtal infection the destruction of the red corpuscles and the fever in the mothcr may produce abortion. It follows that a pregnant woman suffering from malaria should be given quinine in sufficient doses. No doubt in exceptional cases quinine excites uterine contractions and produces abortion, but it is the only means of saving the mother and the fœtus from an infection likely to produce abortion and then kill the mother. In the casc reported above the infection of the fœtus showed that quinine was doubly indicated.

Another undoubted case of quartan congenital malaria is reported by Lemaire, Dumolard, and Laffont,[4] whose paper is reviewed in the *Bulletin of the Pasteur Institute* for 1910, *page* 809. So far as India is concerned a great deal of information regarding malaria will be found in the *Transactions of the Bombay Medical Congress* for 1909, in Hehir's monograph on prophylaxis, and in a paper by Leslie.[5] He points out that many of the deaths from malaria in India are due to the withholding of food. He gives interesting statistics regarding prevalence and death-rate.

It is now time to turn to questions of prevention and treatment. As regards the former, we propose to avoid controversial papers, of which there are more than enough, and so will say nothing regarding Mian-Mir, that pet theme of those to whom the question of malarial prophylaxis appears to be equivalent to a summons to wordy warfare. In the first instance

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[1] Urriola, C. L. (January 4, 1911), "Sur un nouveau signe pathognomonique du paludisme." *Semaine Médicale.*

[2] Kirkovic, S. (1909), "Zur Diagnose der malarischen Splenomegalien." *Wien. Klin. Woch.*, No. 3.

[3] Thayer, W. S. (April, 1911), "Intermittent Fever in Influenza simulating Malarial Fever." *Bulletin The Johns Hopkins Hospital.*

[4] Lemaire, Dumolard, and Laffont (June 24, 1910), "Un cas nouveau de paludisme congénital." *Bull. Soc. Méd. des. Hôp.*

[5] Leslie, J. T. W. (November 20, 1909), "Malaria in India." *Lancet.*

Malaria—*continued*

the prophylactic use of quinine demands attention. In the *Journal of Tropical Medicine and Hygiene* of September 15, 1908, *page* 283, there is an interesting account of the results of an inquiry into this subject set afoot some time ago in Uganda. The various systems of taking quinine were classified as follows :—

System I. 5 grains of quinine daily.
„ II. 10 grains of quinine every Wednesday and Sunday.
„ III. 15 grains of quinine every eighth and ninth day.
„ IV. Quinine taken irregularly.
„ V. No quinine taken except when actually suffering from fever.

and judging by the results

it would appear that those who followed system I. (*i.e.* taking 5 grains of quinine daily) suffered least from fever, while those who followed systems II. and III. were affected most frequently. Unfortunately, the number of persons in all the categories, save system IV. (taking quinine irregularly), was not sufficiently large to warrant much reliance being placed on the results of this interesting experiment.

The attached extract from a report by Colonel Will, Principal Medical Officer, British East Africa, is also quoted :—

In East Africa, quinine is much less used as a prophylactic against malarial attacks. A favourable opportunity occurred during the months of January, February and March for testing its efficacy as a prophylactic. At Samburu, where there is always a certain amount of malaria, an average daily number of 250 men were working on railway diversion works. Each man was given 5 grains of quinine daily during the above period. The daily number in hospital with malarial infections during the previous three months was 3·10 per cent. of the daily strength, and during the three months in which daily issues of quinine were made, 7·68 per cent. The lesser rains ceased in December. January, February and March were dry months, and although an increase in the number of infections was expected in January, just after the decline of the rains, February and March are two of the healthiest months of the year. The highest number of admissions was recorded in February. It is not suggested that quinine, which is our sheet-anchor in malarial infections, increased the incidence of the disease in this instance, but it is evident that it did not diminish it.

I am convinced that too much reliance is placed in the prophylactic action of quinine, to the neglect of such simple anti-malarial precautions as avoiding an unprotected verandah after sundown, the use of wire gauze, the provision of a thoroughly effective mosquito sleeping net, etc.

Bouffard,[1] speaking of Upper Senegal and the Niger territories, advocates a daily dose of 0·25 gramme of the hydrochloride of quinine, a practice which should be continued for fifteen days after leaving an area in which infection might be derived. He points out that while this will protect against ordinary infections, it is not efficient against heavy doses of the virus, and recommends doubling the dose for three or four days if one has been much exposed to infection.

Stitt [2] holds that quinine by itself, without effective mosquito protection, is disappointing. He thinks that if one takes quinine for a long time its curative effects, when fever is acquired, are lessened. He gives the following interesting details :—

In a body of marines stationed near Panama every man took 9 grs. quinine daily as a prophylactic. Few of the men thus treated developed fever, but on having Panama (Colon) by boat twenty of the marines developed fever on the first day at sea, fifty-three on the second day, and forty-five on the third day, despite the fact that quinine in 9 gr. doses was exhibited prophylactically during the voyage. Of the 298 marines who composed the party no fewer than 215 had acute malarial paroxysms during the eight days' voyage to Boston, U.S.A. The patients did not respond satisfactorily to quinine even when given hypodermically. Diagnosis of malaria in these circumstances is rendered difficult, for not only are the parasites difficult or impossible to find in the peripheral blood whilst quinine is taken, but "ague" symptoms are for the most part absent. This is more especially the case when the infection is of the æstivo-autumnal type. Schaudinn's explanation may serve to explain the phenomenon. "The sexual forms in æstivo-autumnal fever do not develop for about ten days after the first paroxysm. In case we are giving quinine prophylactically we do not recognise the first attack, and as time goes by the gametes develop. These, being resistant to quinine, as shown by the experiments of Gauldi and Marirano, are not extirpated. Later on the microgametocytes die out, leaving only the macrogametes. These, by a parthenogenetic reproduction, give rise to another non-sexual cycle, and we have a relapse."

As regards the relative merits of quinine prophylaxis and protection from mosquitoes, Celli gives the following figures :—

Treatment	Infected
Mosquito protection plus quinine prophylaxis	1·75 per cent.
Mosquito protection alone	2·5 „ „
Quinine prophylaxis alone	20 „ „
No protection at all	33 „ „

The immunity the parasite of malaria may acquire to quinine is a subject that requires more careful investigation than it has hitherto been subjected to.

From the administrative point of view a study of the report and recommendations of the

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[1] Bouffard (January 13, 1909), "Prophylaxie du paludisme chez l'Européen dans le Haut-Sénégal et Niger." *Bull. Soc. Path. Exot.*

[2] Stitt, E. R. (May 23, 1908), "Quinine as a Prophylactic in Malaria." *Journal American Medical Association.*

Malaria—*continued*

special French Commission [1] on the question of quinine prophylaxis in the French colonies is useful. The measures employed in Greece, Italy, and India are detailed, as well as those already adopted in French possessions. The forms of quinine recommended are :—

For adults. Compressed but not sugar-coated tablets of the hydrochloride, each containing 0·25 gramme. The sugar-coated preparation is quite as efficient, but is too expensive for general use.

For children. (1) Chocolate pastilles containing tannate of quinine, each with the equivalent of 0·15 gramme of active quinine. (2) The tannate in powder in flasks containing in addition to the dose a small measure. The tannate, while insoluble in water, is absorbed from the alimentary canal. It may be given in milk, and is tasteless. For adults the doses recommended are those adopted by Bouffard (*loc. cit.*). Werner [2] also recommends the tannate for children, but points out that the tannates of quinine on the market vary as regards the amount of alkaloid they contain, which is the reason why some have found them unsatisfactory. A very interesting paper, which is partly a review of the methods of quinine prophylaxis and partly a record of personal experience in India, is that by Acton,[3] who gives for Nowshera in the North-West Provinces the following rules, neglecting quartan infections which there are very uncommon.

(*a*) When Benign Tertian infections are prevalent (*i.e.* when they form 70 per cent. of the weekly malarial returns) two consecutive doses of 5–10 grains should be given at intervals of eight days, but if the epidemic is a severe one, the intervals may have to be shortened down to six days.

(*b*) When Malignant Tertian infections are prevalent (*i.e.* when they form 30 per cent. of the cases or over) two consecutive doses of 10–15 grains should be given at intervals of four days, but if the epidemic is a severe one, these intervals may have to be shortened down to two days and the maximum dose given.

These rules are devised to ensure a maximum amount of protection with a minimum amount of personal inconvenience, and are founded upon the life histories of the respective parasites and our knowledge of the action of quinine on these parasites at various stages of their life-cycles. Two consecutive doses are recommended in benign tertian cases, because double infection is commonly met with in this type of malaria.

So much for quinine prophylaxis. Other preventive measures cannot well be dealt with in a short review of this nature, for they are made up of details which it is not easy to describe and comment upon in a very limited space, and, moreover, many excellent text-books and monographs now exist to guide the student. A few papers, however, will be mentioned. Thus there is the article entitled "Practical Methods of Anti-malarial Sanitation," written by the medical officer of the Duars, Eastern Bengal, and published in the *Journal of Tropical Medicine and Hygiene* of October 15, 1908.

There is nothing new in it, but we note its advocacy of the Vermorel nozzle for spraying apparatus, and its statement that, to be effectual, treatment with kerosene oil should be applied to all possible breeding-places within a quarter of a mile of every inhabited spot. The question of mosquito nets falls for consideration under the heading "Mosquitoes," but the following note may here be quoted :—

The net should be of ample size, at least 7 ft. long and 3 ft. wide, and not less than 5 ft. high. There should be 2 ft. of calico sewn round the bottom outside the net. This saves the netting, and keeps it from tearing where it is tucked under the mattress, and also protects the sleeper from getting bitten through the net. The size of the bedstead is also very important. It should measure not less than 7 ft. 6 in. by 3 ft. 6 in. With a large bedstead the net is well stretched out and therefore cooler, while the sleeper is much less likely to rest any portion of his body against the sides of the net.

Once the mosquito-net habit is formed there is no temptation to give it up. It is a wonderful protection, not only against mosquitoes, but also against many other things that are likely to disturb the night's rest in the Tropics, such as bats, snakes, flies, rats, etc.

A net should last a year, even with the rough usage necessitated by travelling; if stationary, it will last double the time. An accidental tear can be patched up, but when the threads become rotten and minute holes begin to appear all over, it is useless to attempt to mend it, and the net should be destroyed. A net with holes is worse than none—and, we may add, so is a net not tucked in under the mattress. "It gives a false sense of security, and is really a mosquito trap."

Besides the books and papers already mentioned, valuable information as regards general anti-malarial measures will be found in the yearly reports *Campagne Antipaludique*, issued

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[1] Bertrand and others (May 12, 1909), "Sur les mesures à prendre pour développer dans les Colonies françaises l'usage préventif de la quinine contre le paludisme." *Bull. Soc. Path. Exot.*

[2] Werner, H. (1909), "Erfahrungen über Chinintannat bei Malaria." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XII.

[3] Acton, H. W. (August, 1910), "The Rationale of Quinine Prophylaxis." *Indian Medical Gazette.*

Malaria—*continued*

in connection with the excellent work carried out under the direction of the Sergents [1] in Algiers, in the voluminous report by Watson [2] on the work done in the Federated Malay States, in the Proceedings of the Imperial Malarial Conference held at Simla in 1909, in the annual publications of the Italian Society for the Study of Malaria edited by Celli, and in papers and reports dealing with the colossal undertaking in the Panama Canal Zone. So far as Khartoum is concerned further information regarding regulations for irrigated areas, with a few notes on the breeding-places of anophelines, will be found in the *Fourth Report* (1911) of these Laboratories. The following passages on rice cultivation in relation to malaria, a subject of great importance, are taken from Hehir's exhaustive monograph (*loc. cit.*) :—

Until a few years ago authorities were not agreed as to whether rice cultivation is unhealthy or innocuous. A rice-field under irrigation might be regarded as a type of swamp or marsh. The varying physical states of the soil in *paddy-fields* is precisely such as we should expect to find associated with a prevalence of malarial fevers ; they have the characters of marshes—alternately saturated with water and drying-up. It is an important point therefore to decide the distance paddy-fields should be from inhabited places, towns, barracks, etc. Amongst medical officers in India opinion is in favour of making this as great as possible. Personally one considers that rice cultivation should not be permitted within a mile of towns and cantonments in India. In Italy it is not allowed within five miles of towns.

Rice cultivation is undoubtedly inimical to health under certain circumstances. In India, without adequate subsoil drainage, it is undoubtedly injurious to the health of the cultivators, and will continue to be so under existing agricultural methods.

The healthiness or unhealthiness of a rice-field to some extent depends on the amount of water available for irrigation. Revenue officers in India used to classify these fields as " one crop," " two crop," or even " three crop " fields. It might perhaps be safe to say that " one crop " cultivation is almost certain to cause malaria in the vicinity ; that " two crop " cultivation is less dangerous, and that, other causes being absent, there is much less malaria in the vicinity of " three crop " cultivation.

It has been ascertained that the rice grounds in some parts, such as Trichinopoly, Tanjore, and other places in Southern India, where the plantations are almost constantly inundated, are less fertile in the production of malaria than those which, after inundations, are exposed to the action of a powerful sun. This consideration will assist in explaining the varying degrees of unhealthiness in the neighbourhood of the rice grounds in different parts of India.

As stated above, the varying conditions found on the paddy-fields of this country are essentially those of marshes, which have long been notorious for malaria production. Hence, if a site in a malarious locality must be selected for habitations in the neighbourhood of wet cultivation, it is essential that surface drainage should be carefully attended to, so that the " tail " of water beyond that requisite for plant shall be correctly disposed of.

As now carried out wet cultivation is responsible for an enormous amount of malaria in this country, and in Burma, Manipur, and Assam. It is possible by legislation to prevent such cultivation within a certain limit of densely inhabited towns, cantonments and civil stations, as is done in Italy, but under the general conditions of agricultural life in India it is not possible to adopt this measure in rural malarial districts, as the small collections of huts called villages are in most districts scattered in the very heart of the rice-fields themselves. In endemic malarious districts it is theoretically justifiable to condemn rice cultivation, but in this country, where millions depend on rice crops for their existence, this rigid attitude towards rice production cannot be adopted. It is often, in severely endemic malarial districts, a question of allowing the lower classes to die of famine or die of malarial disease, and the former is the worse of the two evils.

Lastly, we turn to papers dealing with treatment, which practically spells quinine, but, despite all that has been written it still retains much both of interest and even of novelty.

Brunton,[3] quoting Fayrer, points out, what is not infrequently forgotten, that quinine does not exert its full action, and may indeed fail to act at all, if the liver be engorged. Hence the necessity for a mercurial and saline before the dose of the specific.

Harding [4] has a paper on the value of Koch's method of treatment, more especially with regard to the continuance of quinine administration in 15-grain doses at intervals for three months from the date of the attack. After the blood has been cleared of intra-corpuscular parasites in the usual way by a 15-grain dose given on each of five consecutive days, and the patient discharged, the dates for further doses are calculated by taking the tenth and two subsequent days from the first dose and every tenth day after them for three months.

For instance, a man in whom the parasite was found on May 1, would receive doses on May 1, 2, 3, 4, 5, 6, 7, 11, 12, 13, 21, 22, 23, and 31 ; June 1, 2, 10, 11, 12, 20, 21, 22, and 30 ; July 1, 2, 10, 11, 12, 20, 21, 22, 30, and 31—*i.e.* not fewer than thirty doses.

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[1] Sergent, Ed., and Et. (1908–1909), *Campagne Antipaludique.* Algiers.

[2] Watson, M. (1911), " The Prevention of Malaria in the Federated Malay States." *Liverpool School of Tropical Medicine.*

[3] Brunton, L. (1907). *The Action of Medicines.* London.

[4] Harding, N. E. (September, 1908), " The Value of Koch's Treatment of Malaria." *Journal Royal Army Medical Corps.*

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Malaria— *continued*

The author points out that this method appears to have been overlooked by the text-books, and concludes :—

> It will be noted that, as was the experience of Koch, treatment for a month or six weeks was not invariably sufficient to prevent relapse even in the case of the—supposedly—less resistant benign tertian parasite, whereas treatment for three months certainly was, as it can hardly be doubted that all the cases of malignant tertian were cured, with the possible exception of No. 20, and I think in all probability he was. Is it, then, too much to say that, having regard to the enormous importance of malaria, alike from the point of view of the sanitarian and the economist, this method of treatment of Koch's is the most marked therapeutic advance of recent years, one only to be compared with the discovery of diphtheria antitoxin, and that such a thing as a relapse from malarial fever should for the future be unknown ? It must be added, however, that unless the diagnosis is made by the microscope, failure and disappointment are bound to ensue, for to cases of liver abscess, enteric fever, septicæmia, pneumonia, and syphilis, all of which I have known treated as malarial, not to mention the various undifferentiated Indian fevers, quinine is more likely to prove harmful than beneficial.

Vassal [1] has shown that atoxyl alone has no specific action in malaria, but he finds it of undoubted value when combined with quinine, and cites several cases in support of his contention. It has a tonic action, and is superior to other arsenical preparations in this respect. It has proved itself of benefit in malarial splenomegaly. Large doses may be dangerous. Cohen is an advocate of quinine and urea hydrochloride given hypodermically in doses of 15 grains. It is very soluble, and if the usual precautions are taken there should be no risk of abscess formation. An injection three or four hours before an expected paroxysm usually prevents the attack. The drug can also be given by the mouth, two capsules of 10 or 12 grains each being taken four or eight hours respectively before the anticipated chill. To check relapses Cohen [2] recommends a dose of 10 grains on the evening of the sixth day and 10 grains on the morning of the seventh day, calculating from the date of the last paroxysm, and continuing this procedure for at least three months. He also speaks to the value of the combination in chronic cases. Ulmer [3] also uses quinine-urea in the form of quinine hydrochloro-carbamide. It is apt to cause a slough when used hypodermically, and hence the following technique is indicated :—

> All the instruments to be used are sterilised by boiling. The part into which the injection is to be made is cleansed with green soap and water ; a high-pressure syringe is used, and after painting an area of some two inches in diameter with tincture of iodine, the long needle attached to the syringe is plunged deeply into the muscle. Care is taken to expel all the contents of the syringe so that in its withdrawal none of the solution will be dropped on the surrounding tissue. The puncture is then sealed with iodoform collodion.

A review of the pamphlet by James [4] is given in the *Indian Medical Gazette* for January, 1909. This is a useful monograph wherein intramuscular injections of the bihydrochlorate of quinine or of the bichlorate of quinine and urea are recommended, while there is a caution to avoid phenacetin in conditions where it might seem indicated in the after-treatment. A letter to the *Journal of Tropical Medicine and Hygiene* advocates a resumption of treatment by the old combination of quinine and opium. It is said to be specially valuable in the hot stage, 9 grains of quinine and 1 grain of opium being given. This, it is asserted, cuts short the hot stage and favours sweating. The letter was the outcome of a note on a paper by Nogara,[5] who in a case of quinine tolerance found a previous administration of morphia and atropine most beneficial. Another method of preventing quinine intolerance is by giving chloride of calcium. Gros [6] has a paper on the subject. The most common symptoms of intolerance are gastro-intestinal troubles, skin eruptions, more especially urticaria, a state of lymphatism, or of vertigo. It is, he says, of rare occurrence. Apart from the indication for the use of calcium chloride, in blackwater fever (*page* 31), he believes it is very useful in quinine intolerance even when there has been a great destruction of red cells. Külz,[7] like Nocht, believes in treating malaria by giving fractional doses of quinine. One gramme is divided into five doses, which are given at two-hourly intervals.

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[1] Vassal, J. J. (November 11, 1908), " L'Atoxyl dans le traitement de la fièvre paludéenne." *Bull. Soc. Path. Exot.*

[2] Cohen, S. S. (September, 1908), " Observations on the Hypodermic Use of Quinine and Urea Hydrochloride in the Diagnosis and Treatment of Acute and Chronic Malarial Infections, etc." *American Journal of Medical Science.*

[3] Ulmer, E. H. B. (October 1, 1910), " On the Effect of Quinine and Urea Hydrochloride upon a case of Double Tertian Malarial Infection, etc." *New York Medical Journal.*

[4] James, S. P. (1908), *Malarial Fevers.* Calcutta.

[5] Nogara, G. (September 20, 1908), " Contributo alla terapeutica dell'intolleranza del chinino." *Gazz. d. Osp. e d. Clin.* Quoted in *Journal Tropical Medicine and Hygiene*, January 15, 1909.

[6] Gros, H. (May 12, 1909), " Le traitement préventif de l'intolérance quinique par le chlorure de calcium." *Bull. Soc. Path. Exot.*

[7] Külz (1909), " Behandlung der Malaria mit fraktionierten Chinindosen." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIII.

Nocht,[1] in an important paper wherein he advocates this method, also states that—

When vomiting or other conditions render it difficult or impossible to give quinine by the mouth, subcutaneous or intramuscular injections may be resorted to. Among the preparations recommended for this purpose, Nocht advises Giemsa's formula. Quinin. hydrochlor. 10 grammes, aq. dist. 18 grammes, and ethyl-urethane 5 grammes. The urethane favours the solution, and the volume of the solution thus prepared is 30 c.cm., so that 0·5 gramme is contained in 1·5 c.c. of solution. When contra-indications against quinine exist, methylene blue must be given.

Fisher [2] states that during twenty years of practice in a malarial country he has never seen any permanent damage to hearing from quinine even when given in large doses.

Chauffard [3]—

has studied the spleno-hepatic syndrome in two cases of acute malaria, and shown that as the volume of the spleen *decreases* under quinine treatment, that of the liver *increases;* the liver becomes, so to speak, the receptacle for the splenic débris brought to it by the splenic vein. This increase in volume is only transient, and then the liver, like the spleen, subsides in those cases where quinine has killed the parasites. This reaction on the part of the liver is not purely a mechanical one, but is accompanied by glandular activity, shown by cholæmia, subicterus, urobilinuria, intestinal polycholia with excess of stercobilin. The hepatic changes are still more serious if parasites from the spleen reach the liver capillaries unkilled by quinine; they include hepatitis, which may end in cirrhosis. In these cases the spleen also presents sclerosis of the pulp and perisplenitis, and there is also endophlebitis of the splenic vein. The author, in fact, considers the hepatitis as in the main dependent on the condition of the spleen.

Ashley-Emile [4]—

advocates the use of hypodermic injections of quinine in those who have established a tolerance to the drug by excessive daily usage, and in severe cases, such as those characterised by excessive vomiting and pronounced nervous symptoms, especially coma, the intramuscular method is employed; but in order to avoid abscesses or other dangerous sequelæ, strict precautions must be taken. The hands are carefully washed several times with warm water and biniodide soap, and finally in sublimate (1–1000) and sublimate alcohol. The skin is also washed, and rubbed with Scrubb's cloudy ammonia until all dirt is removed, then with 1–20 carbolic, finally with absolute alcohol. Syringes, test-tubes, etc. are washed in warm water, and kept in 1–20 carbolic. The quinine hydrochloride solution 5 gr. is boiled once or twice in a test-tube. The injection is made into the muscle (deltoid or interscapular) by pinching it up. The seat of puncture is painted with liniment of iodine, and a pad soaked in alcohol subsequently applied. If the solution is not injected warm, a drop or two of hydrochloric acid is added, producing a clear solution.

Surveyor [5] mentions the use of picric acid by the mouth or of injections of picrate of soda in cases harbouring crescents. These methods seem to cause a speedy disappearance of the sub-tertian gametes. The dose of picric acid is 2 grains twice or thrice a day, while the following are the directions for preparing the picrate of soda solution :—

Add 4 grammes of picric acid to about 75 c.c. of boiling distilled water, and to this add, drop by drop, a strong solution of sodium hydrate, taking the reaction at the same time, with a solution of di-methyl-amido-azo-benzol till the latter no longer turns red. (Do not stop when the dimethyl turns red and subsequently fades, but go on adding the sodium hydrate solution till no change of colour occurs.) Confirm with phenol-phthalein to see that no change of colour occurs; this latter is necessary to ascertain whether the solution has become too alkaline or not. At this stage, most of the picric acid is dissolved up. Make up the solution to 100 c.c. with distilled water; 3 c.c. of this solution is put up in test-tubes and sterilised at 120° C. in the autoclave. As the water evaporates in these tubes crystals are deposited, which can be readily dissolved either by slightly warming the tube or adding a few drops of sterile distilled water. The injections are no more painful than ordinary injections of vaccine, and do not produce any marked reaction, nor is there any nodule or swelling noticed at the site of injection. Scarcely any pain is present after 24 hours, so that there is no difficulty in injecting about 3 c.c. of this solution on consecutive days.

Lemanski [6] recommends intramuscular quinine injections, hydrotherapy, or a course of Vichy treatment in cases of hepatic disease, splenomegaly, or cachexia, and the opotherapic treatment, *i.e.*, daily doses of 60 or 100 grammes of fresh raw spleen in cases of extreme malarial splenomegaly. Whelan's [7] view of the action of quinine in malaria is that it causes the infected red cells to break down prematurely before the parasites can sporulate, in other words it destroys their homes and food. This theory, however interesting, is not generally accepted, and Craig's observations on the subject have already been mentioned (*page* 174).

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[1] Nocht, B. (March 25, 1909), "Die Therapie der Malaria." *Deut. Med. Woch.*

[2] Fisher, W. (June 1, 1909), "Is Quinine Injurious to Hearing?" *Journal Tropical Medicine and Hygiene.*

[3] Chauffard, A. (January 20, 1909), "Le syndrome spléno-hépatique dans le paludisme aigu." *Semaine Médicale.* Quoted in *Medical Annual,* 1910.

[4] Ashley-Emile, L. E. (1910), "The Treatment of Malarial Fever by Intramuscular Injections of Quinine." *South African Medical Record.* Quoted in *Medical Annual,* 1911.

[5] *Loc. cit.*

[6] Lemanski (1909), "Note à propos du traitement du paludisme." *Bull. Gén. de Thérap.* Quoted under "Paris" in *Lancet,* December 25, 1909.

[7] Whelan, J. H. (April 23, 1910), "On Malarial Fevers and Quinine." *British Medical Journal.*

Malaria— *continued*

Lemoine [1] gives the following formulæ for hypodermic quinine solutions which are to be deeply inserted into the subcutaneous tissues :—

Quinine hydrochloride	gr. 7½ to 15
Sterilised water	M 30
Glycerine	M 25
Quin. dihydrochloride	gr. 7·5
Distilled water	dr. 2½
Quin. hydrobromide	gr. 3 to 5
Tartaric acid	gr. 7½
Distil. water	dr. 1
Quin. dehydrobromide	gr. 3 to 5
Distil. water	M 15
Quin. sulphate	gr. 15
Tartaric acid	gr. 7½
Distil. water	oz. 2½

Thayer [2] is accustomed to use the following formula of Bacelli :—

Quinin. dihydrochlor.	1 gramme
Aquæ	10 grammes
Sod. chlorid.	0·065 gramme,

giving one-half in one median basilic and one-half in the other. He emphasises the danger of greater concentration in the dose, and cites a case in which death followed intravenous injection when a dose of double the above concentration was given. The possibility of hyper-susceptibility of the patient to quinine must be remembered, as also the possibility of a very heavy infection even when, after frequent examinations during a whole week, very few parasites are found in the peripheral blood.

The action of quinine on the kidneys has been the subject of investigation by Ferrannini,[3] who—

has carried out a series of researches *in vitro* and *in vivo* with a view to determining what action, if any, quinine in moderate or in prolonged doses has on the kidneys. In the doses usually given it appears to have a slightly deleterious effect on the secreting portion of the kidney substance. Although it is true under average doses the kidney lesions after prolonged use of the drug are very slight, yet they are recognisable, and the author gives photomicrographs of the histological appearances. From the cryoscopic experiments *in vitro* it appears that to be innocuous the quinine must not pass through the kidneys in stronger solution than 1 per cent.; above this it injures the kidney tissues. In the ordinary doses, by the time the quinine reaches the kidney *in vivo* it is in solution at a percentage well below the danger index.

There are several papers on quinine-resistant strains of the malarial parasite. Neiva [4] has dealt with the subject. In Brazil he found that: (1) The doses of quinine which suffice to prevent malaria at first have to be increased later on in order to remain effective. (2) Individuals who do not become attacked in the endemic area, contract fever if they cease to take quinine after they have left the infected region. (3) Doses of quinine employed at first with success as a therapeutic measure, fail to cure in malarial subjects who have taken quinine for long periods. Curiously enough, it was also in persons from Brazil that Nocht and Werner [5] found a remarkable degree of resistance of the parasites to quinine, both in benign and sub-tertian cases. The drug, even in doses of 2 grammes and more, failed to prevent relapses, and methylene blue also failing, recourse was had to salvarsan with considerable success.

The question of the administration of quinine during the puerperium is an important one. Atkinson [6] deals with it, describing cases, and finding that any ecbolic action it may have must be very slight. He believes it acts more as a general stimulant and promoter of vital energy and functional activity, and that even in large doses it can be safely given in severe malignant cases, for it seems to expend its energies in killing the parasites. A good paper is

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[1] Lemoine, G. H. (1901). *Manuel de Therapeutique Clinique.* Paris.

[2] *Loc. cit.*

[3] Ferrannini (March 28, 1910), *Rif. Med.* Quoted in Epitome, *British Medical Journal,* June 4, 1910.

[4] Neiva, A. (April, 1910), "Über die Bildung einer chininresistenten Rasse des Malariaparasiten." *Mém. Inst. Oswaldo Cruz.,* Vol. II., No. 1.

[5] Nocht, B., and Werner, H. (August 25, 1910), "Beobachtungen über relative Chininresistenz bei Malaria aus Brasilien." *Deut. Med. Woch.*

[6] Atkinson, J. M. (July, 1910), "Malarial Fever during the Puerperium." *Philippine Journal of Science.*

Malaria—*continued*

that by Boccarro,[1] who quotes the report of an old Committee held on the subject in India in 1892. With its findings he agrees, but mentions the following precautionary measures :—

(1) As far as possible it is best to avoid administering quinine on the empty stomach of the patient.

(2) To avoid giving the drug by mouth if the liver is functionally out of order (except, perhaps, in cases of malarial origin), as it is not likely to be well tolerated. In such cases my practice is to relieve the liver first and give quinine afterwards, or if quinine must be given at once, I prefer to inject the drug subcutaneously.

(3) Quinine is safest administered in pill or tablet form, or encapsuled in cachets, as being least likely to cause nausea or any irritability of the stomach.

(4) If idiosyncracy or a tendency to abortion exists, quinine, if given by mouth, should be combined with a sedative, opium or bromides, otherwise such cases are best treated with a subcutaneous injection of the drug.

The French view is much the same, to judge from a paper by Montel,[2] who recommends the hydrochloride as the most suitable salt. Turning now from the question of quinine, one finds Stephens [3] inclined to think that good results may be obtained by the use of calcium salts in cases which do not react well to the alkaloid. He mentions a few cases treated by 5-grain tablets of calcium lactate before meals and a $\frac{1}{4}$ grain of calcium permanganate after meals and which improved greatly under this treatment. His paper, however, is somewhat lacking in detail. A few words now as to treatment with arsenical preparations. Bowman [4] recounts his experiences with arsenophenylglycin. He finds that it produces no definite effect on the life of the malarial parasite and has seemingly no effect on the crescent body, while an overdose may produce symptoms of arsenical poisoning. Salvarsan has already been mentioned; Werner [5] has employed it at Hamburg both in benign and sub-tertian cases :—

In the tertian cases injection was followed, in an average period of 24 hours, by disappearance of parasites from the peripheral blood ; moreover, so far as observations covering some weeks show, they did not reappear except in three cases in which the dosage had been below the average of 0·6 gramme. In the æstivo-autumnal cases the results were by no means so encouraging. In five instances a single dose sufficed to banish the parasites from the peripheral blood, but this was only temporary, and within a few days they reappeared. In the remaining six cases of the æstivo-autumnal type the treatment had no effect upon the circulating parasites. Various methods were used ; at first intramuscular injection was practised, then the subcutaneous and intravenous methods, and in the last case a combination of the two latter. Apparently no untoward consequences were noted. Werner's opinion is that "606" is a powerful anti-malarial remedy, but its use should be restricted to cases resistant to or intolerant of quinine.

Nicolle and Conseil [6] record its use in six cases, and sum up their impressions as follows :—

(1) The action of "606" in malaria is very marked.

(2) This action is very rapid. There is an almost immediate amelioration of general symptoms, a fall in temperature, and a lessening of the number of parasites in the blood.

(3) This action, however, is not permanent. After some days of apyrexia the temperature rises and the parasites increase.

(4) The action also is not complete. Some parasites can always be found by prolonged search.

(5) The schizonts are specially susceptible to the drug, ring forms less so, crescents least of all.

They consider "606" of value, but think it should be combined with quinine.

Flexseder [7] has used enesol and "606." The former he finds, if persisted with, can bring about complete cure, in the case of the latter relapses occur. These are points in his paper, an extract from which will be found in the Epitome, *British Medical Journal* of January 21, 1911. There are other papers on the subject, but these must serve.

Pierpoint and Acton [8] find the arylarsonates, especially soamin, most useful in malarial

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[1] Boccarro, J. E. (April, 1910), "A Note on the Administration of Quinine in cases of Fever during Pregnancy." *Indian Medical Gazette.*

[2] Montel, M. L. R. (November 9, 1910), "Quinine et Grossesse." *Bull. Soc. Path. Exot.*

[3] Stephens, G. A. (April 1, 1910), "Malaria treated with Calcium Permanganate." *Journal Tropical Medicine and Hygiene.*

[4] Bowman, F. B. (August, 1910), "The Incidence and Complications of Malaria in the Philippine Islands, with Special Reference to its Treatment with Arsenophenylglycin." *Philippine Journal of Science*, B.

[5] Werner, H. (September 29, 1910), "Das Ehrlich-Hata-Mittel 606 bei Malaria." *Deut. Med. Woch.*

[6] Nicolle, C., and Conseil, E. (December 14, 1910), "Action du 606 sur le paludisme." *Bull. Soc. Path. Exot.*

[7] Flexseder, R. (September 8, 1910), "Behandlung der Malariainfektion mit Enesol 'Clin' und Ehrlich's Dioxydiaminoarsenobenzol." *Wien. Klin. Woch.*

[8] Pierpoint, H. W., and Acton, H. W. (April, 1911), "Malarial Cachexia and the Value of Arylarsonates in the Treatment." *Indian Medical Gazette.*

Malaria—*continued*

cachexia, and conclude a valuable paper with the following rules for treating this cachexia, excluding cases of pernicious anæmia :—

(1) Rid the host of all parasites by quinine in adequate doses.

(2) Stimulate the hæmopoietic organs by intramuscular injections of soamin in the following way :—

Give 5 grains of soamin every second day—six injections in all. An interval of ten days is then allowed to elapse and another six injections are given as above. In no case should 100 grains be exceeded as the total amount injected.

From our experience we should say that practically every case in the first and second stage of splenic enlargement will yield in forty to sixty days' time to a treatment with 60 grains of soamin.

In the advanced third stage the patients will be markedly benefited by the same treatment, and only the dense fibrous tissue of the old inflammation will be left to cause a slight degree of splenic enlargement. It is in this stage that the operation of splenectomy becomes justifiable, and it is only in those cases (*a*) where owing to the weight of the organ and consequent pressure on the stomach, life is made a burden, partly by the dragging pain that is caused and partly by the discomfort after every meal; or (*b*) in acute and chronic twisting of the splenic pedicle. From our experience of splenectomy in animals, we should strongly advise those who are undertaking this operation to transfix and tie the pedicle, before cutting it through, because, owing to the retraction of this structure, it will be extremely difficult to tie when it is tucked up near the diaphragm, and the second point to note is that any great traction on the pedicle is bound to give rise to shock.

In the class of case with splenomegaly Skinner and Carson [1] speak highly of the value of Röntgen rays and give illustrative cases, while in acute pernicious malaria Church [2] advocates transfusion with a hypotonic saline solution (30 grains to 1 pint) given at the rate of 20 ounces in ten minutes on the lines of Rogers's treatment for cholera.

We may perhaps suitably conclude what has proved a very lengthy section by quoting the views of Mircoli,[3] who—

Objects to the statement that malaria is cured when a patient recovers from the febrile attack and is restored to his normal health. All that is really cured in these cases, he says, is the fever; the disease still remains in a more or less latent condition, as is proved by the frequency of relapses in non-malarial districts, and by the long train of malarial symptoms. A true cure would mean that no relapses occur without a fresh infection, and that we are cognisant of all the processes of destruction, not only of the malarial parasite, but of its reproductive elements. Quinine never accomplishes the destruction of all the hæmosporoids circulating during a given attack. The protozoa may even themselves acquire an immunity against quinine. The very reproductive elements themselves (? spores) have been classed in the category of the ultra-visible, so that statements as to their destruction become still more valueless. The so-called race immunity against malaria is a figment, in the author's view, and mulattos and negroes are refractory only because they are already affected with malaria, just as a syphilitic is immune against fresh syphilis. The hard, enlarged spleen in malarics is an expression of the sequelæ of malaria and not of malaria itself; the spleen acts passively as a mere reservoir. No true cure of malaria can therefore be accepted; it can only be cured in the same sense and to the same degree that, for example, syphilis or trypanosomiasis can be. Prophylaxis by means of arsenic is one of the best means we have at present towards a real cure of the disease.

There may be some truth in these remarks, but few, I think, will endorse them in their entirety. In any case it is now known that a syphilitic is not immune to fresh syphilis, so this argument does not hold good.

Additional Notes

Fowler [4] mentions primary cases occurring in Gibraltar, where no anophelines could be found. He asks if another genus and species may be the transmitter. He does not think ships introduced infected anophelines, but it is not clear that he wholly excluded this source, and we know that vessels can harbour malaria-carriers. Fowler, however, confesses himself at a loss to account for the causation of the cases which were benign tertian. Carnegie Brown [5] recently reviewed the question of quinine prophylaxis. He summarises the present position as follows :—

(1) Quinine prophylaxis was now fully accepted as an auxiliary method of the greatest importance in the prevention of malaria; it was essential in dealing with infected native populations, and was specially valuable when (as in the case of detachments of soldiers, railway employees, etc.) general measures were out of the question, individual control and supervision being on the other hand practicable.

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[1] Skinner, B., and Carson, H. W. (February 25, 1911), "Curative Influence of Röntgen Rays in Malaria." *British Medical Journal.*

[2] Church, D. M. C. (January 28, 1911), "Treatment of Pernicious Malarial Fever." *Ibid.*

[3] Mircoli (February 13, 1910), *Gazz. d. Osp. e d. Clin.* Milan.

[4] Fowler, C. E. P. (June, 1911), "Malarial Fever in Gibraltar." *Journal Royal Army Medical Corps.*

[5] Brown, C. (June 1, 1911), "The Present Position of the Quinine Prophylaxis of Malaria." *Journal Tropical Medicine and Hygiene.*

Malaria—*continued*

(2) When general quininisation of a native community was advisable, it should be carried out systematically on an approved plan by a special staff of distributors under a medical director.

(3) The most suitable salts for purposes of prophylaxis were the sulphate, tannate, and nucleinate, and the best method of administration was a daily dose of 3 to 5 grains for adults, and for children (for whom the tannate was best adapted) 1 grain daily for every three years of age.

Werner [1] recommends the intravenous injection of urethanquinine in cases of malarial coma, and records a case where 1·5 grammes was given in 200 c.c. of physiological salt solution with good results.

Malta Fever. Papers dealing with bacteriology first claim attention. Pollaci and Cannata [2] maintain that the *Micrococcus melitensis* is motile, although they do not say that they have attempted to stain possible flagella. They give the rate of development of the organism in different culture media, and state that they have been able to grow it in acid potato, and in both acid and alkaline urine. A laboratory infection showed the incubation period to be 20 days. Cannata [3] has shown that the organism is comparatively long lived in certain culture media—292 days in Lœffler's broth, 278 days in sterile milk, and as many as 313 days on agar slope. On potato, gelatine, and in urine, its life is short (25 to 50 days). Pollaci and Ceraulo [4] have found that blister serum in cases of the disease agglutinates the micrococcus, and also showed [5] that the same property exists in the salivary secretion. In a supplement to a paper by Strachan and himself, Birt [6] gives some very useful notes on the agglutination test and blood culture. His conclusions may be stated :—

(1) Examination of the blood of 177 persons resident in South Africa has shown that they have been infected with the *M. melitensis.*

(2) The *M. melitensis* has been isolated from 1/50 to 1/10 c.c. of blood preserved in glass capsules for three to six weeks in thirty-three cases.

(3) Emulsions of the *M. melitensis* sterilised at 55° C. with the subsequent addition of 0·5 per cent. phenol mixed with the diluted blood serum, and drawn into glass tubes of 1 mm. in diameter, afford a sure and ready method of the diagnosis of Malta fever. This plan can be adopted by any practitioner, though unprovided with laboratory facilities.

(4) Specific blood retains its agglutinating property for weeks or months, even when contaminated.

(5) There is a widespread epizootic of Malta fever among the goats of South Africa. Their milk conveys the infection to man.

In the course of the paper he points out that using the carbolised emulsion of the micrococcus a reaction in a $\frac{1}{20}$ dilution of a serum is diagnostic of Malta fever, past or present. He also says :—

After long subculture, some strains of *M. melitensis* become agglutinable in saline fluid, or when not so clumped they may react to a mere trace of serum from any source. The necessity of controls with normal blood is apparent. Manipulations with the living microbe are fraught with danger. A large proportion of workers with it have been infected. But apart from the safety and convenience of using sterilised cultures there is another great advantage. Anomalous reactions are suppressed. If living suspensions are employed, it sometimes happens that a specific serum reacts when highly diluted, but may cause no agglutination if more concentrated. In an experience of between 2000 and 3000 agglutination tests with dead emulsions, no instance of such an inhibited reaction has come under my notice. The density of the emulsion has been measured by mixing it with an equal volume of water, and drawing it into a glass tube 1 mm. in internal diameter. The opacity should be well marked. This corresponds to about 50,000 million micrococci per cubic centimetre. Since several cubic centimetres of the suspension were prepared at one operation, the estimations of the agglutination were comparable with one another. The ratio of the number of bacteria to the volume of the emulsion is a factor in determining the clumping index of the blood. The simplicity of the sedimentation method with killed cultures, which involves no more apparatus than a few glass tubes and a small amount of a preparation which retains its activity for years, brings the diagnosis of Malta fever within the range of every practitioner.

He also says that though a positive clumping reaction predicates the existence of the infection, yet the absence of agglutinins does not necessarily exclude Malta fever. Such cases are unusual. The failure of the blood to react to the invading micro-organism is a sign of evil omen. The *M. melitensis* has such well marked characteristics that no other organism

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[1] Werner, H. (1911), "Intravenöse Injektion von Urethanchinin bei Malaria comatosa." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XV., No. 11.

[2] Pollaci, G., and Cannata, S. (1908), "Contributo alla morfologia e alla biologia del melitense." *Arch. di Anat. Patol.*, Vol. IV., No. 2.

[3] Cannata, S. (1908), "La vitalita del melitense nei terreni di cultura." *Osp. di Palermo.*

[4] Pollaci, G., and Ceraulo, S. (1908), "La siero-diagnosi da vescicante nelle febbre mediterranea." *Rif. Med.*

[5] *Idem* (1908), "La salivo-reazione nella diagnosi della febbre mediterranea." *Gazz. Siciliana di med. e clin.* All quoted in *Bull. de l'Inst. Past.* (1909).

[6] Strachan, P. D., and Birt, C. (August, 1909), "Malta Fever in South Africa." *Journal Royal Army Medical Corps.*

Malta Fever— *continued*

is likely to be mistaken for it. For laboratory workers, Eyre's [1] paper on animal inoculations and the properties of the sera of infected animals is likely to be useful. Lagriffoul and Roger [2] record the case of a laboratory boy whose blood, four years after an illness like Malta fever, readily agglutinated *M. melitensis* in a dilution of 1 in 30. Nicolle and Comte [3] have made the important observation that the blood serum of patients ill with typhus fever frequently agglutinates *M. melitensis*. They used dilutions varying from 1 in 10 to 1 in 50.

Nègre [4] finds that normal human sera are able to agglutinate *M. melitensis* in 1 in 30 at 37° C. within one hour, and at the room temperature within 5 hours. With 1 in 50 dilution 5 hours at 37° C., and 24 hours at laboratory temperature are the figures. With 1 in 100 no agglutination occurs. Heating these normal sera to 56° C. for half-an-hour destroys this agglutinating power, which is also seen in the normal serum of goats, sheep and rabbits, in 1 in 30 and 1 in 50 dilutions. The author therefore recommends that in sera-diagnosis the serum used should be heated to 56° C. for half-an-hour, employed in dilutions of 1 in 50, and the mixture observed for 4 or 5 hours.

Darbois [5] has determined the resistance of the organism of Malta fever during lactic fermentation in milk foods. He finds (1) That the supposed fragile *M. melitensis* actually resists lactic fermentation better than the tubercle bacillus. (2) Milk-foods, cream, butter, whey, curds, and white cheese, prepared from contaminated milk, can contain the organism in a living state during a period of about the first three months after manufacture, and must be considered as capable of propagating Malta fever during this period. Cantaloube's clinical observations confirm this so far as cheese is concerned. (3) On the contrary, cheeses which are not eaten until they have undergone preparation for more than a month, ripened checses, and cheeses which are allowed to ferment, may be considered as incapable of conveying the infection. Rouslacroix [6] recommends the macroscopic Widal test in Malta fever in a dilution of 1 in 50 with a time limit of 5 hours. He regards it as more reliable than the microscopic method, and the reaction is much more easily observed. He thinks that enteric and Malta fever not uncommonly co-exist in the same subject. Bacteriologists are referred to recent work on the endotoxin of *M. melitensis* by Bernard.[7] Broth cultures containing it are very fatal, but their toxicity is lessened by boiling for 5 minutes, heating to a temperature of between 78° and 80° C., and by filtration through a Chamberland filter. Prolonged boiling abolishes the toxicity altogether. Passing now to papers of a more general nature we find Simpson and Birt [8] describing an interesting case from the Anglo-Egyptian Sudan, where infection was apparently obtained through drinking goat's milk at Roseires on the Blue Nile. Simpson mentions two points as worthy of note ; the first being the long duration and severity of the fever, without the occurrence of any of the usual complications ; the second the prolonged latent period, apparently at least two months. Birt, who deals with the bacteriological aspects of the case, states as regards the patient, that—

> On his return to the Sudan he searched for and discovered the goat which had given his milk supply. He took a sample of its blood and labelled it, "Blood of a goat whose milk I drank about fifty-four days before I was laid up with Malta fever." This blood, notwithstanding a delay in transit of two months before examination, clumped his micrococcus in a 20-fold dilution, while the blood of a normal goat was without action on it. The goat whose milk he drank was therefore infected. The period of incubation may appear long, but it is not exceptional. In 8 per cent. of attacks this extends to eight weeks or over (Reports, *Med. Fever Com.*, Part VII., *page* 102). A case is recorded in which the onset occurred six months after infection (*Journal of Royal Institute of Public Health*, December, 1907, *page* 748). At the same time he despatched the blood of a native who had suffered from fever for ten months on the Blue Nile, and was slowly recovering, though still troubled with joint pains. The native's serum agglutinated the Sudan *M. melitensis* in 160-fold dilution, and in a 40-fold a Mediterranean variety.

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[1] Eyre, J. (1909), "The Pathogenesis of *Micrococcus melitensis*." *Proceedings Royal Society of Edinburgh*, Vol. XXIX.

[2] Lagriffoul, A., and Roger, H. (January 15, 1910), "Sur la persistence de la réaction agglutinante dans la fièvre de Malte," *C. R. Soc. Biol.*

[3] Nicolle, C., and Comte, C. (April 13, 1910), "Sur la présence fréquente d'un pouvoir agglutinant vis-à-vis du *Micrococcus melitensis* dans le sang des malades atteints de typhus exanthématique. Sa valeur diagnostique." *Bull. Soc. Path. Exot.*

[4] Nègre, L. (December 17, 1910), "Sur l'agglutination du *Micrococcus melitensis* par les sérums normaux." *C. R. Soc. Biol.*

[5] Darbois, P. (January 27, 1911), "Résistance du *Micrococcus melitensis* pendant la fermentation lactique, dans le laitage." *Ibid.*

[6] Rouslacroix (March 17, 1911), "A propos du séro-diagnostic de la Fièvre de Malte." *Ibid.*

[7] Bernard, C. N. (1911), "On the Endotoxin of *Micrococcus melitensis*." *Ibid.*

[8] Simpson, R. J. S., and Birt, C. (December, 1908), "Malta Fever from the Blue Nile." *Journal Royal Army Medical Corps.*

Malta Fever—*continued*

Bousfield [1] has also dealt with the disease in the Sudan, especially in the Kassala district. Of nineteen cases observed, which were almost certainly Malta fever, only one was fatal. The complications are mentioned. Among them we note cancrum oris and severe diarrhœa, not of a " pea-soup " character. A point of importance is the fact that the disease has been found to be very widespread. Thus Danlos, Wurtz, and Tanon [2] have recorded two cases from the neighbourhood of Paris, infection being derived from drinking the milk of goats introduced into France from Spain. Simond and others [3] describe cases in Marseilles, and mention a case found by Sicard and Lucas at Malaga. Aubert, Cantaloube, and Thibault [4] state that—

An important nidus of Malta fever exists in the department of Gard, in the Cevennes, a region where goats are very abundant. They have investigated an epidemic of this disease which broke out in 1909 at Saint-Martial, a hamlet situated in this district. Clinically, bacteriologically, and epidemiologically the epidemic was without doubt attributable to infection with the *Micrococcus melitensis ;* and it was preceded by an epizootic amongst goats which was also directly associated with infection by this micrococcus. The inhabitants of the infected area consumed a large quantity of goat's milk, and the authors have no doubt that this was the medium in which the infection was conveyed. They have not been able to discover how the epizootic originated, but they ascertained that it spread from a particular farm where a large number of goats had been brought together. Investigation of the domestic animals in the affected area by means of the serum agglutination test yielded the following results : Out of 213 goats 67 (31·9 per cent.) were found infected, and out of 74 sheep and 96 rabbits infection was found respectively in 7 (1·9 per cent.), and in 20 (20·8 per cent.). With regard to the sheep, they state that ewe's milk is hardly ever consumed now as human food, but when not used for feeding the young lambs is turned into cheese. Whether the *Micrococcus melitensis* may be present and retain its vitality in such cheese is a point which they have not yet determined (*see page* 188). The authors think that the frequency of infection amongst the rabbits investigated is a matter of some significance ; if these animals excrete the micrococcus in their urine, they may prove to be a dangerous means of spreading the disease (but see *infra*). They appear to have no doubt as to the reliability of the serum test (dilution 1 in 20) on rabbits, since they investigated a large number of control rabbits at Marseilles and found that none of them gave a positive result, even with a dilution of 1 in 10.

Dubois [5] has found what he believes to be Malta fever in fowls in the region of Nimes in France. The disease is very fatal, and the serum of infected birds agglutinated *M. melitensis* in dilutions of from 1 in 50 to 1 in 600 in 60 per cent. of the cases. Naturally this observation requires confirmation. Later work by Simond, Thibault, and Brun [6] goes to show that the rabbit is refractory to infection—*i.e.* the organism does not multiply in the rabbit, nor even after massive doses can it be recovered, though an agglutination action may be obtained with the rabbit's serum. Healthy rabbits do not acquire infection if kept in contact with inoculated rabbits or affected kids. They carried out experiments with milk and cheese, finding that the micrococcus can remain alive in inoculated milk for two months, while in cheeses of different kinds they have recovered the organism up to the fifteenth day. They recommend certain prophylactic measures, amongst others vaccination of animals like goats, which serve as a reservoir for the virus. Darbois and Vergnes [7] have shown that ewes which furnish milk used for the preparation of Roquefort cheese may be a source of infection in France, while Du Bourguet [8] has proved the presence of Malta fever in Corsica. As regards other places one need merely mention its recognition in Lisbon, in Uganda by Bruce and his colleagues,[9] and in French tropical Africa.

Nicolle and Conseil [10] state that—

While it is not easy to infect a guinea-pig with Malta fever, recent observations show that it may become naturally infected. In five guinea-pigs purchased from a Maltese goat-keeper, two were found to have an agglutinating power of 300, and from one of these the authors were able to isolate easily the micrococcus from the spleen and liver. It was also found that the agglutinating power was transmitted hereditarily to the young. Three others similarly infected have since been discovered.

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[1] Bousfield, L. (December, 1908), " Malta Fever in the Sudan." *Journal Royal Army Medical Corps.*

[2] Danlos, H., Wurtz, and Tanon (December 4, 1908), " Deux cas de fièvre de Malte observés aux environs de Paris." *Bull. et Mém. Soc. Méd. des Hôp. de Paris.*

[3] Simond, Aubert, Blanchard, and Arlo (July 21, 1909), " La Fièvre de Malte à Marseille." *Bull. Soc. Path. Exot.*

[4] Aubert, P., Cantaloube, P., and Thibault, E. (May 25, 1910), " Une épidémie de fièvre de Malte dans le département du Gard." *Ann. de l'Inst. Past.* Quoted in *British Medical Journal,* November 12, 1910.

[5] Dubois (August 1, 1910), " La fièvre de Malte chez les poules " (note préliminaire). *Revue Vét., Toulouse.* Quoted in *Bull. de l'Inst. Past.,* October 15, 1910.

[6] Simond, P. L., Thibault, and Brun, P. (October, 1910), " Propagation et prophylaxie de la fièvre ondulante en France." *Proc. VI. Congrès de l'Alliance d'Hyg. sociale.* Marseilles.

[7] Darbois and Vergnes, J. (November 12, 1910), " La brebis agent de propagation de la fièvre de Malte." *Journal des Praticiens.*

[8] Du Bourguet, J. H. (December 14, 1910), " La Fièvre de Malte en Corse." *Bull. Soc. Path. Exot.*

[9] Bruce, D., Hamerton, A. E., Bateman, H. R., and Mackie, F. P. (1910), " ' Muhinyo,' a Disease of Natives in Uganda." *Proceedings Royal Society,* B., Vol. LXXXII.

[10] Nicolle, C., and Conseil, E. (1909), " Infection naturelle à *Micrococcus melitensis* chez le cobaye." *C. R. Soc. Biol.*

Malta Fever— *continued*

Samut [1] has recorded the onset of Landry's paralysis in a case of Malta fever, while Cazeneuve [2] writes of the renal troubles which may supervene. Hæmaturia is not uncommon, but a good deal appears to depend on the previous soundness or otherwise of the patient's kidney tissues. As regards prophylaxis the question of vaccinating animals against the disease has already been mentioned. Other measures consist in notification, periodical testing of the blood and milk of goats and ewes, the provision of hygienic stabling for animals, the prevention of contamination of milk by urine, the boiling of milk, and administrative measures, such as registering the individual animals in herds and flocks, preventing importation of infected stock, etc. Some of these measures were advocated by Billet as applicable to Corsica (*loc. cit.*), and some have been adopted at Tunis.[3] Brumpt points out that goats love to drink the urine of man, especially if they are deprived of salt, so in countries where Malta fever occurs this should be prevented as far as possible. There is not much to be said regarding treatment, but De Brun,[4] who, in describing a case closely simulating liver abscess, mentions that quinine in massive doses appears to be the treatment *par excellence*. He gave 2½ grammes of the neutral hydrochlorate by subcutaneous injection, either once every morning, or even morning and evening, and found it well tolerated and beneficial. In ordinary doses it is of no use. This author [5] had previously advocated these heroic doses, and cited a case where a rapid cure was effected. Kennedy [6] describes the treatment of a prolonged and intractable case where infection was acquired at Kassala, by means of an autogenous vaccine given in small repeated doses varying from 6 to 9 million cocci. The doses were given at intervals of a few days, and with marked benefit, though the case was of what he calls the chronic remittent type. We transcribe the following classification table which he appends to his article :—

Class	Type	Local symptoms and sequelæ
I.	Malignant	Fatal : usually in three weeks.
II.	Undulant—	
	(*a*) Severe	Moderately severe or mild.
	(*b*) Mild	Mild.
III.	Chronic—	
	(*a*) Remittent	Usually very severe.
	(*b*) Irregular	
IV.	Other irregular types ...	Varied.
V.	Abortive	Nil.

Prynne [7] records a case in which a vaccine was given by the mouth, 2½ million micrococci to the dose, every alternate morning. It appeared to do good, but did not prevent a relapse. Eventually, however, the treatment apparently cut the disease short.

Additional Note

Ross [8] gives an interesting account of how Malta fever was stamped out of Port Said by destroying all dangerous goats in the town and by laying an embargo on the importation of infected animals. He states that—

> unfortunately the exact way in which Malta fever is conveyed from one goat to another is, at present, unknown. It is possible that the *Micrococcus melitensis* has some existence elsewhere besides goats or men.

[1] Samut, R. (January, 1911), "Landry's Paralysis and Malta Fever." *Journal Royal Army Medical Corps.*

[2] Cazeneuve, H. J. (February 8, 1911), "Les troubles rénaux dans la fièvre méditerranéenne. Crises d'hématuries à la période critique de l'affection." *Bull. Soc. Path. Exot.*

[3] Nicolle, C., and Conseil, E .(1909), "Recherches sur la fièvre méditerranéenne entreprises à l'Institut Pasteur de Tunis." *Ibid.*

[4] De Brun, H. (November 11, 1908), "Fièvre de Malte simulant un abcès du foie. Guérison rapide par la quinine à haute dose." *Ibid.*

[5] *Idem.* (October 14, 1908), "Fièvre de Malte. Inefficacité de la Quinine à dose ordinaire. Guérison rapide par la Quinine à dose massive." *Ibid.*

[6] Kennedy, J. C. (September, 1910), "Vaccine Treatment of Malta Fever." *Journal Royal Army Medical Corps.*

[7] Prynne, H. V. (November, 1910), "Case of Mediterranean Fever Treated with Vaccines." *Ibid.*

[8] Ross, E. H. (June, 1911), "The Elimination of Malta Fever from Port Said." *Ibid.*

Malta Fever—*continued*

In this case the disease may reappear. A repetition of the measures described above will soon cause its disappearance again.

It will be noticed that the evidence of the agglutination reaction was considered sufficient for the slaughter of the goats. On this evidence alone sixty-one animals were killed. This may be criticised. But the presence of the *M. melitensis* in the milk or even in the blood of infected animals is not very constant. As in the case of infected human beings, the micrococcus appears in gushes in the blood, urine, and milk, and then days may pass during which it cannot be found. It was therefore considered that the agglutination test, properly controlled, would give the surest results. It certainly enabled infected animals to be slaughtered with less delay than if the more tedious examination of its milk or blood had been undertaken. It is, of course, possible that more goats were slaughtered than was absolutely necessary, for some of the animals that reacted and were killed might have recovered from the disease. But it erred on the side of safety, and the disease has been completely exterminated. It is also possible that one or two goats might have had the disease in its very earliest stage and thus failed to react—time alone will show if this was the case. The last infected goat was slaughtered at the end of 1910, and fresh importation of the disease is prohibited. In this way Malta fever should cease to exist at Port Said. It will be interesting to watch the results on the human population of the town, but it is a pity that there is not a means of stating accurately the number of cases that occur every year. The question arose as to the advisability of segregating the infected goats until they had completely recovered. It was found that this course would have been more expensive than buying the animals and slaughtering them outright. The disease in the goat is so chronic that it is difficult to say when recovery has actually taken place, and in the meantime the goats must be fed and cared for. It was better to eliminate the disease once and for all.

Measles. Lorey[1] has carried out bacteriological researches in this disease. He finds that the erysipelatous streptococci are the chief cause of complications in measles, and that the severity of a measles epidemic depends on the frequency with which secondary infections with these streptococci occur. The prognosis is specially bad when they are found in the blood, such a condition proving almost always fatal. The starting-place for such secondary invasions is the mucous membranes of the upper respiratory tract, but the false croup so often seen in measles cases seems to be due to a pneumococcal infection. He examined the glands, the middle ear discharge, and the blood. The last named was examined in 22 cases, in 15 of which streptococci were found. In 3, *paratyphosus* B. was discovered, while in the remaining 4 cases the *B. coli*, the pneumococcus with the *B. pyocyaneus*, the *Streptococcus erysipelatosus* with the pneumococcus, and the streptococcus with an anærobic *Streptococcus putridus* were isolated respectively. The streptococci, he believes, are, in hospitals, mostly conveyed from patient to patient by the hands of nurses and other attendants on the sick, food utensils, toys, etc., and also by means of the cough-spray. Hence proper isolation of complicated cases is indicated. Richards[2] shows that measles infection spreads directly from the sick to the healthy. Only in rare instances may infective material on clothing be to blame. There is not a scrap of evidence that the infection clings to walls, floors, or desks.

The *British Medical Journal* of June 25, 1910, has some interesting remarks on King's theory, the foundations for which are distinctly weak, that the microbe of measles comes from the mouse. As the evidence advanced was only presumptive, there is no need to say more about it here, but it might be worth someone's while to investigate the matter on scientific lines.

Kaethe finds a leucopenia is a characteristic symptom of the first week of measles, but if complications occur a leucocytosis is produced. The early leucopenia can be used for differential diagnosis. Ward[3] has a useful paper on measles, and mentions points not usually dealt with in text-books. Thus he describes a mode of onset in which symptoms are present from the time at which the infection takes place, and yet the rash only appears at the end of fourteen days or so, as it would have done if there had been no previous symptoms. He has seen measles without a rash, and measles with a rash but without catarrh, and says :—

It is highly probable that in measles, as well as other endemic specific fevers, the disease spreads from one individual to another as a simple coryza, until at length some suitably susceptible person is attacked, the virulence of the organism is enhanced, and a new epidemic then breaks out.

It is probable also that some of the patients with " morbilli sine morbilli " develop at some time or another a transient rash which may pass unnoticed. In a case of my own in which no rash was noticed, though looked for every day on account of a suspicious coryza, Koplik's spots were present, but disappeared again in two or three days.

In the first Review a French account of Koplik's spots was given. Here is what Ward says about them :—

A careful search for Koplik's spots on the buccal mucous membrane in the 100 cases which came under observation at a sufficiently early date has convinced me that they are as constant in occurrence as the rash itself; indeed, in one case previously mentioned Koplik's spots were present without the rash.

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[1] Lorey, A. (1909), " Bakteriologische Untersuchungen bei Masern." *Zeit. f. Hyg. u. Infekt.*, Vol. LXIII., No. 1.

[2] Richards, H. M. (September, 1909), " The Cleansing of School-rooms." *Public Health.*

[3] Ward, E. (May 30, 1908), " On Measles." *British Medical Journal.*

Measles—*continued*

To see them and be sure of their presence requires some experience; for on the one hand they are difficult to identify until the medical man is used to their appearance, and on the other hand there are certain appearances in the mouth which are normal and which may yet be easily mistaken for the spots unless one is aware of this difficulty. A good light is essential; they should be looked for only in bright daylight by any one who is not quite familiar with them.

The spots have been differently described by different writers, but none of the descriptions seem quite satisfactory. They may best be likened to miliary tubercles, especially to the fine tubercles that are seen on the brain in cases of tuberculous meningitis; and, just as in the case of these tubercles, the Koplik spots are often best seen by noting small irregularities in the light reflected from the surface of the mucous membrane. This is especially so when the light available is not very good, as, for instance, that given by a candle or a match. The spots are scattered irregularly over the mucous membrane of the cheeks and gums, and I have also seen them on the soft palate and fauces. They occur in groups most frequently, that remind one somewhat of the blotches formed by groups of papules in the measles rash on the skin, and the spots of a group may coalesce and form a whitish patch. There is generally some reddening of the mucous membrane.

It may be considered fanciful to describe anatomical groups of spots when they are distributed irregularly; none the less it is convenient to bear these groups in mind, as it leads to a more systematic examination of the mouth. There are:—

(1) A group round the opening of Stenson's duct.

(2) A group above and behind this opposite the upper molar teeth.

(3) A group opposite the lower posterior molar teeth, spreading on to the gum behind the teeth.

(4) A group in the vertical fold behind the teeth where the labial mucous membrane becomes continuous with that over the ascending ramus of the mandible.

Of the appearances likely to be mistaken for Koplik's spots there may be mentioned a number of small pale projections found normally in the fold mentioned in (4) and spreading in front of this; and there is also seen in many mouths a tiny speck on the labial mucous membrane, about $\frac{3}{4}$ in. below the parotid papilla, which may be mistaken for a Koplik's spot, but which is, I believe, a tiny congenital projection, possibly an accessory Stenson's papilla. Small white ulcers, too, due to stomatitis, may be mistaken for groups of spots.

With the outbreak of the measles rash on the body there generally is an accompanying stomatitis, which reddens the whole of the buccal mucous membrane, sometimes in patches at first; and in this general catarrhal stomatitis Koplik's spots rapidly disappear. The spots are sometimes late in appearing, and may not appear till after the rash; if catarrhal stomatitis is then present they may easily be missed. This stomatitis occasionally causes a peeling of the tongue exactly like the "strawberry" tongue of scarlet fever. In 2 per cent. of cases I have seen petechial hæmorrhages in the mouth at an early stage of the disease, and have been able to correctly prognose a severe attack.

He divides the rash into three types—fine, medium and coarse. The first is apt to be mistaken for rubella or scarlet fever; the last, which often goes with a mild attack, may be taken for a simple urticaria. He says, further, that the first appearance of the rash is not on the face but on the buttocks and round the anus. Amongst complications he mentions a corneal lesion in which there appears to be an abrasion of the surface which may be due to an irregular sub-epithelial collection of lymph. His notes on prognosis are suggestive:—

It is useful to be able to tell the parents of a child with measles whether the attack will be severe or not, and to be able to foretell a special liability to broncho-pneumonia or other complication. As measles is usually a mild complaint and is quickly over, most authors do not dwell on the prognosis.

In the cases I have seen, the patients on whom the rash came out slowly had a severe attack, as a rule, while those with a rapid outbreak of a profuse eruption did well. A profuse eruption of Koplik's spots generally preceded a profuse skin eruption, and was therefore an aid to prognosis; the finer the type of rash the more severe the disease.

Broncho-pneumonia occurred more frequently in cases where the physical signs found at the first examination were mostly at the base of the lungs, or were confined to one lung only. The cases with extensive signs in both lungs, with dyspnœa and slight cyanosis, occurring early in the disease, quickly recovered, although the general condition of the child seemed at first sight to justify a guarded prognosis.

In a case of extensive eczema of the head and face it seemed to me that eczema would probably be worse after the attack; but it was distinctly better. A week later, however, the eczema relapsed, and was worse than ever before.

He mentions the immunity of infants, and believes the immunity of the mother is partially transmitted by the milk as well as through the placenta. Altogether this is an interesting and valuable paper, and justifies a somewhat lengthy review, for measles is well-nigh as important in the Tropics as in temperate climates, though possibly not so deadly.

Tylecote [1] points out that in a small, struggling child it is not always easy to see Koplik's spots, especially when there are but few of them. According to him a more certain and quite as early a sign is an intense gingival hyperæmia. The gums become red, injected, and slightly swollen. They are also injected here and there with a patchy, whitish scum which is easily removed, and which consists of epithelial squames and debris. The hyperæmia lasts longer than Koplik's spots, sometimes even till the rash begins to fade. It is not seen in scarlet fever, rubella, or influenza.

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[1] Tylecote, F. E. (August, 1908), "The Condition of the Gums in Measles." *Practitioner.*

Measles—*continued*

Pathologists will find much of interest in an illustrated paper by Ewing [1] on the changes in the epithelial cells in measles. Here one can only quote his final sentences. He concludes :—

In the writer's opinion all the indications drawn from these cases point to the existence in measles of an infection by an actively multiplying micro-organism of the class of bacteria. Although one finds in the epithelial cells many structures which bear some resemblance to protozoa, and the origin of one group of these structures could not be satisfactorily determined, yet the general characters of the disease, and especially the widespread occurrence of very acute degeneration and necrosis of epithelial cells, all suggest that measles is referable to infection by a bacterium which produces an active toxin having special affinity for superficial epithelial cells.

A paper by Armstrong [2] is likely to interest the epidemiologist. He deals with school epidemics, and believes that infection is always due to direct personal contact. As regards pre-eruptive symptoms he mentions Meunier's sign—a marked lowering of body-weight during the incubation period. It lasts several days and its intensity varies. In the light of Kaethe's findings it is worth noting that Renaud and Tileston, whom Armstrong quotes, find that there is a leucocytosis beginning early in the period of incubation. As regards glandular enlargement the mastoid and sub-occipital glands seem to escape in measles. Those in the cervical and axillary regions are specially affected. The association of malignant measles with insanitary conditions is mentioned in an article in the *British Medical Journal* for December 18, 1909.

For the prevention and treatment of measles Milne [3] advocates the procedure which has given him such excellent results in scarlet fever, and which may possibly revolutionise our ideas as regards prophylaxis in these two exanthemata. Briefly put, it consists in gently rubbing pure eucalyptus oil, morning and evening, all over the body from the crown of the head to the soles of the feet, during the first four days of the disease, commencing at the earliest possible moment. Afterwards this is repeated once a day until the tenth day of the disease. At the same time the tonsils and pharynx are thoroughly swabbed with 1 in 10 carbolic oil every two hours for the first twenty-four hours, rarely longer. He claims for this method :—

(1) When this treatment is commenced early—and this is vital—secondary infections never occur, and consequently complications are unknown.

(2) With this treatment carefully carried out the children may occupy the same room without risk of infection.

(3) The economy of the treatment. An ordinary case in the isolation costs £10 ; this, perhaps, 2*s*. Therefore it means a saving of millions of pounds annually.

(4) Its household economy. The mother is free to attend both the patient and her duties. The father is free to go to work without the slightest risk, and the children equally free to attend school.

(5) No after-disinfection is necessary, for, the disease having been destroyed, nothing remains.

(6) I have frequently been asked about the disinfection of the patient's spoons, crockery, etc., as these are such a trouble in an ordinary household. Well, the fact is, there is no disinfection or in any way a keeping them apart. They are all collected together, washed in the ordinary way, and served out indiscriminately on the next occasion.

Thus there is no interruption of the domestic, scholastic, or business affairs of the household.

Further, he states :—

The tendency to complications is greatly lessened by this method of treatment with eucalyptus oil, and with the more recent use of carbolic oil 10 per cent. for the tonsils and pharynx. I may say that, from my experience, it has proved equally as efficacious as it has proved to be in scarlet fever cases ; for, with the exception of broncho-pneumonia in very delicate children, such are unknown. Even the broncho-pneumonia is, I fondly hope, a thing of the past. When the patient is first discovered, if possible when suffering from coryza, or if Koplik's spots are visible before the rash appears, as well as when the rash is appearing or out, the patient is treated at once and put to bed. A large bed-cradle is placed over the child's head and chest. This is then covered with a light fleecy gauze and sprayed or moistened from time to time with eucalyptus oil. This is done to entangle the phlegm, and prevent the germs in coughing being carried beyond the disinfecting power of the eucalyptus oil, and so infecting the other children ; for in coughing, these germs may be carried to the distance of 20 or 30 ft. It is a great advantage that the child is thus able to see all that is going on around.

For the healthy children who have been exposed to infection I have a little eucalyptus oil sprinkled on their bed at bed-time, and in the morning, noon, and evening a little placed on a handkerchief and carried in their bosom. Thus they have a continuous aroma of eucalyptus being inhaled. It is to this treatment that I attribute the fact that for all these years we have required no isolation hospital for these diseases for the children under my care. In corresponding schools the necessary isolation accommodation is, I believe, from one-third to one-half or one-half to two-thirds of the number of children in residence. The economical saving thus effected is very great, while the benefits to the patient are incalculable. It is worthy of note too, that, in these cases I have given, our cubic space is only about 750 cub. ft., while in the isolation hospitals it is 2000 cub. ft. and the beds 15 ft. apart.

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[1] Ewing, J. (February 18, 1909), "The Epithelial Cell Changes in Measles." *Journal Infectious Diseases.*

[2] Armstrong, H. G. (December, 1909), "The Case-Incidence in Nine Epidemics of Measles at a Public School, with Notes on the Pre-eruptive Symptoms." *Proceedings Royal Society of Medicine*, Vol. III., No. 2.

[3] Milne, R. (April 22, 1911), "Measles : Its Treatment and Prevention." *Lancet.*

Measles— *continued*

These are certainly very remarkable statements which are now being put to the proof, and certainly Milne's method, so-called, might with advantage be applied to cases of measles in tropical countries where facilities for isolation are often lacking.

As regards therapeutic measures Servoss [1] states that :—

> A warm, well-ventilated, darkened room is required. The air should be kept moist by the liberation of steam, which has a tendency to relieve the cough. The bowels should be thoroughly cleared out at the outset by the administration of calomel and podophyllin, followed by an effervescent saline carrying 60 per cent. of pure magnesium sulphate. After clearing the bowels they should be kept clean by the use of sulpho-carbolates. To control the fever a combination of aconitine gr. $\frac{1}{134}$, digitalin gr. $\frac{1}{67}$, and strychnine arsenate gr. $\frac{1}{134}$ should be given until an effect is obtained. In using this combination Shaller's rule of administration to children should be followed : One granule of the above or any other active principle for each year of the child's age, and one additional granule dissolved in 3 oz. of water, the dose being a teaspoonful of the solution at such intervals as may be indicated to obtain the desired effect. For the cough, emetine gr. $\frac{1}{67}$ should be exhibited at hourly intervals or oftener, bearing in mind not to produce nausea but to bring the action almost to that point. Codeine gr. $\frac{1}{67}$ will relieve the irritation and overcome the tendency to cough. Owing to the absence of leucocytosis, nuclein is indicated from the beginning, the dosage being 10 drops or more per day, divided. Where there are pulmonary complications veratrine is especially valuable. To bring forth a tardy eruption a cold pack and powerful stimulation of the vitality is necessary. In this connection a combination of glonoin, atropine, and strychnine valerianate, each gr. $\frac{1}{250}$, and capsicin gr. $\frac{1}{67}$ every ten minutes will be followed by prompt reaction. This treatment is also useful in hæmorrhagic cases where the vitality is low. As in all infectious cases, calcium chloride is indicated, and should be given until its action is apparent by the sulphurous odours emanating from the mucosa, skin, and secretions. The action of the calcium chloride is to overcome infection, and it does so if pushed to its full effect. Complications should be met and treated symptomatically as they occur.

This is certainly a much more energetic line of treatment than is usually carried out in measles, but when one remembers how very fatal the disease is in young children, and what a terrible malady malignant measles is, such indications as are here given may be considered of value, based as they appear to be on sound scientific principles.

Milk. One cannot devote so much space to this subject as in the First Review, and hence papers with a distinct bearing on tropical life and tropical conditions as affecting milk will chiefly be considered. Even so a considerable number fall to be reviewed. A vast deal of information as regards milk in its relation to the public health will be found in the record of work carried out by Rosenau and his collaborators.[2] One cannot do more than outline some of the principal sections. Milk as a cause of epidemics is fully considered ; enteric fever, scarlet fever, diphtheria, sore throat, and Malta fever in their relation to infected milk all being passed in review. Milk and tuberculosis are discussed, and then the condition known as milk sickness, which is of importance in certain parts of the United States. There seems little doubt that the disease is acquired by the ingestion of milk, butter, cheese, or flesh from an animal suffering from trembles.

The relation of cow's milk to the zoo-parasitic diseases of man is discussed, but the rôle which milk plays in this connection is not an important one. It is a question of possibilities, and these should be entirely obviated by cleanliness, honesty, and propriety. Chapters follow on the morbidity and mortality statistics as influenced by milk, on ice cream, the chemistry of milk, its bacteriology and germicidal properties, the question of its leucocyte and streptococcic content, the conditions and diseases of the cow injuriously affecting the milk. General papers on sanitary inspection, milk depôts, dairies, markets, pasteurisation, and infant feeding conclude a compilation of the greatest value, and one which should be in the hands of every medical officer of health.

Rosenau [3] has also a bacteriological paper on the thermal death-points of pathogenic micro-organisms in milk. He points out that the tests applied were severe, as the milk used was very heavily infected with virulent cultures, and was in a condition to which natural milk practically never attains. As regards tubercle bacilli he says that if 60° C. for twenty minutes is sufficient to destroy the infectiousness of a milk containing them, when such milk is injected into the peritoneal cavity of a guinea-pig, it is justifiable to assume that after this treatment the milk would be safe for human consumption. His remaining conclusions are as follows :—

> The evidence is plain that milk heated at 60° C., and maintained at that temperature for two minutes, will kill the typhoid bacillus. The great majority of these organisms are killed by the time the temperature reaches 59° C., and few survive to 60° C.

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[1] Servoss, G. L. (April, 1910), "Measles." *Pediatrics*, New York. Quoted in Epitome, *British Medical Journal*, August 6, 1910.

[2] Rosenau, M. J., and Others (1908), "Milk and its Relation to the Public Health." *Bulletin No.* 41, *Hygienic Laboratory, Public Health and Marine Hospital Service of the United States.*

[3] Rosenau, M. J. (1908), "The Thermal Death-points of Pathogenic Micro-organisms in Milk." *Bulletin No.* 42. *Ibid.*

Milk—*continued*

The diphtheria bacillus succumbs at comparatively low temperatures. Oftentimes it fails to grow after heating to 55° C. Some occasionally survive until the milk reaches 60° C.

The cholera vibrio is similar to the diphtheria bacillus so far as its thermal death-point is concerned. It is usually destroyed when the milk reaches 55° C.; only once did it survive to 60° C. under the conditions of the experiments.

The dysentery bacillus is somewhat more resistant to heat than the typhoid bacillus. It sometimes withstands heating at 60° C. for five minutes. All are killed at 60° C. for ten minutes. However, the great majority of these micro-organisms are killed by the time the milk reaches 60° C.

So far as can be judged from the meagre evidence at hand, 60° C. for twenty minutes is more than sufficient to destroy the infective principle of Malta fever in milk. The *M. melitensis* is not destroyed at 55° C. for a short time; the great majority of these organisms die at 58° C., and at 60° C. all are killed.

Milk heated to 60° C. and maintained at that temperature for twenty minutes may, therefore, be considered safe so far as conveying infection with the micro-organisms tested is concerned.

Moulds are so common in hot, dry countries that a note by Bastian [1] drawing attention to their existence in milk is of interest. He finds that lactic bacteria must make the milk acid before moulds appear, but in four or five days at a temperature of 70° F. to 65° F. torula-like bodies or conidia occur in such numbers that he is constrained to ask what their source may be and to point out that their presence is generally overlooked. This is true, but they have received some attention from Weigmann and Wolff [2] in connection with the flavour they may impart to butter. The most important has the characters of an *Oidium*. Others approach the genera *Mycoderma* and *Monilia*.

Condensed milks are naturally much used in tropical countries. Klein [3] has worked at the bacterial content of the sweetened varieties. His results are interesting, and his conclusions are here given. He says :—

The mode of producing the sweetened condensed milk does not permit of sterilisation, such as is the case in the production of tinned meats or tinned fruits, and it is therefore obvious that no brand of sweetened condensed milk can be free of microbes. The presence of microbes *per se* in sweetened condensed milk does not in general make it unfit or unsound any more than in fresh milk; as a matter of fact, fresh milk perfectly wholesome and sold by the best dairies will be found to contain large numbers of microbes, ærobic and anærobic, often amounting to many thousands or even hundreds of thousands per cubic centimetre, and it is one of the most difficult problems to determine what should be a permissible number—that is to say, at what number of microbes should the line be drawn between sound and unsound milk. Quite recently the *U.S.A. Bureau of Animal Industry, Bull.* 104, published the results of the findings of a considerable number of "Medical Milk Commissions," in which the somewhat arbitrary line is drawn at from 10,000 to 30,000 microbes per 1 c.c. I do not think that a satisfactory line can be drawn as regards the number of general microbes. I have examined milk which was perfectly wholesome and sound, although it contained over 100,000 microbes, including streptococci, per 1 c.c. The only safe bacteriological standard of soundness is that the milk must not contain specifically pathogenic microbes, that it is not obtained from diseased cows, and that it is produced, collected, transmitted, and stored under clean and sanitary conditions.

And the same would apply to sweetened condensed milks. As the analyses show, no brands, not even those brands that have the best reputation and have never been challenged, are free of ærobic or anærobic microbes, some samples containing them in considerable numbers.

Dold and Garratt [4] classify condensed milks, give an account of the preparation of some of the forms, and obtained bacteriologically results somewhat similar to those of Klein. Even in so-called sterilised milks certified absolutely free from bacteria, organisms were found. In a sample of "Ideal" there were 40 in 1 c.c. At the same time the number is much less than in market milks. *B. coli communis* and *B. enteritidis sporogenes* were absent in every case, but streptococci were sometimes found. Pathogenic organisms were absent, and bacteriologically they declare these condensed milks to be satisfactory considering the usual standard for ordinary market milk.

Still considering bacteriological papers, we give some of the points brought out by Anderson [5] on his investigations into bacteria in top and bottom milk with special reference to infant feeding. He finds that top milk (the cream layer) contains sometimes from 10 to 500 times as many bacteria per cubic centimetre as the mixed milk. This may explain why infants sometimes do not thrive on modified milk made from top milk. When milk is centrifugalised the great mass of bacteria go up with the cream; a lesser number is carried down in the sediment. The skim milk contains many times less numbers of bacteria per

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[1] Bastian, H. C. (October 31, 1908), "The Contamination of Milk." *Lancet.*

[2] Weigmann, H., and Wolff, A. (1909), "Über einige zum Rübengeschmack der Butter beitragende Mycelpilze." *Cent. f. Bakt.*, II. Orig., Vol. XXII., Nos. 24/25.

[3] Klein, E. (March, 1909), "The Bacterial Character of Sweetened Condensed Milk." *Public Health.*

[4] Dold, H., and Garratt, E. (May, 1910), "The Bacteriological and Chemical Examination of Certain Brands of Condensed Milk." *Journal Royal Institute of Public Health.*

[5] Anderson, J. F. (June 12, 1909), "The Relative Proportion of Bacteria in Top Milk (Cream Layer) and Bottom Milk (Skim Milk) and its Bearing on Infant Feeding." *Journal Infectious Diseases.*

Milk—*continued*

cubic centimetre than the cream or sediment layers. Centrifugally-raised cream contains more bacteria per cubic centimetre than the gravity-raised cream from the same milk.

The distribution of bacteria in bottled milk has formed the subject of work by Torrey and Rabe,[1] who find—

(1) The upper 2 ounces of the cream of fresh bottled milk of fair quality contain on the average 50 to 100 per cent. more bacteria than an equal amount of the lower cream. In older and more grossly contaminated milk the lower cream may embody as many as or even more bacteria than the upper layers.

(2) By removing these 2 top ounces from a milk bottle and using the remaining top milk (8 ounces) for infant feeding, as Hess has suggested, there generally results a reduction of from 30 to 50 per cent. in the bacterial count.

(3) The dominant controlling factor in the primary disposition of bacteria in a milk bottle is the upward "rafting" activity of the fat globules. A higher percentage of bacteria are brought to the surface layers in a milk rich in cream than one poor in that substance.

(4) At ice-box temperature the rate of increase of bacteria in the cream and that in the skim milk are practically identical. As the temperature is elevated the rate of multiplication in the skim milk outstrips that of the cream, until at 30° C. it may be many times as rapid.

(5) In certain samples of rather highly contaminated milk the abrupt change in the temperature of the environment from 5° C. to 30° C. caused a striking bacteriolysis in both the cream and the skim milk. This was probably an expression of bacterial antagonism.

(6) The sediment portion of the average bottle of fresh milk contains frequently fewer bacteria than any other region of the fluid. A marked excess of bacteria in the sediment indicates that the milk is old or that it has been kept in a warm place.

Hess,[2] whom they mention, has also worked at the subject, and considers it also from the point of view of infant feeding. He finds that—

In bottled milk the bacteria are by far the most numerous in the upper layers of the cream, becoming gradually fewer in its lower portion.

The upper 2 ounces contain the greatest number of bacteria.

This is true of tubercle bacilli as well as of streptococci and other bacteria.

Therefore, instead of using the upper cream, as is now practised, it is preferable to discard the upper 2 ounces.

The average bottle of such *partially skimmed milk* contains 3 per cent. fat and 3·5 per cent. proteid, and is well adapted for infant feeding.

If we discard the upper 2 ounces we have: next 7 ounces, a 12 per cent. milk; next 8 ounces, a 10 per cent. milk; next 12 ounces, a 7 per cent. milk. With these figures as a basis the usual top-milk formulæ may be prepared.

Chatterjee[3] has a most interesting paper on fermented, soured or curdled milk. It is, he says:—

to the Eastern tropical countries that we must look for the special form of fermented milk in which the milk is curdled by means of a special ferment which is kept in stock in every household and is handed down from generation to generation, the milk being taken in the shape of curd. These ferments are much more active and give a much more solid curd of agreeable aroma than in the case of the fermented milk in use in Europe and America. The extensive use of one or other varieties of fermented milk produced by means of a special ferment in Eastern countries probably owes its origin to the difficulty of preserving milk in a sweet condition for a long time, in comparison to cold countries. Milk when undergoing spontaneous decomposition in hot climates becomes changed within a few hours to a foul-smelling fluid in which the caseine and the fat have undergone liquefaction, whereas when fermented by means of the special ferment, the decomposing, gas-producing proteolytic bacilli are killed off by the more vigorous organism of the ferment, which has no destructive action on the fatty or albuminous constituents of milk, so that by this means milk can be kept in a condition fit for consumption for a long time. In this way the economic problem of preservation of milk is solved. The following are some of the known varieties of curdled milk in use in Eastern countries, some of which have been made the subject of bacteriological study:—

Mazun of Armenia, Kephyr and Koumiss of Russia, the Leben of Egypt, the Oxygala and Chiston of Rome and Greece, and the Rayet of Algeria.

As regards the Egyptian variety he states that it has been fully studied by Rest and Khoury, who found in it—

(1) A big bacillus with square ends called the *Streptobacillus lebenis.*

(2) A fine bacillus with rounded ends called the *Bacillus lebenis.*

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[1] Torrey, J. C., and Rabe, A. H. (May 20, 1910), "The Distribution of Bacteria in Bottled Milk and Certain Controlling Factors." *Journal Infectious Diseases.*

[2] Hess, A. F. (1908–9), "The Distribution of Bacteria in Bottled Milk and its Application to Infant Feeding." *Collected Studies, Research Laboratory, Department of Health, City of New York.*

[3] Chatterjee, G. C. (1910), "A new lactic acid producing Streptothrix, found in the fermented milk of India, called the Dadhi." *Cent. f. Bakt.*, I. Orig., Vol. LIII., No. 2.

Milk—*continued*

(3) Diplococcus, called the *Diplococcus lebenis.*

(4) An oval-shaped yeast called the *Saccharomyces lebenis.*

(5) A long fungus called the *Mycoderma lebenis.*

Of these the most important are the *Streptobacillus lebenis.* The *Bacillus lebenis,* the *Saccharomyces* and the *Blastomyces lebenis,* being separately inoculated into milk, do not clot it. The *Diplococcus lebenis,* however, rapidly coagulates milk.

The *Streptococcus lebenis* is described, and some of its cultural characteristics given. In India there are two varieties of curdled milk named respectively Dadhi and Khilat. His paper concerns the former, and he states regarding it that—

(1) The fermented milk of India called the Dadhi resembles in all essential points the Bulgarian fermented milk as well as the Leben and other forms of fermented milk in use in the East.

(2) The causative element of the curdling process of Dadhi is a *Streptothrix* having characters similar to *Bacillus bulgaricus, Streptobacillus lebenis, Bacillus caucasicus* and the long bacillus of Mazun in (1) not growing in ordinary media, (2) producing a large amount of lactic acid in milk, (3) producing besides coagulation of caseine and splitting sugar of milk into lactic acid, no other change in milk, (4) not producing any indol, nor peptone, saponification of fat, nor formation of any gas.

(3) It differs from the above by showing peculiar pink-stained granules, when stained with methylene blue, and showing peculiarly convoluted chains in glucose agar.

(4) The importance of the organism lies in the fact, as in the case of *Bacillus bulgaricus,* that it kills all pathogenic non-sporing germs and also destroys all proteolytic gas-forming bacilli in milk.

Millard [1] gives an account of the preparation of dried milk which he has used largely at an Infant's Milk Depôt, and with the value of which as a food for infants he has become impressed. He summarises its advantages as follows :—

(1) *Ease of Digestion.*—Milk not " sicked up," as is so often the case with fresh milk, however modified.

(2) *Bacterial Purity.*—Freedom from tubercle bacilli or contamination of flies.

(3) *Conservability.*—No " souring " in hot weather.

(4) *Cheapness.*—No waste.

(5) *Convenience.*—Always ready for use.

(6) *Palatableness.*—Babies love it.

Its disadvantages are of a theoretical nature, and consist in the presumed destruction of the antiscorbutic properties of fresh milk. This, however, can be compensated, if thought necessary, by administration of fruit juice. For domestic purposes apart from infant feeding, dried milk has distinct limitations as a substitute for fresh milk, as, owing to its taste, it is not so suitable for adding to tea or coffee.

At a later period there was an interesting discussion on this subject, the points raised being whether the long-continued use of dried milk might not lead to rickets, and whether such milk was free of all danger from tubercle bacilli. On neither point could an absolute opinion be given, but there seemed to be a general consensus of opinion that dried milk was a valuable product and filled a want. This subject leads us to consider a paper by Lane-Claypon [2] on the influence of heating upon the nutrient value of milk as an exclusive diet for young animals. She states that in Paris, where several thousand babies are fed every year on milk that has been boiled for twenty minutes, rickets is rare, and scurvy almost unknown, and quotes Budin and other authorities to show that when the milk of another species is used there is no marked nutritional difference between raw, boiled or even sterilised milk. Her own experiments on rats confirmed this view. A paper on the administrative aspects of providing good dairy produce in India is to be found in the *Lancet* of September 17, 1910, but the resolutions there detailed go but a little way in solving a difficult problem, and one which is of special interest in the Sudan, as reference to the Third and Fourth Reports of these Laboratories will show.

Blackham [3] deals with the analyses of milk samples in India. These were derived both from the cow and the buffalo. The amount of added water found in milk in various parts of India ranges from 20 to 60 per cent. In Bengal it is the recognised custom to dilute all milk with one-fourth of its bulk of water. The various analyses are detailed, and the author thinks that the results of his investigations appear to establish the following facts :—

(1) The cows' milk supplied to the soldier by Government dairies in India is much above the standard laid down by the Sale of Food and Drugs Regulations of 1901.

(2) It will, moreover, compare favourably with the results obtained in English dairies.

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[1] Millard, C. K. (January 29, 1910), " Dried Milk as a Food for Infants." *British Medical Journal.* See also *Public Health,* June, 1910.

[2] Lane-Claypon, J. E. (September, 1909), " Observations on the Influence of Heating upon the Nutrient Value of Milk as an Exclusive Diet for Young Animals." *Journal of Hygiene.*

[3] Blackham, B. J. (February, 1911), " Milk in India." *Journal Royal Army Medical Corps.*

Milk—*continued*

(3) Buffalo milk obtained from Government dairies in India is, however, in its percentage of fat, much below the standards laid down by all the authorities consulted, with the exception of Richmond and Pappal, and at Peshawar the percentage of total solids has also been uniformly much below the amounts given in all but one of the analyses usually accepted as guides.

(4) The results of analyses of buffaloes' milk in various parts in India, as shown in Tables III. and IV., indicate that the amount of butter fat in buffalo milk is most in warm and moist climates such as Bengal, and least in hot or cold and dry climates such as Peshawar.

(5) The results obtained appear to indicate that no general standard can be fixed for the whole of India, and that the percentage of fat in buffalo milk given by most of the authorities hitherto accepted as standards requires reconsideration.

Snell [1] is the latest advocate of goat's milk in infant feeding, but says :—

It must be borne in mind, however, that with goat's milk the cream is in much finer globules and does not so easily separate out as does the cream of cow's milk, hence testing with a creamometer does not give correct results. The amount of fat must be determined by a proper butyrometer, and no doubt this apparent absence of cream has given rise to the opinion prevalent in some parts that goat's milk is "poor." There is no doubt that as an alternative to cow's milk where the latter disagrees or the child is not thriving, goat's milk is greatly neglected by the medical profession of this country.

A paper of great value, and one which advances a new and interesting hypothesis, is that by Savage [2] on the diseases of the cow (excluding tuberculosis) affecting the milk in their relationship to human disease. He divides abnormal cow conditions into three groups :—

(1) General systemic disease of the cow without local lesions of the milk organs.

(2) General systemic disease of the cow with local lesions in or on the udder and teats.

(3) Local affections, with little or no general systemic disturbance.

In the first group he mentions anthrax, Gaertner infections, gastro-enteritis, septic conditions and Malta fever to which cows are susceptible, but with the exception of anthrax (Chicago outbreak) records of outbreaks of human disease from these causes are either rare or absent. In the second group come foot-and-mouth disease and cow-pox. The former can be transmitted to man, the latter may be, but there is no definite evidence to that effect. In Group III. come mastitis and ulcerated teats. As regards the first, Savage shows that the great majority of cases of bovine mastitis are due to an organism, *Streptococcus mastitis*, which is not harmful to man. Rarely, however, mastitis would appear to be due to organisms highly pathogenic to man and producing sore throat and other septic outbreaks. The question of ulcerated teats and their relationship to human disease is well considered. Any pathological effect may be exerted in three possible ways :—

(*a*) The ulceration may be part of a general disease of the cow, and through the teat ulcerations the milk may become infected. This has been shown to be a cause of human disease in foot-and-mouth disease, and bovine scarlet fever has been advocated as another example.

(*b*) The teat and udder conditions may be purely local, but due to streptococci or other organisms pathogenic to man.

(*c*) The teat condition may be due to purely bovine disease or be traumatic in origin, but become secondarily infected by organisms pathogenic to man.

In other words, we may theoretically have a constitutionally infective cow, a local actively infective cow, and a local passively infective cow.

Savage cites one outbreak of sore throat due to this condition which seems to be associated with the presence of long-chain streptococci. He also notes that such sores may become infected with the diphtheria bacillus from human cases, and thus in an indirect manner spread diphtheria. It is in connection with bovine scarlet fever that his new hypothesis is advanced. He does not regard the existence of this disease as proven, but he does believe that one may have a passively infected cow or cows ; in other words—

(*a*) That the cow may be a source of human disease not because it is constitutionally infective, but because it is acting as a carrier of human infective organisms.

(*b*) That disease of the milk-producing organs of cows is only likely to be harmful to man when the causally associated organisms are of human origin or when human organisms are superadded as a secondary infection.

Of course, tuberculosis is not included in this hypothesis. The first conclusion is more capable of proof than the second, and may be accepted without the second being admitted.

He goes on to advance very cogent proofs in support of his theory, but into these and the discussion we cannot enter here, only advising a careful perusal of this most suggestive and useful paper.

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[1] Snell, S. H. (April 1, 1911), "Goat's Milk for Infants." *British Medical Journal.*

[2] Savage, W. G. (1911), "Diseases of the Cow (excluding Tuberculosis) affecting the Milk in their Relationship to Human Disease." *Proceedings Royal Society of Medicine*, Vol. IV., No. 5.

Horrocks [1] has an article, which must be consulted for details, on the use of lacto-sera as a means of distinguishing goat's milk from cow's milk. In the *Journal of the Royal Institute of Public Health* for September, 1909, will be found notices of three papers dealing respectively with the chemical analysis of stale milk, a new test for watered milk, and the sterilisation of milk by ultra-violet rays. This has been successfully accomplished, the difficulty due to the opacity of milk being overcome by causing the milk to flow in a thin film over the illuminated surface. Milk—*continued*

A good practical paper, with illustrations of milk utensils, milk bottles, and sterilising apparatus is given by Pape,[2] Superintendent of Dairying to the Agricultural Department of the Transvaal Government. There is nothing new about it, but the reference may be found useful by medical officers of health. Many of the excellent publications of the United States Department of Agriculture deal with various aspects of the milk question. Circular 153 of the *Bureau of Animal Industry* is worthy of study, and deals fully with pasteurisation. As Rosenau says, "theoretically it should not be necessary; practically we find it forced upon us. The heating of milk has certain disadvantages which must be given consideration, but it effectually prevents much disease and death, especially in infants during the summer months." This, be it noted, however, applies with most force to countries where bovine tuberculosis exists, while it must never be forgotten that owing to careless or faulty storage, etc., the pasteurisation may be rendered of no avail.

Webster [3] is the author of an admirable circular on the production of sanitary milk. It deals largely with the question of contamination, especially in cow sheds, and gives the types of inspection cards which have been introduced. The following are "the features of inspection":—

The routine of inspection should include—

(1) Health of attendants,

(2) Health of the herd,

(3) Purity of the water-supply,

(4) Methods of the dairyman,

(5) Facilities for producing pure milk, and

(6) Handling and transportation from farm to city.

Another paper of the same type which also gives an example of a "Dairy Score Card" is that by Heinemann, Luckhardt, and Hicks.[4] Some of their work was of a bacteriological nature, and their conclusions may be quoted:—

(1) Separator cream contains a smaller number of bacteria per cubic centimetre than the whole milk from which it is obtained. Separator milk contains more bacteria than the whole milk from which it is obtained.

(2) The bacterial count in milk obtained by mixing the cream and skim milk from the separator is higher than that of the original milk.

(3) Straining milk, during the process of milking, through a brass sieve removes some of the bacteria, and also removes coarse particles of dirt, which otherwise would increase the number of bacteria.

(4) Straining through absorbent cotton before bottling results in a higher bacterial count for the strained milk.

(5) Polymorphonuclear leucocytes of the neutrophile type, large mononuclear leucocytes, and small lymphocytes appear normally in the separator slime of the milk of healthy cows, and as far as we can see they bear no relation to the number of micro-organisms present, inclusive of streptococci.

(6) Eosinophiles may occur in the slime of the separator. The cause and significance of their presence remain problematical.

(7) The white corpuscles in milk of normal and diseased cows and in the blood of the same animals should be studied, differentiated, and classified. Such a study will put the subject of leucocytes in milk on a more exact scientific basis than heretofore, and further our knowledge of the significance of the relative number of the various corpuscles in milk in normal and diseased conditions of the cow in general, and in pathological processes of the mammary glands and the udder in particular.

Another useful paper on milk is that in the valuable New South Wales *Report of*

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[1] Horrocks, W. H. (November, 1908), "On the Use of Lacto-Sera as a Means of Distinguishing Goat's Milk from Cow's Milk." *Journal Royal Army Medical Corps.*

[2] Pape, R. (January, 1909), "Milk for Consumption." *Transvaal Agricultural Journal.*

[3] Webster, E. H. (1909), "Some Important Factors in the Production of Sanitary Milk." Circular 142, *Bureau of Animal Industry, United States Department of Agriculture.*

[4] Heinemann, P. G., Luckhardt, A. B., and Hicks, A. C. (January 15, 1910), "On the Production of Sanitary Milk." *Journal Infectious Diseases.*

Milk—*continued*

the Government Bureau of Microbiology for 1909. Amongst other things it deals with "Manipulated Milk," and gives the following table of the processes to which milk is now subjected :—

A. Mechanical processes—
  (*a*) Centrifugalisation.
  (*b*) Filtering.

B. The application of heat—
  (*c*) Sterilisation.
  (*d*) Boiling.
  (*e*) Pasteurisation
  (*f*) Concentration.
    Desiccation.
  (*g*) Thermophore treatment.

C. The application of cold—
  (*h*) Freezing.
  (*i*) Chilling.
  (*j*) Cooling.

D. The addition of antiseptics—
  (*k*) Carbonate of soda.
  (*l*) Boric acid, borax, or mixtures.
  (*m*) Formalin.
  (*n*) Salicylic acid.
  (*o*) Peroxide of hydrogen.

E. The inducement of alcoholic fermentation—
  (*p*) Koumiss.
  (*q*) Kephir, etc.

It takes up each of these in detail and furnishes a mass of useful information concerning them. Here one would only note that the thermophore, the value of which yet remains to be proved, is an apparatus designed to prevent the growth of bacteria in milk by keeping this fluid continuously warm. It acts, indeed, on the principle of a "Thermos" flask, and it is said to prevent multiplication of bacteria and possibly even to reduce them, the temperature maintained being 40° C. to 55° C. Altogether this is an excellent paper which is apt to be missed, and which we feel we do well to recommend strongly to all interested in the great milk question.

We conclude with a reference to *Bulletin No.* 326 of the *New York Agricultural Experiment Station*, dated December, 1910, which discusses with numerous illustrations different types of milking-pails designed to exclude dust and dirt. The form most highly commended has been fashioned, and is to be tried in Khartoum, for a pail of this kind should have a future before it in a country where, during the summer at least, dust devils and sand storms are of frequent occurrence, and where it is customary to find a heavy deposit at the foot of every cupful of milk, boiled or unboiled, during the hot season of the year. As a rule in the Sudan servants boil all milk to prevent it going bad, and this is probably a custom common throughout the Tropics. Hence the new test of Rochaix and Thevenon [1] for the purpose of ascertaining whether milk has been subjected to a minimum temperature of 85° C. may be mentioned.

It is based on the action of pyramidon in presence of oxidising agents, shown by a violet colour. The test solutions required are the following : (1) a 1 per cent. solution of pyramidon in distilled water, (2) peroxide of hydrogen, 12 vols., (3) a 20 per cent. solution of sulphate of manganese or chloride of calcium, and (4) a 20 per cent. solution of acetic acid.

The test is made with the milk serum. To 20 c.c. of the milk add a few drops of acetic acid, shake so as to separate the coagulated albuminoids, allow the latter to settle, and then decant the supernatant fluid on to a filter. To 2 c.c. of the clear fluid add four or five drops of peroxide of hydrogen, then 2 or 3 c.c. of the pyramidon solution. Shake well and heat gently to 60° C. If it be raw milk the solution at once turns violet, the colour disappearing after attaining its maximum. Boiled milk does not give this reaction.

Mosquitoes. The new books dealing with malaria and mentioned in the section dealing with that subject enter fully into the question of mosquitoes, more especially, of course, those of the family *Anophelina*. Hence we may somewhat curtail our references to those papers which consider this important group of insects. It seems advisable to begin with their

[1] Rochaix and Thevenon. Quoted in *Journal Practical Dietetics and Bacterio-Therapeutics*, January, 1910

Mosquitoes —*continued*

general biology. Banks [1] finds that *Myzomyia ludlowii*, Theob., a species of anopheline which probably transmits the æstivo-autumnal parasite, breeds in the Philippines, both in salt and in fresh water, while altitude (up to 1500 metres) has no appreciable influence upon its development. He thinks that it was originally a fresh-water species only, and has adapted itself to a marine life. *Nyssorhynchus stephensi*, an Indian species and a malaria carrier, has also been found breeding in salt water. Gholap [2] discovered its larvæ in ponds containing sea water at Colaba near Bombay. There were millions of the larvæ present in these water collections. In the light of these observations it is interesting to note that Graham [3] recommends the salting of water containing the larvæ of *Pyretophorus costalis*. He adds common salt in the proportion of 3 per cent., and finds that it causes disintegration and precipitation of the motile algæ upon which the larvæ feed. The latter, being thus deprived of their natural food, become cannibalistic. Salt, he says, in lesser concentration appears to inhibit the growth of young larvæ, probably by diminishing their food supply, but seems to hasten the fully-grown larvæ, which become pupæ more rapidly than usual. In the Sudan *P. costalis* breeds freely in brackish waters, in pools formed by water which has washed the salt out of the banks of irrigation channels, and this is in line with what Willcocks [4] records as occurring in Egypt, for there the larvæ of a species of *Pyretophorus* (*P. cleopatræ*) have been found flourishing in large numbers in brackish waters containing from 2·56 to 3·25 per cent. of common salt. Even 1 per cent. proves fatal to the larvæ of the common Egyptian anopheline, *Cellia pharœnsis*.

Darling,[5] working with the mosquitoes of the Canal Zone, observed the effect of salt and sea water on anopheline larvæ, and says :—

> In general, the effect of an irritating, toxic, or otherwise unusual fluid on mosquito larvæ is to hasten pupation. A number of experiments were tried with sea water, salt water, and solutions of the heavy metals, and in most instances, in the more concentrated solutions, when the larvæ were not killed within twenty-four hours they pupated, and occasionally the period of pupation was shortened ; so that if, for instance, in a district sea water were used as a larvicide, the first effect would be to hasten pupation, and thus increase the number of anophelines in the district, and if later the sea water became diluted by rain several species of malaria-transmitting anophelines might breed in it without difficulty ; notably, *A. albimanus* and *A. tarsimaculata*. On this account, sea water could not be used with any degree of success as a larvicide for anophelines, except in large quantities and in certain locations.

A point of interest is that Ficalbi has calculated that from a mother stem 200,000,000 mosquitoes may be produced in four months.

Darling (*loc. cit.*) has many interesting notes in his useful paper. As regards the incubation of certain of the local species of anophelines he says that sunlight and the abundance of algæ undoubtedly play a great part in the duration of the period of incubation. He has found that the characteristic musical note of anophelines is caused by the vibration of the proboscis, as the following observation indicates :—

> A specimen of *A. malefactor* was badly wet and sprawled ; upon placing her upon a piece of filter paper and touching or approaching her proboscis the latter vibrated visibly, and emitted the characteristic high-pitched note ; the wings were at rest, being stuck to the paper. This was verified again and again. Later I picked up a slightly water-sprawled infected mosquito for dissection and held it over a few drops of chloroform ; both wings were seen to vibrate rapidly, as in flight, but noiselessly ; while holding the mosquito by the last abdominal segment, and touching one wing at its tip the opposite wing would immediately stop vibrating. Upon releasing the wing, both would vibrate noiselessly, as before. The noise of the mosquito is due, then, to the vibration of its proboscis, and the wing vibration is independently and automatically co-ordinated.

He has also notes on the food of anopheline larvæ and on the question of parthenogenesis in mosquitoes.

Legendre [6] furnishes information on the biology of *Stegomyia fasciata* and of *Culex pipiens*. He experimented with the larvæ in the water of the laboratory, in distilled water, and in a water to which sulphate of lime was added in varying proportions. The last, especially the strongest

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[1] Banks, C. S. (September, 1908), "A Mosquito which Breeds in Salt and Fresh Water." *Philippine Journal of Science*, B.

[2] Gholap, R. D. (June, 1910). (?) *Indian Medical Journal.*

[3] Graham, W. M. (April, 1910), "The Study of Mosquito Larvæ." *Bulletin of Entomological Research.*

[4] Willcocks, F. C. (March 21, 1910), "A Preliminary Note on the Prevalence of Mosquitoes in Cairo and its Environs." *Annals of Tropical Medicine and Parasitology*, Vol. III.

[5] Darling, S. T. (1910), "Studies in Relation to Malaria." *Isthmian Canal Commission, Laboratory Board of Health, Department of Sanitation.*

[6] Legendre, J. (July 21, 1909), "Note sur la biologie de *Stegomyia fasciata* et de *Culex pipiens*." *Bull. Soc. Path. Exot.*

Mosquitoes —*continued*

solution (1 gramme to 1 litre), proved the most favourable to development, 12 days being the minimum time, and 22 the maximum, from egg to imago. In distilled water 17 and 33 were the respective figures. The larvæ were found to be very resistant to unfavourable conditions, *i.e.* lack of food. Owing to the fact that spermatozoa persist in the spermathecæ of the female imago, a single fecundation suffices to ensure fertility not only as regards the first egg batch, but as regards several subsequent layings. Ross [1] has something to say on biology, especially as regards its effect on migration. He thinks that the reason why mosquitoes do not fly far from their breeding-places depends on certain biological factors. He holds that only fecundated females feed on blood, and that the hæmatophagus habit depends upon the presence of spermatozoa in the body of the female. In the species with which he experimented he found that eight or nine males to one female hatched out from collected nymphs. Even so, many females escape fecundation. His next observation differs from that of Legendre (*loc. cit.*), for he says :—

> Male mosquitoes do not live for more than a few days. They rarely fly far from the breeding-place where they passed their metamorphoses. As they never suck blood, they prefer to remain near the cesspool or collection of water where they were born, fertilising the females of their own or preceding generations, their testes producing enormous numbers of spermatozoa in the short period of their existence. It would, therefore, be expected that the females, after the successive feeds of blood they require to mature the eggs within them, will return to lay their eggs on the water they themselves were born from, because they know that the water will be suitable for their larvæ when born, and that they will then be able to find males of their own species, but of a later generation, to replenish their spermathecæ, which were exhausted when the eggs were laid.
>
> This theory is supported by the observation that the three spermathecæ of the female culex seem only capable of containing about 400 spermatozoa, which is just sufficient to fertilise all the eggs in one brood, and also by the observation that all females having blood in their stomachs have invariably their spermathecæ full of spermatozoa —never partially filled. The spermathecæ have hard chitinous walls and are inelastic.

Of course the divergent views may be due to different species studied.

He states there is no proof of parthenogenesis, and if food be plentiful sees no reason why mosquitoes should fly far from their breeding-places, but continues :—

> Should a female mosquito, after several meals of blood and with her uterus full of matured ova, return to the water-collection where she herself passed her metamorphosis in order to lay her eggs and then to replenish her spermathecæ from a male of a succeeding generation, and find the water there dried up or covered with a layer of petroleum, she will leave that place in search of another more suitable in which her larvæ, when hatched out, will thrive. Then she will naturally go to that water-collection where there are already some hatched-out males, and thus one sometimes sees two cesspools containing the same type of sewage, adjoining each other and similar in all respects, one containing mosquitoes and the other free from them.

Darling, in a letter to the *Journal of Tropical Medicine and Hygiene* for January 1, 1910, commenting on the above paper, says :—

> Dr. Ross stated that only fecundated females feed on blood. "The desire to suck blood is dependent upon the presence in the spermathecæ of the female of the spermatozoa of the male." This is not true of the mosquitoes, with which I worked, which were *A. albimanus*, *A. pseudopunctipennis*, and *Stegomyia calopus*. My observations were based on virgins bred out from isolated individual pupæ in separate breeding-out tubes. The single virgins after emerging were inspected for the identification of variety and sex, and were then segregated in biting jars made of lantern chimneys, covered on one end with crinoline gauze for ventilation, and the other end placed on a petrie dish containing water and raisins. In every case the females, after twenty-four hours, or more, would bite and suck blood as greedily as fecundate ones usually do. Specimens of *A. pseudopunctipennis* did not bite with alacrity; but this mosquito, I have found, does not visit quarters to the same extent that *A. albimanus* does, and in my infecting experiments only 12 per cent. of *A. pseudopunctipennis* became infected after biting favourable cases of malarial fever, while 60 per cent. of *A. albimanus* became infected. This might be interpreted as meaning that blood-sucking is not a confirmed habit with *A. pseudopunctipennis*.
>
> Virgin specimens of *S. calopus* bred out and segregated in the same way bit and drew blood in every case. From one jar containing nineteen mosquitoes, sixteen drew blood on the first application, and three the next morning. These mosquitoes would bite on successive or alternate days although at the time of their biting their abdomens were already partly distended by food. A number of these mosquitoes were kept for two weeks and over. One jar was kept for seventeen days, and upon killing and examining the mosquitoes there were no males among them, and none had spermatozoa in their spermathecæ. None of the specimens of *A. pseudopunctipennis* showed any development of their ova. One *A. albimanus* contained well-developed ova, 48 mm. in length, almost full size. Two *Stegomyia* contained fully developed ova, 56 mm. in length. As these females had not oviposited, I am inclined to doubt whether their ova would have been fertile.
>
> Dr. Ross made the statement that males do not live for more than a few days. This was also my former opinion, but in my later experiments, after discontinuing the use of bananas as food, males have lived for fifteen to nineteen days, frequently outliving females when both were subjected to a raisin or date diet, the females not being permitted a blood feeding. When the male has suitable food he appears to live in captivity fully as long as females do. This is based on observations with *A. pseudopunctipennis*, *A. albimanus*, *Culex cubens*, and *S. calopus*.

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[1] Ross, E. H. (September 1, 1909), "The Influence of Certain Biological Factors on the Question of the migration of Mosquitoes." *Journal Tropical Medicine and Hygiene.*

Mosquitoes —*continued*

Boyce and Lewis [1] consider the effect of mosquito larvæ on drinking-water, and come to the conclusion that they add considerably to the number of bacteria present, and are to be regarded as a source of pollution. The statement, however, that "if larvæ lead to the increase of saprophytic bacteria, it is reasonable to suppose that they will not diminish pathogenic forms," is one with which *à priori* one would not be inclined to agree. Those who study African mosquitoes will find Wesché's [2] able paper on the larvæ and pupæ of West African *Culicidæ* of great value. It is not easy to review in a short space, but the following list of subjects considered will give an idea of its scope :—

(1) Technique, including measurements and the examination of living larvæ.

(2) Characters of the larvæ and pupæ.

(3) Keys to the species described, larvæ and pupæ.

(4) Separate description of each species.

(5) Plates and explanation.

The seven plates are most useful. As regards the subject-matter, it is interesting to find that so many types and sub-types of the larvæ of *P. costalis* exist. He distinguishes the two main types of larvæ which have a length of 3 mm.

Type I. Head nearly as large as the small thorax.

Type II. Head of usual anopheline type, half the width of the thorax.

The larvæ, 4½ mm. and 6 mm. in length, are also quite distinct. One has noticed, without studying them closely, similar differences in *P. costalis* larvæ in the Sudan, and they are puzzling to those not acquainted with the alterations which take place during the various larval moults. The larva and pupa of *Cellia pharoensis*, *Myzorhynchus mauritanus*, and *Stegomyia fasciata* are, amongst others, fully described.

Howlett [3] considers the influence of temperature upon the biting habits of mosquitoes. His observations were made in India chiefly upon *Stegomyia scutellaris* and *Culex fatigans*. He points out the following attributes of a living warm-blooded host which may be supposed to advertise its presence to an insect such as a mosquito :—

(1) *Motion.*—Probably unimportant. Mosquitoes bite a motionless sleeper.

(2) *Form and Colour.*—They are very obviously attracted by black and dark colours (it is remarkable that tsetse flies are similarly attracted by black), but pay no regard to form as far as can be seen. The fact that black objects are good absorbers and good radiators of heat may be not without significance.

(3) *Smell.*—Blood and sweat without apparent influence.

(4) *Temperature* and air-currents due to the motion of air warmed by the body.

The author records some interesting experiments with mosquitoes enclosed in a loose gauze bag, and brought into close proximity to a test-tube half full of hot water, which stimulated them to great activity and induced them to try and puncture the glass in order to reach the source of heat. A cold tube had no effect, and Howlett concludes :—

(*a*) That the bite of a mosquito is a reaction to the stimulus provided by a hot surface (*b*) that the mosquito is attracted to the hot surface mainly by the warm air rising from it, and (*c*) that the strength of the reaction is, within certain limits, proportional to the "differential temperature" of the surface, *i. e.* the difference between its temperature and the general air-temperature at the time, and that this difference must be positive.

Knab [4] states that normally the eggs of *S. fasciata* (*calopus*) are deposited out of water, at the edge of the water film, and that here they remain until they are submerged, whereupon they hatch out. This is an important matter, and the observation requires to be confirmed. Eggs remaining out of water are said to retain their vitality for a long time. In the laboratory, eggs have been kept dry as long as five months, and then when submerged have produced larvæ. It is possible that under favourable natural conditions they might survive even longer. Galli-Valerio and de Jongh [5] have a paper on the bionomics of mosquitoes, but as it deals exclusively with European species it need merely be mentioned. Balfour,[6] from certain

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[1] Boyce, R., and Lewis, F. C. (March 21, 1910), "The Effect of Mosquito Larvæ upon Drinking-water." *Annals of Tropical Medicine and Parasitology*, Vol. III.

[2] Wesché, W. (April, 1910), "On the Larval and Pupal Stages of West African Culicidæ." *Bulletin of Entomological Research.*

[3] Howlett, F. M. (December, 1910), "The Influence of Temperature upon the Biting of Mosquitoes." *Parasitology.*

[4] Knab, F. (1910), "Mosquito Habits and Mosquito Control." *Science.*

[5] Galli-Valerio, B., and de Jongh, J. R. (March 22, 1911), "Beobachtungen über Culiciden." *Cent. f. Bakt.*, I. Orig., Vol. LVIII., No. 2.

[6] Balfour, A. (January 8, 1910), "Mosquitoes with Reference to Immigration and Horse-sickness." *Lancet.*

Mosquitoes —*continued*

facts observed at Khartoum, suggests (there is no experimental proof) that *S. fasciata* may be the vector of the virus of horse-sickness. Theiler, Pitchford and others have already indicated that a mosquito is in all probability the culprit. Useful notes on bionomics will be found in Hehir's [1] monograph already mentioned under the heading malaria. As regards food, he says :—

> The majority of mosquitoes never taste man's blood, and but comparatively few take vertebrate blood. Certain species are, however, natural blood-suckers, especially the Stegomyias, and certain species of Culex and Anophelinæ. Most mosquitoes feed on vegetable juices. They are very partial to bananas, and sliced banana is one of the best foods to keep them alive. Many mosquitoes take the blood of invertebrate animals, such as insects. They also feed on young fish.

Again, dealing with the length of life of the insects, he writes :—

> Formerly it was believed that mosquitoes lived only for five or six days. Now we know that they may live for months. *Stegomyia fasciata* can certainly live for five months. Anophelines have been kept alive in captivity for 155 days. There are many mosquitoes known to hibernate both as adults and as larvæ throughout the winter. We cannot at present say what the average length of the life of the mosquito in nature is. In captivity we remove them from the dangers of their natural enemies, birds, inclement weather, high winds, excessive rain, etc., although they must be affected by the artificial conditions of life in captivity.
>
> Anophelines can certainly remain alive in huts for one or two months and possibly longer. Subsequent to the drying up of all their breeding-places, it is found that the number of anophelines do not decrease to any material extent for several weeks, but if this drying up continues, their numbers gradually diminish ; species may, however, be caught in the neighbourhood for two months (or even more) afterwards.

Hehir does not neglect the subject of natural enemies, and as regards this point several recent papers may be mentioned. There are but few references to the occurrence of nematodes in mosquito larvæ, as Gendre [2] points out when describing how he found the larvæ of *Mermis* parasitic in the larvæ of *Stegomyia fasciata*. The observation was made in French Guinea, and the worms were found in the general body cavity of the larva, two being present in each, a large and a small form. He describes their appearance, and mentions that they do not appear in any way to harm or incommode the larvæ until the latter are on the point of turning into nymphs. Then the parasites liberate themselves by piercing and traversing the peri-anal membrane, and, probably as a result of the loss of body fluid, the mosquito larvæ perish. The freed mermis larvæ also die some hours after becoming free, and it would not seem that they could be put to any practical use in destroying *Stegomyia* larvæ on a large scale. An interesting discovery made by Gibson in Hong-Kong, and recorded with personal notes by Atkinson,[3] is that flies called *Lispa sinensis* (Schiner) belonging to the family *Anthomyidæ* prey greedily upon mosquito larvæ. The species of the latter devoured or carried away by the flies was not determined. The insect is illustrated and evidently deserves attention.

Nicholls [4] describes some of the natural enemies found in the West Indian island of Saint Lucia. One is a small undetermined Crustacean of the sub-order *Decapoda*. Six of these *Crustacea* were placed in a jar with several hundred mosquito larvæ ; the next day not a larva remained, so it would appear they are likely to be useful, especially as they can be employed in mountain pools which fish may not inhabit. In suitable places beetles and dragon-fly larvæ may be effective. In small pools in the beds of irrigation channels in the Sudan where these were plentiful I have failed to find larvæ, while they were numerous in leakage pools hard by. I believe, however, the absence of larvæ in the first situation was due to her instinct warning the female mosquito that the pools there were unlikely to be sufficiently permanent to permit of the complete water stage being accomplished. Neuroptera are also mentioned by Nicholls, but his most important notes refer to fish, more especially to *Girardinus pœciloides*, the " Millions " fish. He has bred them in barrels, has succeeded in adapting them for life in the water of rusty iron tanks, and in immunising them to darkness and to brackish water. As there has been difficulty in keeping and breeding an allied fish in the Sudan, the following quotation may be useful :—

> I have had great difficulty in getting fish to live and multiply in water at and above 100° Fahr. ; but I have now succeeded, and the difficulty, I believe, was entirely due to the dark incubator with which I was obliged to work, layers of fungi quickly appearing on the surface of the water, and their food material quickly decomposing. Continually changing the water and adding fresh food, and allowing the sunlight to play upon the water each day,

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[1] Hehir, P. (1910), *Prophylaxis of Malaria in India.* Allahabad.

[2] Gendre, E. (February 10, 1909), " Sur les Larves de *Mermis* Parasites des Larves du *Stegomyia fasciata.*" *Bull. Soc. Path. Exot.*

[3] Atkinson, J. M. (September 4, 1909), " A Possible Natural Enemy to the Mosquito." *Lancet.*

[4] Nicholls, L. (1910), *Annual Report,* Saint Lucia. Quoted in *Bulletin of Entomological Research,* October, 1910.

Mosquitoes —*continued*

has enabled me to get fish to flourish at these higher temperatures. I have had difficulties with the lower temperatures; but the experiments conclusively show that these fish can be gradually immunised to temperatures ranging from 101·5° Fahr. to 55° Fahr.; and there appears to me no reason why higher and lower temperatures should not be employed, if a considerable period of time is used to obtain the immunity.

He found that two or three fish soon clear a 10,000 gallon tank and keep it free from larvæ, and believes "Millions" could be conveyed to such a country as India, bred there, immunised, protected, distributed and made to serve a useful purpose. It has already been sent to West Africa and Mauritius. In the former locality the fish did not long survive. Information regarding success or otherwise in the latter is not forthcoming. India, of course, already possesses the "Chilwa," *Chula argentea*, which lives in tanks and feeds well both on larvæ and *imagines*. Balfour (*loc. cit.*) mentions the work carried out by King in the Sudan, where two species of fish have been specially tested, *Ophiocephalus obscurus* from the White Nile and *Cyprinodon dispar*, a fish of the "Millions" type, from Khor Arbat in the Red Sea Province. King[1] enters fully into the matter, but further experiments are required. A review of a lecture by Oswaldo Cruz on the subject of yellow fever prophylaxis will be found in *Public Health* for February, 1910. In Brazil another species of *Girardinus*, *i.e.* *G. caudimaculatus*, is used with success in the case of tanks and boxes containing water for household use. Locally it is known as the "barrigudo," and is very voracious. Before taking up more fully the subject of preventive measures, a few papers dealing with the relations of mosquitoes to disease and other points may be profitably considered. That of Willcocks (*loc. cit.*) on the mosquitoes found in Cairo and its neighbourhood is interesting. He throws doubt on *Cellia pharœnsis* being a malaria carrier. It is very common in certain parts where, however, malaria does not occur. For such cases as do occur, *P. cleopatræ* is probably to blame. He mentions a natural enemy not hitherto recorded, *i.e.* the "back swimmers," aquatic bugs belonging to the *Hemiptera*. He says :—

> These bugs appear to increase rapidly and to become quickly distributed in a district. The adults leave the water with ease and take flight, but if in the course of their flight they hit an obstacle and fall, they appear to have very great difficulty in again taking wing, or even to be unable to do so. They leave the water with the dorsal surface upwards, making a slight whirring noise.
>
> Another but rather rare member of the same family of water-bugs (*Notonectidæ*) has also been found to prey upon mosquito larvæ, and although these insects measure but 2 mm. in length they will attack and destroy almost full-grown mosquito larvæ.

I may mention that they have been tested in Khartoum, where they occur in river pools, etc. They certainly destroy mosquito larvæ, but in practice have proved a failure. They are curious and interesting insects, and were employed after one had heard of Mr. Willcocks's observations. Hehir (*loc. cit.*) gives a list of Indian anophelines—already, it would appear, somewhat out of date. At the time he wrote there were twenty-seven known species, and of these only the following four were proved malaria carriers: *Myzomyia listoni* (Liston), *Nyssorhynchus culicifacies* (Giles), *N. fuliginosus* (Giles), and *N. stephensi* (Liston). Possibly *Pyretophorus jeyporiensis* ought to be added to the list.

Darling (*loc. cit.*) lists the anophelines of the Canal Zone, and finds that *A. albimanus*, the common, white, hind-footed mosquito, a hardy variety, is the transmitter of æstivo-autumnal and tertian infections there. *A. tarsimaculata* seems also implicated, and *A. pseudopunctipennis* only doubtfully so. Other papers which may be consulted are those by the Sergents[2] for Algiers, and by Prout[3] for Jamaica. The latter found anophelines occasionally breeding in wells, and this has also been recently observed in Khartoum. There have been a good many contrary statements as to the possibility of what is now known as *Nyssomyzomyia rossi* being a malaria carrier. The latest work by Bentley[4] probably explains the discrepancies, and as he gives the references there is no need to quote other papers. He says :—

> The result of this series of observations fully confirms the opinion originally expressed by Stephens and Christophers, that in India *N. rossi* is negligible as a factor in the spread of malaria; and consideration of all the known observations relating to this species of anopheles appears to warrant the following conclusions :—
>
> (1) That *N. rossi* is naturally refractory to malarial infection.
>
> (2) But that this immunity may sometimes be broken down, notably under conditions inseparable from feeding experiments conducted with mosquitoes in captivity.

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[1] King, H. H. (1911), "The Control of Mosquitoes." *Fourth Report, Wellcome Tropical Research Laboratories*, Khartoum. Vol. B.

[2] Sergent, Ed. and Et. (1910), "Observations sur les moustiques des environs d'Alger." *Rech. Exp. Path. Alger.* (1902–9).

[3] Prout, W. T. (1910), "Reports of the Twenty-first Expedition of the Liverpool School of Tropical Medicine. Jamaica Malaria." *Annals of Tropical Medicine and Parasitology*, Vol. III.

[4] Bentley, C. A. (1911), "*Nyssomyzomyia rossi* and Malaria." *Paludism*, No. 2.

Mosquitoes —*continued*

(3) That there are strong reasons for assuming that *N. rossi* plays no part in the spread of malaria in India.

(4) And that into any investigation into the distribution of malaria and in any work of practical malaria-prevention it is very necessary to discriminate between the presence of *N. rossi* and other species of anopheles known to carry malaria in nature.

Boyce [1] has a lengthy paper on *Stegomyia fasciata* and its significance in West Africa. He has some good notes on breeding-places and habits. As regards the latter he states :—

> The mosquito avoids windy places, and therefore selects not only quiet stagnant water, but places where the air is stagnant. As soon as the imago emerges from the pupa, it makes for the dark places in the house. It alights preferably on dark or black material. So far as I have been able to judge, I do not think that it flies any distance at one time, although of course its travelling may be very greatly assisted by the cover of trees or a long line of huts, which would enable it to progress from point to point, sheltered from wind and rain. Some observers give 100 yards as its maximum distance of flight. Whatever this may be, however, I consider that it may safely be said that this mosquito does not, as a rule, fly long distances. It seeks cover as soon as it emerges from the pupa but it may travel from house to house, and is certainly capable of entering ships moored in rivers. In conformity with its house-haunting, domestic nature is the fact that it is probably the most common mosquito found on ships ; numerous observations in recent years, and the endless records of yellow fever on board ship in the nineteenth century, amply testify to this fact. Given the suitable condition of freedom from draughts, darkness, and warmth, it can remain secreted for weeks in the holds, galleys, engine-rooms, or bunks of a ship. It is for this reason that it is so essential to screen ships which trade in rivers in yellow fever countries, or to insist that they shall be moored several hundred yards from shore.

He states that *S. fasciata* bites by night as well as by day and is noiseless, and mentions the fact that there is no conclusive evidence that the infected female *Stegomyia* transmits the virus of yellow fever to its eggs and larvæ. He believes the very high mortality rate in the past amongst Europeans on the West Coast of Africa has been due to yellow fever, and not to malaria, a view suggested in part by the great prevalence of *S. fasciata*.

A few papers on preventive and anti-mosquito measures may now be considered. Illustrations of a new portable net with a special support and extension rod are given by Nichol,[2] but the "Mida" net described in the *Journal of Tropical Medicine and Hygiene* for March 15, 1911, and obtainable from the Tarkwa (Gold Coast) Trading Company, Ltd., 164, Palmerston House, Old Broad Street, London, E.C., would seem to be a better type. It is very strong and durable and folds into a small compass. As the notice says :—

> The chief feature of this net are the fineness of the mesh, and the protection it affords to the hands should they come into contact with the net, owing to the lowest two feet of the net being made of stout calico, which is impervious to the bite of the mosquito.
>
> All the foremost authorities on tropical hygiene assert that mosquito nets should invariably be tucked under the mattress of the bed, and this procedure requires the presence of strong material. Without the calico the net soon becomes torn, when it is no longer a protection, but a source of danger.
>
> When ordering a "Mida" mosquito net, care should be taken to state the size and shape required, otherwise the single pyramidal net, as being that in most general request, will be supplied.

An interesting investigation was carried out by Whyte [3] to ascertain the effect of a mosquito net on the air within it. The points considered were (1) The percentage of carbon dioxide in the air inside the net, and (2) the amount of organic matter contained therein. As regards the former there did not seem to be any difference in the air inside and outside the net, but with respect to the latter there was an appreciable increase in the amount of organic matter present. The indication, therefore, is to get rid of the accumulated waste products by ventilating the net in some way, no easy matter. Two papers, the outcome of Whyte's article, are those by Hill and Fink in the *British Medical Journal* for October 15, 1910. The former maintains that the use of a fan inside the net will do away with the discomfort, and that there is no evidence that organic impurities found in traces in the air of rooms occupied by men have any harmful effect. The latter mentions the common Indian types of mosquito nets.

Wolferstan Thomas [4] gives an account of the method now adopted for screening steamers against mosquitoes. This is especially employed in steamers trading from Liverpool to the Amazon, and has proved highly effective in protecting against yellow fever. Mosquito traps were mentioned in the first Review. Legendre [5] describes a form of trap to be used at

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[1] Boyce, R. (January, 1911), "The Prevalence, Distribution and Significance of *Stegomyia fasciata*, F. (=*calopus*, Mg.) in West Africa." *Bulletin of Entomological Research.*

[2] Nichol, C. E. (October, 1909), "A New Portable Mosquito-net Support." *Journal Royal Army Medical Corps.*

[3] Whyte, G. D. (October 1, 1910), "The Effect of a Mosquito Net on the Air within it." *British Medical Journal.*

[4] Thomas, H. W. (July 9, 1910), "A Steamer with Special Mosquito Screens." *Lancet.*

[5] Legendre, J. (July 13, 1910), "Sur la destruction des Culicines à l'aide du gîte-piège." Also "Sur la destruction des moustiques adultes à l'aide du filet à papillons." *Bull. Soc. Path. Exot.*

breeding-places, and the same author also mentions the use of the butterfly net for catching *imagines*, especially in rooms tenanted by yellow fever patients. The usual way of destroying the adults is by fumigation. Trillat and Legendre [1] have tested the toxicity of various vapours in this respect. Their work was only of a preliminary nature, but apparently pyridine and quinoline in high dilution are very effective.

Boyce (*loc. cit.*) has the following useful notes regarding fumigation :—

In my experience, the best, cheapest, and most readily procurable culicide is sulphur, whether used in a small way by burning in sulphur pots, or on a large scale by generating it in a Clayton sulphur apparatus. I always recommend testing the efficacy of fumigation by direct experiment, rather than relying upon calculation. For this purpose I insert living *Stegomyia* in a muslin-covered box, or in some place where they can be observed from outside the room or building. When they are dead I conclude that the fumigation has been successful. The following is a brief statement with regard to the three most generally useful culicides.

Sulphur.—2 lbs. to 1000 cubic feet. The pots containing the sulphur are to be placed in pans containing one inch of water. The sulphur is to be ignited with alcohol, and care must be taken to see that it is well alight. Duration three hours. Brass work and steel goods are liable to injury ; they should therefore be removed.

Pyrethrum powder.—3 lbs. to 1000 cubic feet, applied for three hours ; and it is better that the 3 lbs. be divided amongst three pots than that all the powder be put in one pot. The pots to be placed in pans containing a little water. Pyrethrum powder is used for rooms close to any sick patients, as the fumes which might escape from sulphur fumigation are irritating. This powder is also used in cases where brass work, pianos, telephones, instruments, etc., are present.

Camphor and Carbolic Acid.—The mixture consists of equal parts camphor and crystallised carbolic acid dissolved by gentle heat. It is an exceedingly good fumigator, and does not injure furniture, clothes, or brass work ; the odour is pleasant and smells of camphor. A room has a refreshing smell after its use.

Four ounces are vaporised per 1000 cubic feet for two hours. The material is placed in an open pan placed over a spirit or petroleum lamp ; white vapour is given off.

Avoid risk of setting fire to the premises by using care and foresight.

Ross's important work on the Prevention of Malaria does away with the necessity of reviewing many papers on general anti-mosquito measures. As regards irrigation areas the following regulations have been found useful in the Sudan, and are a combination of those given in the Third and Fourth Reports of these Laboratories.

(1) Irrigation channels should, as far as possible, be so aligned that the water surface will be below land level, thus avoiding infiltration into low-lying adjoining lands. Where the water surface, owing to the requirements of irrigation, must be above land level, the banks should be so constructed as not to allow of leakage into low-lying adjoining land.

(2) Irrigation channels should be graded with the maximum bed slopes which circumstances permit. By this means water tending to remain after irrigation has ceased, will run to the far end of the channel and spread over the land.

(3) Both section and slope of irrigation channels should be as uniform and regular as circumstances permit, and when they tend to become otherwise, holes and depressions should be filled in until a uniform waterway has been obtained.

(4) All borrowpits or depressions adjoining or resulting from the construction of irrigation or drainage channels, banks or roads, should be filled in to the level of the adjacent land.

(5) Dead ends of irrigation channels should be reduced to the smallest size compatible with efficiency, so as to avoid water stagnating on a larger surface than is necessary.

(6) The channels should be periodically cleaned of all vegetation, weeds and refuse.

(7) Sluices, regulators, pipes and outlets generally should be so constructed that leakage through them which might form stagnant pools and puddles is, as far as possible, prevented and, where hollows are worn out downstream of such works, they should be bedded with stones and filled in up to the level of the channel bed. All pools and puddles formed by leakage should be abolished.

(8) Where stagnant pools in spite of the foregoing are unavoidable, petroleum or other larvicide should be used, particularly when the channels are intermittently used, or in the event of the water-supply temporarily failing.

(9) When possible, fish to destroy larvæ should be introduced and kept in the main supply channel.

(10) Lands where water is apt to stand should be filled in to the same level as the adjacent lands, or should be provided with suitable surface drainage.

(11) Crops such as sugar-cane, rice, and others which require a more or less continuous supply of water, should not be grown within one mile of any village or town.

(12) Cases of fever and any excessive number of mosquitoes should be notified to the Governor of the Province by the managers of all estates.

Hehir's monograph, so often quoted, is full of useful hints, and many other papers might be mentioned if space and time permitted. One must, however, again refer to Darling's paper (*loc. cit.*), where there is information about larvicides, agents used to destroy vegetation, grass and algæ, and the composition and size of mesh for wire screens.

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[1] Trillat and Legendre, J. (December 9, 1908), " Étude sur la toxicité des vapeurs de quelques substances chimiques sur les Moustiques." *Bull. Soc. Path. Exot.*

Mosquitoes —*continued*

Hoffmann [1] has recently published a paper on the prevention and treatment of mosquito bites. He mentions a number of substances which can be employed as repellants. For ease at night none seems better than

℞	Ol. caryophyll	5 to 10
	Lanolin	30
	Ung. glycerini ad.	100

with which he claims to have had excellent results, and which is a cleanly application. He gives the following formula for a mixture with which to treat bites—

℞	Menthol	0·2
	Terebinth. laricis	
	Ol. ricini, āā	1·0
	Collod. dupl.	18·0

The preparations are, of course, those of the German pharmacopœia. Thymol and menthol seem the best anæsthetics, and collodion is usually not required. Naphthalene is highly praised. It allays inflammation and has a more lasting effect than other applications. He states that it was used with much success by an expedition to the Argentine. Two papers on technique may be cited. One is by Bentley and Taylor [2] on a new and ingenious method of making permanent preparation of mosquitoes by the use of celloidin, the other by Stephens [3] on the methods for detecting sporozoites and zygotes in infected anophelines. Naturally these papers must be consulted for details, but the appendix to Stephen's paper is so useful and suggestive that it is given here *verbatim*.

PROBLEMS CONCERNING THE INFECTION OF MOSQUITOES WHICH NEED FURTHER INVESTIGATION

(1) *Bodies of uncertain significance found in the Salivary Glands of various Mosquitoes.*

(*a*) In a large Anopheline (*Myzorhynchus* ? sp.), a species not frequenting houses, caught in the bush in Sierra Leone at a considerable distance from human habitations, sporozoits were found in one out of four examined. The nature of these is unknown, and further observations are much needed.

(*b*) The examination of specimens of an undetermined species of *Culex* at Mabang, Sierra Leone, showed that 10 per cent. contained bodies resembling sporozoits, but more slender, twisted and irregular in outline. Some of these Culicines had fed on human blood, others were caught in the bush. Here again we have no knowledge as to the nature of these bodies.

(*c*) In another undertermined *Culex*, 5 to 10 per cent. of the specimens contained straight bodies in the globules of salivary secretion. These resembled sporozoits, but were probably crystalline in nature.

(2) *Alleged transmission of Malarial Infection through the Eggs of the Mosquito.*—Statements have been made, without a vestige of proof, that such transmission occurs. It may be well, therefore, to examine the eggs of Anophelines for sporozoits. Even should infected eggs be found, it would not be clear how they could transmit infection to the adult mosquito hatched from them, as there is no evidence that the sporozoits multiply or undergo further development in the mosquito. If we suppose that hereditary transmission does occur, the form of the parasite may be quite different from anything we know. Hence the study of the contents of normal eggs is of importance.

(3) *What are the conditions which determine successful infection of Anophelines fed on malarial blood?*—In feeding experiments only a certain percentage are as a rule successful. In experiments made by Christophers and myself in India we got no result until we kept the Anophelines in a hot incubator, though in the villages they were naturally infected. Is it quite certain that no Culicines can transmit malaria ?

(4) *How many persons can one Anopheline infect?*—We have no data on this point. In the case of Culicines the brothers Sergent have shown that an infected Culicine can infect two, but not three consecutive birds with *Proteosoma*. Similar experiments might be made in the case of Anophelines and man, but in case this is not possible, the experiments should be made with Culicine sporozoits on birds; and, indeed, if opportunity offers, bird-malaria still affords a fruitful field of research. In the greater part of Africa, however, *Proteosoma* does not exist, but in the mode of transmission of *Halteridium*, Hæmogregarines, etc., there is abundance of work to be done.

(5) *Does the percentage of infected Anophelines vary from month to month, and if so, to what extent?*

(6) *How long does an Anopheline once infected remain so?*

(7) *Penetration of red cells by sporozoïts.*—Using a mixture of finger-blood and sporozoits from the salivary gland, Stephens and Christophers were unable to observe penetration of the red cell by the sporozoits, but the latter appeared to change into rings. Nor did Schaudinn, making the same experiment, succeed, but on using sporozoits

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[1] Hoffmann, K. F. (May 16, 1911), "Über Verhütung und Behandlung von Mückenstichen." *Münch. Med. Woch.*

[2] Bentley, C. A., and Taylor, J. (November, 1910), "A New Method of making Permanent Preparations of Mosquitoes." *Indian Medical Gazette.*

[3] Stephens, J. W. W. (May, 1911), "Methods for Detecting Sporozoits and Zygotes in Mosquitoes Infected with Malaria." *Bulletin of Entomological Research.*

Mosquitoes —*continued*

taken from a large oocyst in the stomach he was successful. These experiments are worthy of repetition, and an explanation should be sought for the difference in the behaviour of the sporozoits from the two sources, if the facts are correct.

(8) *Properties of the Salivary secretion.*—As far as I am aware, nobody has yet repeated Schaudinn's observations. He states that the salivary gland rubbed into an abrasion does not produce the irritation of a mosquito bite, but that, on the contrary, if the œsophageal diverticula be rubbed in, the well-known itching effects are experienced, which he attributes to the enzymes produced by low bacterial forms in the diverticula. Any fact established about mosquitoes is of value, for we never know to what practical purpose such knowledge may not be turned.

SUGGESTED LINES OF RESEARCH IN THE LIFE-HISTORY OF ADULT MOSQUITOES

Finally, in addition to the problems we have indicated as awaiting research dependent mainly on microscopical methods, there are numerous points concerning adult mosquitoes (apart from larvæ) on which further light is required, problems which are to be solved rather in the field than in the laboratory. Such, for example, are :—

(1) Length of life.

(2) Distance of flight. It might be possible to mark mosquitoes, *e.g.* with a stain or powder, and to trap them again.

(3) Habits, especially of the male, and conditions of fertilisation.

(4) Effect of jungle, bush, bamboo-thickets, and banana-clumps as screens. Is it advisable to clear all jungle indiscriminately, without regard to its screening function ?

(5) What are the natural enemies of adult Anophelines ?

(6) Is it possible to discover any plant or substance that will entirely repel mosquitoes, or, on the contrary, that will irresistibly attract them ?

(7) What is the best form of mosquito trap, and to what extent can mosquitoes be diminished by persistent trapping every night in native huts or European bungalows ?

(8) Habits in the dry season.

(9) When does egg-laying of Anophelines take place in nature ? Has it any relationship to food ? What determines selection of any particular water ?

(10) How often does an Anopheline leave a native hut or bungalow ?

Additional Notes

De Fossey [1] raised a point of practical interest by opening a discussion on the influence of prevailing winds on the development of the larvæ of culex and anophelines. He made observations on certain waters exposed to violent winds, and also carried out some artificial experiments. He concludes that the wind is not favourable to the development of the larvæ of certain mosquitoes, and that though it may favour the dissemination of adult insects its influence on the whole is inhibitory. It is worth noting, however, that in the northern Sudan *Pyretophorus costalis* and its larvæ seem to thrive well even when exposed to the strong and often bitterly cold north wind which blows during the winter. One has frequently found active larvæ in pools whose surface was ruffled by a strong and chilly breeze, and such larvæ can develop into pupæ and hatch out under these apparently unfavourable conditions.

Fülleborn [2] describes and figures a new form of mosquito-protected tent which in practice has proved useful. Zoologists and others working at the bionomics of the *Culicidæ* will find much of interest in an illustrated paper by Eysell [3] on the birth of the mosquito, *i.e.* the emergence of the *imago* from the pupal case, every step of which is described with remarkable care and minuteness. A review of the original German article appears in the *Lancet*, June 17, 1911.

Mycetoma. Since Brumpt's classic monograph on the subject there have been no very notable advances in our knowledge of this interesting disease. Surveyor [4] refers to the work of Boyce and himself, which showed that the white variety was due to a streptothrix and the black to a fungus allied to the common moulds. The former, he points out, spreads much more rapidly than the latter, though, even so, its progress is very chronic compared with that of actinomycosis. *Streptothrix maduræ* grows very slowly on glucose-glycerine agar and glycerine potato. In Bombay the cultures never developed the pink tint noted by Vincent in Algiers. There is much more swelling and fatty degeneration associated with the white than with the

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[1] De Fossey, A. M. (May 10, 1911), "Influence des vents dominants sur le développement des larves de Culex et d'Anophèles." *Bull. Soc. Path. Exot.*

[2] Fülleborn, F. (1911), "Ein einfaches mückensicheres Zelt." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XV., H. 11.

[3] Eysell, A. (1911), "Das Schlüpfen der Stechmücken." *Ibid*, No. 9.

[4] Surveyor, N. F. (1909), "Mycetoma or Fungus Foot Disease." *Transactions Bombay Medical Congress.*

Mycetoma —*continued*

black variety. Indeed, in the latter there is a tendency to wasting and shrivelling of the tissues, and partially fatty crystals are not deposited. The author suggests vaccine treatment in the early stages of the white variety. He has never seen the red species. Boccaro [1] gives an account of the disease as met with in India, and enters into questions of pathology and morphology, but as he does not seem to have been acquainted with Brumpt's work, and as there is nothing of special interest in his paper, it need not be considered at length. He draws, however, some interesting analogies between mycetoma and the fungus diseases of plants. In the last Review, culture work by Pinoy was mentioned. This author, along with Nicolle,[2] succeeded in cultivating the fungus from a case in Southern Tunisia. They proposed for the parasite—which may, however, be identical with *Madurella mycetoma*, Laveran—the name *Oospora tozeuri*, from its resemblance to the fungus of favus and the place (Tozeur) from which the case came. They describe the grains, and used as media maltose agar, potato-glycerine, and carrot. The favourable temperature was 35° C. for primary culture, and 37° C. for subcultures. The fungus in sugar media produced tyrosinase, which caused a blackening of the media. Inoculations of the rabbit, guinea-pig and monkey failed, but succeeded in the foot of the pigeon.

Kayser and Gryns [3] discovered in a Javanese a case of what they thought was madura foot, but which on examination turned out to be botryomycosis. There is no doubt that this latter disease may closely simulate mycetoma. Not only so, but it may occur along with it, as Archibald [4] has recently shown in his work on Human Botryomycosis in the Sudan. In the same Report will be found notes on, and illustrations of, types of mycetoma both of the hand and of the foot occurring in the Anglo-Egyptian Sudan. The red variety has been encountered containing granules of a bright red colour, something like those mentioned by Campbell as occurring in Indian cases (discussion on Boccaro's paper *loc. cit.*), but scarcely of a carmine tint.

Musgrave and Clegg [5] have a lengthy paper on the subject, to which is attached a very full bibliography by Polk. It deals with a great deal more than mycetoma, and need not be reviewed at length. A comparative table giving the cultural characteristics of various types of streptothrix and actinomyces will be found useful by those working at the subject.

A new mycetoma deserves attention. It has been found by Lindenberg [6] in Brazil, and has been named by him *Discomyces brasiliensis*. It began as a small growth in the left popliteal space, and finally involved the whole leg. Painless fistulæ formed, the pus from which, contained white granules. These consisted of felted masses of fine filaments. The fungus, which did not affect the foot, was cultivated on agar, and, unlike other pathogenic fungi, showed its optimum growth at room temperature, and not at 37° C. The author has shown that the growth always starts in a giant cell. He gives a table showing how its cultural characteristics differ from *Discomyces bovis* and *Discomyces maduræ*.

Babes [7] has a note on the black variety of mycetoma, but seems ignorant of all the previous work on the subject. He states that the parasite degenerates in the form of huge spheres 0·02 to 0·05 millimetres in diameter. He also compares the white and black varieties. A good general review of the subject, which does not, however, contain any new facts, is that by Boehm,[8] while Fülleborn [9] describes the disease as encountered in German South-West Africa, apparently a new locality for madura foot. To judge from the appearance of the accompanying photo-micrographs the parasite implicated is *Indiella somaliensis*. This is one of the forms which occur in the Anglo-Egyptian Sudan. The exact method of infection in mycetoma still remains unknown, though thorns and other foreign bodies have from time to time been found in the tumour masses.

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[1] Boccaro, M. E. (1909), "On Mycetoma." *Transactions Bombay Medical Congress.*

[2] Nicolle, C., and Pinoy, E. (1908), "Un cas de mycétome à grains noirs. Culture et inoculation expérimentale." *Bull. Soc. Path. Exot.*

[3] Kayser and Gryns (1907), "Een geval van Botryomykose zeer veel gelijkende op maduravoet." *Geneesk. Tijdschr. voor Nederl. Indie*, Vol. XIII.

[4] Archibald, R. G. (1911), "Human Botryomycosis." *Fourth Report, Wellcome Tropical Research Laboratories*, Vol. A.

[5] Musgrave, W. E., Clegg, M. T., and Polk, M. (December, 1908), "Streptothricosis, with Special Reference to the Etiology and Classification of Mycetoma." *Philippine Journal of Science*, B.

[6] Lindenberg, A. (September 30, 1909), "Un nouveau mycétome." *Revista Medica de S. Paulo*, and in *Archives de Parasitologie*, Vol. XIII., p. 265 (with illustrations).

[7] Babes, V. (January 20, 1911), "Note sur la variété noire du pied de Madura." *C. R. Soc. Biol.*

[8] Boehm, W. (1910), "Mycetoma." *Sep. Abd. aus. Real Encycl. der gesam. Heilkunde*, No. 4.

[9] Fülleborn, F. (1911), "Madurafuss aus Deutsch-Südwestafrika." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XV., No. 4.

Myiasis. A few more or less general papers will first be considered. Of this nature is one in Italian by Splendore.[1] He gives a list of all known human myiasis, dividing the parts affected into external cavities, the skin and the gastro-intestinal tract, and grouping the parasites concerned under each of these three headings, placing them also under the two families *Œstridæ* and *Muscidæ*. He also describes a new intestinal form in Brazil due to one of the *Calliphorinæ*. A valuable paper is that by Austen.[2] After a useful introduction he takes up the subject geographically. Under Africa he describes *Cordylobia anthropophaga*, Grünb, known in Sierra Leone as the Tumbu or Tumba fly, and as Ver de Cayor in Senegal, where actually more than 300 larvæ were found in a single spaniel puppy. This fly was mentioned at some length in our first Review, so all that need be said is that it has been confused with *Bengalia depressa*. There is no evidence to show that the larva of the latter is a subcutaneous parasite. The *Sarcophaga* are considered, although in Africa there is no absolutc evidence that they produce myiasis. Suspicious behaviour on the part of a female *Sarcophaga* is, however, recorded from Nyasaland in a human case, while from Angola, infection of a goat by an undetermined species is recorded by Wellman. The larvæ were deposited in the nostrils and caused erosion and necrosis. There is also a case of apparent human intestinal infection from Natal. A similar case due to *Anthomyia desjardensii* is also reported from Angola. This species is allied to the well-known *Homalomyia* (Wellman [3] mentions that the species of *Sarcophaga* with which he infected goats were *S. africa* and *S. albofasciata*). Austen next considers Asia. *Aphiochæta ferruginea* is extremely small but specially interesting, because it may be capable of passing through its entire life-cycle in the human colon. It is not confined to Asia, being found in West Africa and Central America, and it seems to have been introduced into fresh localities by human agency. A case of infection from eating candied bael fruit has been recorded, and there seemed little doubt that in this instance the fly propagated itself while sojourning in the human intestine. Both flies and maggots were said to be passed per anum, and the infection lasted for nearly a year. Laurence [4] describes a West Indian case where the infection lasted at least eight months. Austen mentions that some of the *Phoridæ*, the family to which this fly belongs, have been found alive in corpses exhumed after being buried for two years. *Sarcophaga* are operative in India (see below), and *S. ruficanis* may be one of the species concerned. *Pycnosoma* can cause nasal myiasis in India. In Tropical America, including the West Indies, *Aphiochæta* exists, and one encounters *Chrysomyia macellaria*, the well-known screw-worm fly. Another of the *Chrysomia* causing facial myiasis is *C. viridula*, a larger species. *Sarcophaga*, and especially *S. chrysostoma*, have been found implicated, while *Dermatobia*, a genus of the œstrid flies, represented probably by *D. cyaniventris*, and possibly a distinct *D. noxialis*, gives rise to the "Ver macaque," and causes myiasis in man. Austen concludes with a plea for the necessity of breeding out the adult flies from the larvæ. He says :—

> All that is necessary is to place the maggots on the top of a pot containing some fairly dry earth, and to cover the vessel with muslin. The flies, which will thus be caught on making their appearance, should be killed by exposure to chloroform or cyanide, but, since it is absolutely essential to give the integument, legs, and wings time to harden and to assume their natural colours, from twelve to twenty-four hours should be allowed to elapse before transferring the insects to the lethal chamber. For transmission to England they should be screwed up loosely in cigarette paper, and packed in a small metal box. The sexes can be distinguished by the eyes in the male being either actually in contact, or close together on the top of the head, while in the female the eyes are wider apart. Three or four examples of each sex are necessary, and they should be accompanied by their puparia, and by some of the larvæ and pupæ in spirit.

In his introduction Austen referred to myiasis of the urinary tract, and we proceed to consider two papers on this subject. The one is by Chevrel,[5] a long and illustrated paper, of which we can only consider some of the conclusions. These are :—

(1) Twenty-one cases of the condition have been recorded (up to 1909), of which seven are authentic.

(2) The infection in man may be direct or natural, indirect or accidental.

(3) It is improbable that accidental infection is derived from water or instruments used in washing out the bladder, and in any case it is very rare.

(4) Infection is nearly always direct, *i.e.* natural. In order that this may be realised the urinary organs must permit the passage of an organic liquid arising from an affection of the bladder or urethra, or some severe general disease.

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[1] Splendore, A. (1908), "Contribuzione allo studio delle miasi." *Arch. de Paras.*

[2] Austen, E. E. (March, 1910), "Some Dipterous Insects which cause Myiasis in Man." *Transactions Society Tropical Medicine and Hygiene.*

[3] Wellman, C. (1910), "Diseases in the Tropics." *American Society of Tropical Medicine.* Collected Papers.

[4] Laurence, S. M. (August 13, 1910), "Intestinal Myiasis." *British Medical Journal.*

[5] Chevrel, R. (February 10, 1909), "Sur la Myiase des Voies Urinaires." *Arch. de Paras.*, Vol. XII.

Myiasis—*continued*

(5) Given these conditions, flies must be able to obtain access to the urinary orifices, as when a patient lies uncovered at night, etc.

(6) There are two stages in the process, the deposition in the neighbourhood of the urinary meatus, and the penetration of the young larvæ developing from them into the urethra and bladder.

(7) These then obtain darkness, humidity, warmth, food and oxygen, the conditions necessary for their existence and development.

(8) Their food is derived from the muco-purulent secretion and the albuminous filtrate which bathes the walls of the urethra and bladder.

(9) These fly larvæ can be immersed in urine for several consecutive hours without suffering in any way. They regain their activity as soon as they leave the liquid.

(10) They are able to resist asphyxia, and require very little oxygen.

(11) The most common insect producing this curious condition is the little room-fly *Fannia canicularis L.*, a full account of the larva of which is given.

(12) A streptococcus and a protozoon are often found along with other organisms in the intestinal contents of these larvæ.

The second paper is by Tribble,[1] and records a case in the Philippines where severe abdominal symptoms, due to an acute cystitis, were set up by the presence of dipterous larvæ in the deep urethra and bladder. The parasites were found in urine withdrawn by the catheter. A cure resulted following irrigation with potassium permanganate and boric acid solutions. In the discussion Chevrel's work was not mentioned, and was apparently unknown. The larvæ were not identified, but were said to be like those of *Musca domestica*.

Turning now to cases of specific infection we find that McCampbell and Corper [2] have described a case of triple intestinal infection due to the larvæ of *Anthomyia canicularis*, the small black flower or privy-fly; *Musca domestica* and *Eristalis tenax*, the drone or flower-fly. The larvæ were passed for many years, the source of infection being unknown, and the continuance of the phenomenon a mystery. Sorel [3] has recorded an interesting case where intestinal myiasis due to larvæ of a fly belonging to the *Sarcophaga* produced an illness closely resembling enteric fever. There was a continued temperature and severe diarrhœa, at one time of a choleriform type. A skin eruption and stupor were also present. The observation was made in French Guiana. For an account of the larvæ of the genus *Cordylobia*, the reader is referred to a short paper by Gedoelst.[4]

The same author [5] describes a new species, *C. rodhaini*, producing cutaneous myiasis in the Congo Free State. He describes and figures three stages of the larva, which seems to be the larva of Lund, previously described by him. Broden and Rodhain [6] describe the cutaneous myiasis which it produces. A good illustrated account of *Cordylobia grünbergi* (Dönitz) is given by Fülleborn.[7] A picture of the fly is given and photographs and drawings of the larva and the boil it produces. Patterson,[8] who was quoted by Austen, records a very terrible case of facial myiasis due to what he calls an "Indian Screw Worm," but which, as above mentioned, Austen proved to be larvæ of *Sarcophaga*. Possibly several species of maggots accounted for the horrible condition and death of the coolie woman infected, and from whose sloughing face large numbers of maggots were removed daily. The nose and eyes were practically wholly destroyed, but the brain and its membranes escaped. Cameron [9] records cases of nasal myiasis in Northern India, probably due to *Pycnosoma*, and obtained good results by syringing out the nose with chloroform 1 part, and rectified spirits 2 parts. This induced violent sneezing and expulsion of dead maggots. Swan [10] records severe cases of facial and cervical myiasis occurring in the United States. One fatal case was due to the larvæ of *Lucilia sericata*,

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[1] Tribble, G. P. (November, 1910), "Unidentified Larvæ of some Dipterous Insect developing in the Deep Urethra and Bladder of Man, producing Severe Abdominal Symptoms." *Philippine Journal of Science*, B.

[2] McCampbell, E. F., and Corper, H. G. (October 9, 1909), "Myiasis intestinalis due to Infection, with Three Species of Dipterous Larvæ." *Journal American Medical Association.*

[3] Sorel, F. (June 10, 1908), "Cas de myiase intestinale simulant une maladie typhoide." *Bull. Soc. Path. Exot.*

[4] Gedoelst, L. (December 9, 1908), "Note sur les larves parasites du genre *Cordylobia*." *Ibid.*

[5] *Idem* (1910), *Cordylobia rodhaini*, nova species, Diptère Congolais à Larve Cuticole." *Arch. de Paras.*, Vol. XIII.

[6] Broden, A., and Rodhain, J. (1910), "La Myiase Cutanée chez l'Homme au Congo." *Ibid.*

[7] Fülleborn, F. (November, 1908), "Beobachtungen über Cordylobie Grünbergi (Dönitz)." *Beihefte* No. 6, *Arch. f. Schiffs-u. Tropen-Hyg.*

[8] Patterson, R. L. (October, 1909), "An Indian Screw Worm." *Indian Medical Gazette.*

[9] Cameron, A. (November, 1909), "Cases of Myiasis in Northern India." *Ibid.*

[10] Swan, J. M. (January 1, 1910), "A Report on Two Cases of External Myiasis." *Journal Tropical Medicine and Hygiene.*

Myiasis—*continued*

Meigen. This fly takes between 15 and 16 days to develop fully from egg to adult insect. The eggs turn into larvæ in 24 to 48 hours, the larvæ to pupæ in 3 or 4 days, and the pupæ to imagines in 10 days. Other cases were due to *L. cæsar*, which takes 19 or 20 days to develop from the egg. Garrod [1] records an intestinal case due to *Homalomyia* larvæ. As a rule the eggs or larvæ probably enter the body with the food, but he quotes Hewitt,[2] who states that the eggs of *H. canicularis* may be deposited on the lips or nostrils of children and pass thence into the stomach and intestines. Hewitt also states that the larvæ may enter the rectum, being splashed up from below, if the old type of privy be used. Diarrhœa is the most common symptom of infection. This author mentions a case due to *C. erythrocephala*, and notes that in certain cases the larvæ may wander from the mouth or alimentary tract and get into the nasal passages or other ducts, in which cases complications may ensue and result in the death of the patient. Fenwick [3] has an interesting paper on the existence of living creatures in the stomach as a cause of chronic dyspepsia. Amongst the diptera he deals with some already mentioned, and in addition cites two apparently authentic cases of infection with the larvæ of *Tipulidæ*, the family to which the daddy-long-legs belongs. These are crane-flies, and infection takes place through unwashed fruit or vegetables. He also mentions a case where immense numbers of the eggs and larvæ of mosquitoes were vomited at intervals (Allonneau), and instances of infection with the bots of *Gastrophilus equi*. He has interesting notes on *Coleoptera* and *Lepidoptera* found in man, but these come under the heading "Parasites." As regards the infection he remarks :—

> The clinical details of many of the cases of internal myiasis, while deficient in several important particulars, conclusively prove that under certain circumstances the eggs of insects are hatched in the human stomach, and the resultant larvæ grow to their full size; while in rarer instances all the various metamorphoses which precede the development of the perfect insect may be completed in the organ. Thus more than 45 cases have been recorded in which a vast number of maggots were evacuated as the result of the ingestion of insects' eggs, and in many of these the length of time which elapsed between the probable date of infection and the first discharge of living larvæ correspond with that required for the hatching of the eggs and the development of the maggots. In others again, as in that related by Cavenne, the appearance in the stools of chrysalids suggests that the pupal as well as the larval stage was completed in the alimentary tract, while the case of Mary Riordan and others, in which larvæ, pupæ, and the perfect insects were discharged at intervals for years, can only be explained by the assumption that the insects actually multiplied in the digestive canal of their host.

He also says that :—

> It is well known that certain functional disorders of the nervous system, including neurasthenia, hysteria, and some forms of insanity, are not infrequently accompanied by a marked deficiency of hydrochloric acid in the gastric juice; and since all varieties of primary inflammation of the stomach produce a similar diminution of digestive activity, it is obvious that the gastritis which ensues from the presence of living animals must indirectly favour their longevity. It is also highly probable that the condition known as *achylia gastrica*, in which the stomach never secretes any acid, is far more common than is usually supposed, and consequently in many apparently healthy individuals the stomach may prove an excellent incubator for the development of any eggs that happen to gain entrance to it.

His notes on symptoms are of value :—

> The symptoms that ensue from the presence of larvæ in the alimentary tract vary according to the numbers and nature of the parasite. In the case of the *Muscidæ*, the passage of maggots by the rectum is often the first indication of the disease; but when larvæ of the *Œstridæ*, *Tipulidæ*, or *Coleoptera* are present, their large size and sharp appendages always give rise to considerable irritation. An interval of four to twelve days usually intervenes between the ingestion of the eggs and the appearance of the first symptoms, during which time the patient either feels perfectly well or complains of vague abdominal discomfort, restlessness, and want of appetite.
>
> At the end of this incubation period general malaise is experienced, accompanied by headache, thirst, anorexia, and faintness, while in children rigors, convulsions, and delirium are not infrequent. Extreme vertigo has been mentioned in so many cases that its occurrence cannot be regarded as purely accidental. Fever occurs in more than half the cases, and may persist for ten days or longer, although as a rule it tends to subside within forty-eight hours. In several instances continued pyrexia for three weeks, accompanied by loose stools, caused the disease to be diagnosed as enteric fever. When dipterous larvæ inhabit the intestine the abdominal symptoms are usually slight, and chiefly consist of distension, uneasiness, or of pinching and pricking sensations in the region of the navel; but if those of beetles, bot-flies, or crane-flies are present, severe tearing or gnawing pains are often complained of, or genuine colic is experienced. Retching and vomiting occur in the majority of the cases in which the latter larvæ exist, and in more than one instance hæmatemesis has been observed.
>
> The crisis of the complaint, which appears to coincide with the maturity of the larvæ, is heralded by a sudden evacuation of the parasites, dipterous maggots being usually discharged by the bowel as well as by emesis, but beetle larvæ chiefly by vomiting. Occasionally only a few specimens are eliminated at a time, but as a rule their numbers have been reckoned by the pint, quart, or litre, or are described as "innumerable."

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[1] Garrod, J. R. (September, 1910), "Note on a Case of Intestinal Myiasis." *Parasitology.*

[2] Hewitt, C. G. (December, 1909), "The Structure, Development, and Bionomics of the House-Fly." *Quarterly Journal of Microscopical Science.*

[3] Fenwick, W. S. (February 11, 1910), "The Existence of Living Creatures in the Stomach as a Cause of Chronic Dyspepsia." *British Medical Journal.*

Myiasis—*continued*

A sharp purge constitutes the best treatment in mild cases, while in the more troublesome forms thymol, santonin, or other anthelmintics have been successfully used.

Miller [1] has reported a human case of *Myiasis dermatosa* due to ox-warble flies. The condition is very rare, and the patient, a boy, presented a swelling under the chin. A lump below the left knee had been the first symptom, and this had shifted during two months from place to place finally appearing sub-mentally. On incision a larva was found which Stiles identified as that of *Hypoderma lineata* in the second stage. Previously the patient himself had removed another larva from the occipital region. It had first shown itself in the left groin.

Weinberg [2] has experimented with the larvæ of œstridæ, and finds that :—

(1) The larvæ of Œstrus, which fix themselves on to a point in the intestinal tract, live on the blood of the host.

(2) They suck blood intermittently.

(3) The parasites secrete substances which have the property of hindering the coagulation of the blood, of re-dissolving a clot already formed and of dissolving red corpuscles.

(4) The substances are not specific, and appear to be reduced, but not destroyed by heat.

(5) They are elaborated by the digestive organs of the larva. They are also found in the adipose tissue and red cells of that organ.

Brief mention may be made of a paper by Surcouf and Gedoelst,[3] in which they describe a new œstrid from a hippopotamus. They have named it *Rhinœstrus hippopotami*. We conclude with an interesting extract of a paper by Portier [4] on a possible remedy for the bots of *Gastrophilus* :—

He points out that hitherto all attempts to destroy the bots of *Gastrophilus* in the stomach of the horse have failed. Such remedies as corrosive sublimate, salts of arsenic, thymol, spirits of turpentine, tincture of pyrethrum, etc., have been used with little effect, or have even proved fatal to the horse.

He attributes these powers of resistance on the part of the larvæ to the possession of an extremely effective mechanism in the tracheal system, which prevents the invasion of the body by poisonous liquids. So effective is this contrivance, that these larvæ have been placed for three or four hours in alcohol, spirits of turpentine, corrosive sublimate, castor oil, etc., without being seriously affected thereby. From his examination of the tracheal system, he concluded that a remedial liquid to be effective must possess the following properties: It must be capable of moistening the chitin, which is a hydrofuge ; it must have a very feeble surface tension, in order to prevent the phenomenon of gaseous absorption, which is so marked in these insects, and which is so efficacious a means of protecting the stigmata from the invasion of external liquids ; and finally, it must possess these qualities in an acid as well as a neutral medium.

When almost on the point of abandoning his search for such a liquid, it occurred to him that bile possesses all these properties ; and actual experiment showed that when *Gastrophilus* larvæ were placed in even a weak solution of bile (1 per cent.), the liquid rapidly entered the tracheal system. By adding suitable remedies to the bile, the largest larvæ could be killed in less than an hour.

M. Portier points out that larvæ of *Gastrophilus* have only been found in just those very animals in which a gall-bladder is wanting, namely, the Equidæ, the elephant and the rhinoceros ; but, as a matter of fact, this is by no means a complete list of the mammals in which there is no gall-bladder. The author argues that this correlation cannot be regarded as a simple coincidence, and suggests that in animals having a gall-bladder the bile may regularly regurgitate into the stomach and so destroy any larvæ. He also suggests that ruminants are protected by the fact that the bots can only permanently establish themselves in an acid medium ; in a neutral or alkaline medium they are rapidly attacked by parasitic organisms.

Cutaneous and intestinal myiasis are both exceedingly common in wild and domesticated animals in the Sudan. Some notes on certain of the parasites found and studied appear under the Entomological Section of the Fourth Report of these Laboratories, Volume B, but there is still a large field for study in connection with these conditions.

Ophthalmia. It seems advisable to discuss a few papers on this disease which is so prevalent and important in certain tropical and sub-tropical countries. Brooke [5] has a useful paper on the contagious form. He deals only with the less definite catarrhal and granular types, and does not consider the purulent, membranous and phylctenular varieties. Acute

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[1] Miller, R. T. (December 3, 1910), "Myiasis dermatosa due to the Ox Warble Flies." *Journal American Medical Association.*

[2] Weinberg, M. (1908), "Substances hémotoxiques secrétées par les larves d'œstres." *C. R. Soc. Biol.*, Vol. LXV., No. 25.

[3] Gedoelst, L., and Surcouf, J. (December 8, 1909), "Description d'un Œstride nouveau, parasite de l'hippopotame." *Bull. Soc. Path. Exot.*

[4] Portier, M. P. (1910), "A possible Remedy for the Bots of *Gastrophilus*." *C. R. Soc. Biol.* Quoted in *Bulletin of Entomological Research*, October, 1910.

[5] Brooke, G. E. (August, 1910), "Notes on Contagious Ophthalmia." *Philippine Journal of Science*, B.

catarrhal ophthalmia can be caused by at least three different organisms : (*a*) The Koch-Weeks' bacillus ; (*b*) a Gram-positive organism ; (*c*) The Morax-Axenfeld bacillus. He describes the first which is so largely a factor in Egypt, where it was discovered. He found it in 54·7 per cent. of his cases in the East, and believes it to be a common cause of ophthalmia there. The second is rather like the Koch-Weeks' bacillus, but is Gram-positive. It is non-motile, and does not form spores. It occurred in 14·6 per cent. of his cases. The third has been found in Europe, Africa, North America, and Asia, and frequently occurs in pairs. It is Gram-positive unlike the Koch-Weeks' bacillus. (It has a square, well-defined outline.) Only 4·4 per cent. of Brooke's cases were due to this organism. As regards symptoms he says that they

Ophthalmia—*continued*

> call for little remark, and their severity will vary in many cases. There is intense infection of the conjunctivæ, more or less œdema of the tissues and eyelids, lachrymation and muco-purulent discharge. There is a pricking and burning feeling, and photophobia in the worst cases. As a rule, the pain is slight. The lymphoid follicles may, or may not be elevated. Normally, these follicles are found scattered in the sub-epithelial tissue of the conjunctival reflections, and become widely developed in inflammatory conditions. If they become prominent they are then easily visible to the naked eye, but it is highly important not to mistake them for the large "sago-grain" prominences of granular ophthalmia.
>
> All forms of catarrhal ophthalmia appear to be highly contagious. Both eyes are usually attacked, either simultaneously or within a short time after each other. If untreated, in quite a large number of cases marginal corneal ulcers occur which frequently coalesce and involve considerable areas, and this is a serious Eastern scourge.

He gives as essentials of treatment—(*a*) remove the germ by medication, (*b*) take care of the cornea, (*c*) maintain the patient's health. In Koch-Weeks' infection he finds silver salts best, a few drops of silver nitrate (2 grains to the ounce). A stronger solution may result in sloughing of the lids or corneal opacities. Boric acid irrigations are useful, and a shade should protect the eye. On no account should a bandage ever be used. Weak oxide of mercury ointment prevents the lids sticking together. Corneal ulcers may necessitate atropine, corneal necrosis eserin (2 grains to the ounce). Tonics are indicated. When the second bacillus is present the same treatment is effective, but if the Morax-Axenfeld bacillus be found, silver nitrate does no good and may be harmful. Copper sulphate, 0·25 per cent. solution, is indicated, applied with a cotton-wool mop.

Granular conjunctivitis or trachoma is of great importance, and the definite causative organism has not yet been discovered. The usual symptoms are as follows :—

> There is a preliminary, acute congestion of the conjunctiva : very soon small, grey spots, rather smaller than a pin's head in size, appear in the tarsal conjunctiva of the upper lid. These have been called by Von Græfe "primary granulations," but if there is much congestion accompanying the conjunctivitis, they may be obscured. Translucent "sago-grain" granules speedily form in the cul-de-sac and palpebral conjunctiva. The plica semilunaris and caruncle are congested, and chemosis may be present. There is intense photophobia and considerable discharge. After a week or two the acute condition passes into a chronic state, which is often highly intractable. The chief sequelæ (and these together are pathognomonic) are—(*a*) corneal ulceration and pannus, leading to opacity ; (*b*) formation of scar tissue, leading to entropion and trichiasis ; (*c*) conjunctival xerosis and shrinking.
>
> Thus it is seen that the disease is highly contagious, very chronic, and leads to grave results.

He has the following short notes on therapeutics :—

> The *modes of treatment* are multitudinous.
>
> 1. The best result seems to be secured by—
>
> (*a*) Expressing the follicle with a flat Grady's forceps, or the roller forceps of Knapp. This is best done under an anæsthetic.
>
> (*b*) Painting the ruptured surface with a little bichloride of mercury.
>
> (*c*) After a day or two the daily application of solid sulphate of copper should be begun and continued until all traces of hypertrophy have vanished.
>
> Various other methods of treatment have been advocated, as (2) Galezowski's excision of retotarsal folds ; (3) Kuhut's removal of tarsus ; (4) Merck's extract of abrin (sequiritol) ; (5) X-rays, introduced by Mayon in 1902 ; (6) radium, tried by Treacher Collins in 1904.
>
> However, none of these methods has been as successful as the first mentioned. Cases are frequently eventually cured, but seldom in less than several months, often years.

One has gone into this question at some length, as Dr. Squires of the Sudan Medical Department has found trachoma common amongst the boys attending the Gordon Memorial College, and it is probable that the disease is more prevalent in the Sudan than was at first supposed.

Hewitt,[1] in his paper on the house-fly, has some notes on the conveyance of the infection of ophthalmia by flies, and quotes Axenfeld, who says that in acute epidemics of catarrhal

[1] Hewitt, C. G. (December 3, 1909), "The Structure, Development, and Bionomics of the House-Fly, *Musca domestica*, Linn," Part 3. *Quarterly Journal of Microscopical Science.*

Ophthalmia—*continued*

conjunctivitis almost the only organisms occurring are the Koch-Weeks' bacillus, perhaps, also, the influenza bacillus and the pneumococcus (in Egypt the gonococcus also, rarely *B. subtilis*). MacCallan, whom he also quotes, says that acute ophthalmias in Egypt are more liable to transmission by flies than is trachoma. The spread of the latter is mainly effected by direct contact of the fingers, clothes, etc.

Articles on the "trachoma" bodies of Halberstädter and v. Prowazek will be found in the *Medical Annual* for 1910 and 1911, where there is a great deal also about the treatment of conjunctivitis. Whatever the nature and significance of these bodies, and they appear to belong to the Chlamydozoa, it has not been proved that they occur in other conditions besides trachoma. Working in Manila, Edwards[1] has isolated from trachoma cases a small organism to which he has given the name of *B. trachus*, but, as he himself admits, there is no evidence that it is a cause of trachoma.

Oriental Sore. This is a bad name for the condition we are about to discuss. Perhaps it had better be termed "Cutaneous Leishmaniasis," and yet this again would appear to be scarcely correct, as quite recently the condition has been found affecting the buccal mucous membranes. Perhaps "Superficial Leishmaniasis" would serve, but, however that may be, fresh interest has been evinced in the subject, doubtless in part from Manson's pronouncements and suggestions regarding it, and still more from the discovery of infantile Leishmaniasis, the success which has attended cultural methods, and the ever-growing enthusiasm for working out the problems presented by tropical medicine. Most of the papers for review deal each with so many aspects of the condition that it is not easy to group them, but those dealing specially with treatment will be taken last.

A general paper is that by Marzinowsky[2] which, however, is now somewhat out of date, and contains nothing very special except possibly some therapeutic notes, which will be mentioned in due course, and the observation that he succeeded in infecting himself by employing a special technique.

Nattan-Larrier and Bussière[3] have studied *L. tropica*, finding the parasite best stained in sections by means of Unna's polychrome blue, followed by differentiation with oil of cloves. The stain should act for half-an-hour. Carbol thionin also gave good results. Careful preliminary fixation is required. The majority of the parasites are contained in the large macrophages. A great number are found in the connective tissue cells, but none in the plasma cells. The endothelium of blood capillaries may harbour them, but none were seen in the lumina of blood-vessels. Some, however, were observed floating in the cavity of the lymphatics. They find the *Leishmania* most abundant in the spreading part of the sore, and therefore in its depths and at its periphery. Free forms, besides occurring in the lymphatics, may be found in the connective tissue spaces, and even on the surface of the lesion. Important work has been carried out in the Pasteur Institute at Tunis, and perhaps it will be best to take all the papers describing it together.

Nicolle and Sicre[4] describe the parasite, and note its absence from the peripheral blood. They found an increase of the mononuclear elements at the expense of the polymorphs. Culture on blood-salt-agar, and also on Novy-MacNeal, was successful, and the flagellated culture forms are described. They were grown at a temperature of between 19° and 23° C. Subcultures were easy, and at a temperature of 22° C. vitality was maintained for two months. The cultural forms differ from those of kala-azar. There is an early division of the flagellum in *L. tropica*, and it is longer and more flexible than in *L. donovani*. The authors record that a

monkey (*Macacus sinicus*) inoculated with the virus of the disease on the upper lids and on the root of the nose in the skin, and on both sides of the forehead by scarification, developed highly characteristic lesions in the two first situations, but only a very small and transient papule on the forehead. The primary lesions lasted twenty-one days, and smears taken from them showed the undoubted presence of *Leishmania*. One out of two *M. sinicus* inoculated under the same conditions as the first, with second cultures eighteen days old, developed, after an incubation of thirty-eight days, a nodule which persisted for thirty days, when it was excised. Smears taken from it showed parasites, generally much altered, within the mononuclears and extra-cellular bodies of quite normal appearance.

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[1] Edwards, R. T. (1910), "Conjunctival Infection in Manila." *American Society of Tropical Medicine.* Collected Papers.

[2] Marzinowsky, E. J. (December 28, 1908), "Die Orientbeulen und ihre Ätiologie." *Zeit. f. Hyg. u. Infekt.*, Vol. LVIII.

[3] Nattan-Larrier, L., and Bussière, A. (January 13, 1909), "Répartition des Leishmania dans le Bouton d'Orient." *Bull. Soc. Path. Exot.*

[4] Nicolle, C., and Sicre, A. (1908), "Recherches sur le Bouton d'Orient." *Arch. de l'Inst. Past., Tunis*, No. III.

Oriental Sore—*continued*

Experimenting further with another species of monkey, these observers [1] found that cultures of *L. tropica* exhibited but a feeble virulence. They failed with intradermic, corneal, and ocular inoculations on the dog, cat, and rabbit (*see also page* 222). Row [2] was one of the first to cultivate *L. tropica* successfully, using serum cultures. He did so in Bombay, and concludes a well-illustrated and interesting paper as follows :—

(1) The parasite of the Oriental sore when full developed into the flagellate form, under ordinary conditions of culture, is much longer and bigger than that of kala-azar, in which one meets with short and fat forms as a rule.

(2) The parasite of the Oriental sore is more resistant to external conditions than that of kala-azar—in other words it is much less delicate, as it is found possible to obtain developmental forms up to the flagellates from this parasite (of the Oriental sore) three days after the parasites are removed from the lesion—while the parasite of kala-azar, according to Rogers, dies within twenty-four hours after it leaves the spleen, if it is not cultured within that period.

(3) The flagellum of the parasite of the Oriental sore is much longer, and presents more regular wavy undulations than that of kala-azar, where it is shorter, and where the undulations, if any, are not regular or uniform.

(4) Although contamination of the material with extraneous germs is inhibitory to the early developmental progress of the parasite of the Oriental sore, it is not so destructive to its further development into flagellates as in the case of the parasite of kala-azar where, according to Rogers, even the slightest contamination with staphylococci is sufficient to destroy the culture.

(5) The parasite of the Oriental sore develops into fully mature flagellate forms between forty-eight and seventy-two hours, while that of kala-azar takes twice as long, if not longer.

(6) The best culture medium (according to my results) for the parasite of the Oriental sore is human blood serum, by preference that from tuberculous patients, while that for the parasite of kala-azar is, according to Rogers, sodium citrate 2 to 8 in sodium chloride 0 to 8 solution mixed up with splenic puncture blood.

(7) The optimum temperature for the growth of the parasite of the Oriental sore is between 25° and 28° C., or even up to 30° C., while for that of kala-azar, it is 22° C., or even less (according to Rogers).

Marzinowsky [3] has also succeeded in cultivating the parasite, and as he found Nicolle's special medium the best, its composition and method of preparation may perhaps be given. It has been found very useful in these laboratories and consists of agar 14 grammes, sea-salt 6 grammes, water 900 c.c. This mixture is tubed and sterilised in the autoclave. Defibrinated rabbit's blood is then added in the proportion of 2 of agar to 1 of blood. The tubes are placed for twelve hours in the incubator in an inclined position. Before use they are kept for some days at laboratory temperature to ensure their sterility. The original agar should have a feeble alkaline reaction. After complete neutralisation with litmus, 7 c.c. of a normal solution of soda are added to the litre. The author also used human blood to which 10 per cent. citrate of soda solution had been added. Like other observers he points out the absence of any undulating membrane in the otherwise trypanosome-like culture forms. He gives a schematic drawing showing the supposed cycle of the parasite in the human being, *i.e.* multiplication by binary division of the nucleus and blepharoplast, and the cycle found in culture forms, and, presumably, also in the insect vector. He shows male and female forms, and illustrates conjugation, but it is doubtful if this is a correct interpretation of the phenomena he has observed. Markham Carter [4] has added considerably to our knowledge of the condition as met with in India, and holds somewhat different views to other observers. In his first paper he says :—

In the light of the experiments described below, it is certain, in the first place, that true Oriental sore is due to a localised cutaneous infection by one or more species of protozoon which can under suitable conditions in culture develop from the early inert torpedo or cockle-shaped forms found in the infected tissues to the fully-developed monadine flagellated organism crithidial in type.

In the second place, it is certain that the view held by Manson and other workers, that the parasite of Oriental sore represents a localised infection by *Leishmania donovani*, whereas kala-azar is a generalised infection of the body with the same parasite, is entirely wrong. The parasite, though morphologically somewhat similar in the early form of Oriental sore, differs from Leishmania as much in culture as it does in the manner it attacks man, in that the parasites develop to their final stage of flagellated organisms in symbiotic relationship with cocci and bacteria. Further, it is interesting to note that two forms of the parasite occur in culture, the one a blue-staining flagellated organism, the monadine form, representing, in my opinion, the motile sexual form, possibly the male element ; the other a red-staining flagellated organism entirely different, possibly the female element. The fact that these two latter forms are found frequently in pairs is highly suggestive of sexual interchange of elements

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[1] Nicolle, C., and Sicre, A. (1908), "Faible Virulence des Cultures de *Leishmania tropica* pour le Singe" (bonnet chinois). *Arch de l'Inst. Past., Tunis,* No. IV.

[2] Row, R. (1909), "Observations on the Development of Flagellated Organisms from the Parasite of Oriental Sore." *Transactions Bombay Medical Congress.*

[3] Marzinowsky, E. J. (December 8, 1909), "Cultures de *Leishmania tropica* (s. *Ovoplasma orientale*, s. *Helcosoma tropicum*) parasite du Bouton d'Orient." *Bull. Soc. Path. Exot.*

[4] Carter, R. M. (September 11, 1909), "Oriental Sore of Northern India a Protozoal Infection." Preliminary Note. *British Medical Journal.*

Oriental Sore— *continued*

previous to the gregariniform phase. The third type found in culture are minute coccoid-like protozoa, the resistant gregariniform phase, or the earliest form of the parasite from which the common types found in the Oriental sore arise.

He then passes on to a discussion on *Leishmania*, *Leptomonas*, *Herpetomonas*, and *Crithidia*, in the course of which he says :—

Both herpetomonas and crithidia are genera whose distinction is based upon the size and shape of the monadine form, and show in general an alternation of monadine flagellate, with gregariniform resting or non-flagellate phases. In the latter the parasites are seen as small rounded pear-shaped or oblong bodies, attached in great numbers to epithelial cells, etc.

The parasites present in this stage two chromatic elements ; a nucleus with its intranuclear centrosome lie close to each other at the base of the cell. In some species a trace of the flagellum attached to the extranuclear centrosome is seen.

and he notes that both the fully developed monadine and the gregariniform phases were present in his cultural forms. He then passes to methods of cultivation, the differentiation between kala-azar and Oriental sore, and other matters of such interest and importance that we feel justified in transcribing the greater portion of the notes.

As a result of experimenting with a series of over fifty different blood media at different temperatures, the medium that was found to exactly meet the requirements of the protozoal parasite was made as follows :—

To 29 c.cm. of sterilised citrate solution 10 per cent. add about 3 c.cm. of fluid expressed from the edge of the sore, which contains myriads of the tiny torpedo-shaped and cockle-shaped parasites typical of the disease.

It is advisable to bore through the rosy margin of the sore to a depth of about 1/4 in., or 1/4 in. towards the centre of the infected area, with a short, fairly fine glass pipette, whose tip has been broken off. Smart pressure will give a steady flow of infected blood and serum.

This infected mixture should now be covered, ringed with vaseline, and placed on ice until the remainder of the medium is made up. Take 50 c.cm. of normal human venous blood and allow to stand in an ice-chest for an hour. At the end of this time break up the clot with a fine glass rod and stir until the whole mass is finely broken up. Pour the fluid portion of the blood and serum into sterilised centrifugal tubes, seal with waxed corks, and centrifugalise until large columns of clear serum are obtained. Place these tubes of blood in an incubator, and keep them at 56° C. for five minutes, then allow to cool to 28° C., or laboratory temperature.

Make a series of fifteen pipettes for cultures as follows : Blow a large glass bulb in the centre of a 3½-in. piece of ordinary glass rod, then make a long, narrow drawn-out area above it, twist this whilst soft so as to make a circular tube of narrow calibre above the bulb. Flame the tube until very soft below the bulb, and draw out until a long, thick capillary tube, 7 in., is made. Cut and seal this capillary tube. Plug the short upper end of the tube above the circular tube with wool, and sterilise in hot air.

Following the usual laboratory methods, make a mark on the capillary tube about ½-in. from the bulb. Take the volume of the tube from this point to the other end as one unit, and draw fluid up in the bulb with a large rubber teat on the plugged end of the tube. To four units of clear non-activated serum add four units of red blood cells collected below the fine white cell buffy layer. To this add three units of sterilised citrate 10 per cent., and mix the constituents freely in the bulb by shaking. To the mixture add four units of infected citrate taken from the sedimented organisms which lie with red blood cells at the bottom of the watch-glass. Mix thoroughly in the bulb ; seal the capillary tube.

Thread the tubes so prepared on a glass rod bent to three sides of a rectangle, and just able to slide into the upper shelf of an incubator. Keep this incubator at 22° C.

At the end of thirty-six hours, practically every tube shows myriads of single protozoa and large clumps of the parasites in all stages, from those found in the sore to the free flagellar forms.

There are many limits within which I have altered my constituents and temperatures and got positive results, but the above is the most certain and most perfect as yet attained.

The important points to be noted are : (1) The red cells and serum must be heated to 56° C. for five minutes ; (2) the medium must be highly acid ; (3) the parasites must be freely mixed up with the constituents of the medium ere the red cells deposit with them in the capillary tube ; (4) white cells should be avoided as much as possible.

In a successful culture, flagellar forms increase in enormous numbers up to 120 hours, and live symbiotically with masses of cocci and bacilli. Parasites are found in large clusters (flagellates) in 48 hours. In 72 hours pairs of flagellated organisms are frequently found, the one parasite crithidial in shape and staining blue, the other oval or circular and staining rosy-pink ; the two organisms are apposed to each other at or about the level of the nucleus of the crithidial form. These pairs are first seen in cultures 48 hours old ; the rosy flagellate form then is usually smaller and stains deeper.

DIFFERENTIATION BETWEEN KALA-AZAR AND ORIENTAL SORE

KALA-AZAR	ORIENTAL SORE
Family Distribution	
An extraordinary tendency to attack a number of persons in the same family or household, this family incidence clearly pointing to house infection.	Rarely, if ever, more than one person attacked.
Age Incidence	
Children most commonly attacked.	Adults the rule.

Oriental Sore—*continued*

KALA-AZAR	ORIENTAL SORE
Race Incidence	
Immigrants rarely attacked before eight years' residence in the East. The majority of patients seen are natives.	Immigrants attacked within a few months' to a year's residence in the East. The majority of patients seen are natives.
Seasonal Incidence	
No seasonal incidence known, though it is probable that the majority of cases are infected in the cold season.	Affection first appears usually from September to April, and may last for sixteen months and more.
Fevers Typical of the Disease	
Double remittent type of fever in certain cases. Double continued type. Low continued type. Frequency of different types of fever in various stages of the disease.	No fevers.
Recovery after Septic Complication	
Such as cancrum oris.	Septic complications no effect, as the parasite thrives best in cultures with masses of cocci and bacteria.
Effect of Quinine	
Large doses in early cases have cured.	No result.
General Symptoms in Kala-azar	
Early cases gave history of rigors daily.	
Headache.	None.
Sickness.	None.
Bowels. One-third of cases in hospital show diarrhœa; dysentery in 7 per cent. of such cases.	No bowel trouble.
Spleen and Liver	
Enormous enlargement of both viscera.	None.
Coagulability of the blood decreased.	Increased.
Distribution of the Parasite	
Polynuclear leucocytes infected.	Superficial polynuclears rarely, if ever, contain the parasites, whereas they swarm in the large mononuclear cells seen in a smear.
Spleen, liver, bone-marrow infected heavily.	
Intestinal ulcers and cutaneous ulcers contain the parasite.	
Cultivation and Development of the Flagellated Stage of the Parasite Showing Differences between the Two Parasites	
At 27° C., in blood containing citrate 10 per cent., parasites live for several days and multiply, but there is no material alteration in their form, and no increase in size.	At 28° C., in infected unheated undiluted serum with no citrate, flagellar forms appear in five days.
At 22° C., and not above 25° C., flagellated forms appear.	At 28° C. flagellar forms have been obtained.
Exposure to a temperature of about 25° C. causes rapid death and degeneration of the developing forms.	
Sterility of the culture tubes of crucial importance. Contamination with micrococci and bacteria causes rapid death and degeneration of the parasites, staphylococci the most deadly contamination for the parasite.	Contamination with micrococci and certain bacteria highly favourable, as the parasites develop symbiotically with masses of these organisms.
	Staphylococci the most favourable contamination. Further, the most perfect monadine forms are seen attached to large masses of staphylococci.

STAGES IN LIFE HISTORY NOTED IN THE PARASITE OF ORIENTAL SORE

(1) Monadine crithidium, very large, and several times the length of a red cell; staining blue, with a scarlet flagellum, carmine extranuclear centrosome, and rosy-violet nucleus.

(2) Flagellated rosy-pink parasite; body oval or circular; apposed to the above at about the level of the nucleus of the monadine crithidium. This presents a small dark-violet staining nucleus, and an extranuclear centrosome staining carmine, from which a long scarlet flagellum arises.

(3) Gregariniform phase of clusters of small parasites, circular, ovoid, or bean-shaped, like enormous cocci. In these the nucleus stains violet. The extranuclear centrosome, when seen, stains red-rosy, and the cytoplasm of the cell pale pink. A few are rose-coloured throughout. These clusters are usually found surrounded by masses of bacteria and cocci staining pale blue.

(4) Early forms of the parasite, showing pyriform, ovoid, and torpedo-shaped elements as ordinarily seen in the infected tissues.

Oriental Sore—*continued*

(5) Larger pyriform cells.

(6) Larger rosy bodies.

The two latter frequently occur in the same group, which may consist of 120 to 200 parasites.

The best method of obtaining clumps of the protozoa from cultures is as follows :—

Blow the contents of the infected tube into a sterile watch-glass gently, then suck up a large drop of red blood deposit ; drop this on one end of the slide, and with a fine glass pipette, avoiding actually touching the slide, draw a level film of infected blood serum and citrate to within an inch of the other end of the slide. On removing the glass pipette a large streak of blood mixture remains. Stand the slide on its end against a bottle so that this slowly streams towards the centre of the slide again ; when a thickish film is thus made, dry in air and fix in methylic alcohol for five minutes.

The most satisfactory stain for the parasite in all its stages is made up as follows : To 10 c.cm. distilled water add 12 drops of Giemsa solution, shake and pour on the slide, film upwards. Leave to stain for twenty minutes.

At the end of this time the slide will be dark purple. Wash under the tap for thirty seconds, and dip into a watery solution of eosin, 1 in 50,000, for about thirty-five to forty seconds. The film should then seem light rosy-violet. Care must be taken not to stain the film too red.

On examination of a perfectly stained film the torpedo and cockle-shaped forms show up clearly against the faint rose-coloured red cells ; the early pyriform and large flagellated monadine forms show up light blue, with scarlet flagella, their nuclei stain purple, their extranuclear centrosomes stain scarlet.

Bacilli and cocci stain deep violet.

The gregariniform phase of the parasite stands out clearly, for these are seen to be four or five times the size of the cocci ; their cytoplasm stains rosy-pink, their nuclei violet-blue.

In a later paper Carter[1] draws attention to the various types of Oriental sore which exist in India, mentions a non-ulcerating form, and takes exception to the term Oriental sore. He also refers to the possibility of there being different varieties of Leishmania producing these skin lesions. The mention of a non-ulcerating form draws attention to a paper by Thomson and Balfour.[2] In two cases from Egypt they found curious and multiple growths containing *L. tropica*, coccoid forms, and curious bodies which may or may not have been connected with the specific infection. They suggest the name Leishman nodules for these skin lesions, and enter fully into their histo-pathology. This answered closely to the description given by Jeanselme and Rist in their text-book, and differed in certain respects from the earlier descriptions. They agree with Carter's views above mentioned, and give illustrations of one case and photo-micrographs of sections of the growths, some of which presented the aspect of mountains on a relief map viewed from above. There were frequently secondary growths in the neighbourhood of the main growths with which eventually they coalesced. Leucopenia was present, and the blood from the nodules coagulated rapidly. The second case was apparently infected from the first. Further notes on the parasite and other forms found are given in the Fourth Report of these Laboratories. Culture was only partially successful, flagellated forms not being obtained, but the methods employed scarcely received a fair trial. At the time the paper was written only one instance of a similar condition had been published. As the authors say :—

The exception mentioned is given by Cambillet,[3] who recently described the case of a small native boy in Algiers, who presented on the right cheek a tumour, which, to judge from the photograph given, must be almost identical with the face growth in our case. It commenced as a small papule, increased in size until, at the time the paper was written, it measured three centimetres in diameter, and showed no sign of ulceration or discharge. It had persisted for a year in this state. On puncture it yielded blood and *de petits grumeaux blancs*, and in smears *Leishmania tropica* was found. He concluded that the case was one of "Bouton d'Orient," and certainly this term is much more applicable to his case and ours than that of Oriental sore. The latter, in any case, is a misnomer, as instances have been described from Bahia by Juliano Moreira, and recently from Bauru in Brazil by Lindenberg,[4] who found Leishman bodies present. His work has been confirmed by Carini and Paranhos.[5]

Thomson and Balfour also suggest that the occurrence or non-occurrence of ulceration may depend upon the reaction of the tissue to the virus. If this be strong the epidermic layers thicken ; if weak they are destroyed. It may be so, or special forms of Leishmania may produce their own specific results ; or again, symbiosis with cocci or bacteria may play a part.

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[1] Carter, R. M. (November 6, 1909), "A Note on Oriental Sore." *British Medical Journal.*

[2] Thomson, D. B., and Balfour, A. (1910), "Two Cases of Non-Ulcerating 'Oriental Sore,' better termed Leishman Nodules." *Transactions Society Tropical Medicine and Hygiene.* Also *Journal Royal Army Medical Corps*, January, 1910.

[3] Cambillet (July 21, 1909), "Un cas de Bouton d'Orient à Flatters (Alger)." *Bull. Soc. Path. Exot.*

[4] Lindenberg, A. (May 12, 1909), "L'ulcère de Bauru ou le Bouton d'Orient au Brésil." *Ibid.*

[5] Carini and Paranhos, U. (May 12, 1909), "Identification de l'ulcère de Bauru avec le Bouton d'Orient." *Ibid.*

Oriental Sore—*continued*

Apparently similar growths were soon afterwards described by Ferguson and Richards [1] in Egypt. Bitter and Ferguson had previously found Leishmania in ulcerated papillomatous lesions on the limbs of Egyptian fellaheen, and Ferguson and Richards describe that condition, the warty form, more fully, and also a flat, non-ulcerating form. They were unable to differentiate the parasite from the typical *L. tropica*, and state :—

The examination of a large number of specimens has shown that in those cases in which bacteria were most plentiful, parasites occurred in very scanty numbers or not at all. Our opinion is that, so far from there being anything of the nature of a symbiosis between the two, the appearance of bacteria involves the extinction of the parasite. The reason why we have failed to find the parasites in so many of the cases reported, is probably that this process of extinction had reached a point where exceedingly few, if any, parasites had survived. The specimen which contained the parasite in largest numbers was one which contained no bacteria. Whether the bacteria ever destroy the parasites sufficiently to bring about a natural cessation of the process we have no means of judging, but it seems quite possible.

The result of their researches they summarise as follows :—

(1) Certain forms of skin affection caused by *Leishmania tropica* occur not infrequently in Egypt.

(2) They may be solitary or multiple, and in the latter case are almost certainly the result of auto-inoculation.

(3) They consist essentially of a mononuclear infiltration of the subcutaneous tissues which harbour, sometimes, large numbers of the parasites.

(4) The lesions manifest themselves clinically under two forms : the one, a slightly raised, smooth, flat patch ; the other, a prominent warty growth. They run a chronic course, and are unaccompanied by constitutional disturbance.

(5) They are best treated by excision and immediate skin-grafting.

Recently Carter [2] has again returned to this interesting subject of the non-ulcerating sore, and in a well-illustrated paper states that with our present knowledge we may distinguish three types of Oriental sore : (1) the non-ulcerating Oriental sore ; (2) the superficial flat Oriental ulcer ; (3) the deep-seated Oriental boil. He gives an interesting account of both non-ulcerating and ulcerating forms in natives and Europeans, mentions the Indian names, and states that around Kohat, natives believe the lesions follow the bite of the sand-fly, an opinion which Fink expressed several years ago. Carter says that

the points of interest in the first set of cases as compared with the last are—

(1) Non-ulcerating character.

(2) Increased coagulability (of the blood).

(3) High constant infection of mononuclear cells.

(4) Rare infection of polynuclears.

(5) Long history, and appearance of other similar lesions at long intervals.

(6) Possible infection from another case in close daily contact.

(7) Primary itching followed by anæsthesia.

(8) Lesion presents constantly a central smooth surface, papery epithelial scales at periphery, margin indurated and visible to the naked eye.

(9) Liver and spleen unaffected.

(10) Possible exacerbations at irregular periods.

(11) General malaise.

(12) Occurs at all stages, and in Europeans as well as natives.

(13) First area affected usually on exposed surface.

He stains smears and films, whether from the patient's tissues or from culture tubes, as previously, stating in addition that

the films should be fixed in methyl alcohol for five minutes and blotted dry before the stain is applied.

The results of his examination of the material obtained from the lesions were very similar to those of Thomson and Balfour. He then enters more minutely than in his first paper into the appearances found in culture, and amongst other notes says :—

A curious feature in cultures of non-ulcerating Oriental sore, first noted by me in October, 1909, is the constant occurrence of enormous clusters of what seem at first sight to be giant cocci. These bodies stain purple, and have often a reddish margin or film round them. They vary from forms the same size as an erythrocyte to smaller forms, altogether like cocci, diplococci, etc. This suspicious and interesting point has since been confirmed by Thomson and Balfour in their work on non-ulcerating Oriental sore in Egypt. In the description of material from an

[1] Ferguson, A. R., and Richards, O. (July 25, 1910), "Parasitic Granuloma ; a Condition Allied to Oriental Sore occurring in Egypt." *Annals Tropical Medicine and Parasitology*, Vol. IV., No. 2.

[2] Carter, R. M. (April 20, 1911), "Non-Ulcerating Oriental Sore, the Cultural Characteristics of the Parasite as compared with a new similar Parasite in *Erthesina fullo* (Thumb.), a Pentatomid Bug." *Ibid*, Vol. V., No. 1.

Oriental Sore—*continued*

affected area on the neck, they note, in addition to the parasites found free and in mononuclear cells, groups of what seem to be large cocci, also a number of pale blue homogeneous structureless masses—a condition which is seen to occur also in cultures of the parasite from the intestinal tract of *Erthesina fullo*, to be described later. In material from affected areas on the thigh similar coccoidal bodies were found. These observers describe these blue coccoidal bodies as four to six times the size of the small cocci present. They stain feebly in their centres, often present unstained areas, occur in clumps or pairs, and may resemble huge gonococci.

In the light of recent experiments I am of the belief that the life history of the parasite of non-ulcerating Oriental sore is as follows :—

The cockle-shaped form found in the tissues and mononuclear cells represent the form of the parasite which multiplies in the cells of the host by simple fission. In their earliest form they are seen as an exceedingly minute protoplasmal ring, containing a dot-like nucleus. Such forms are occasionally seen amongst the more maturely developed forms.

After a series of divisions by simple fission in cultures, what would seem to be sexual elements are formed, which stain differently. These seem to pair with interchange of elements. From this point the cycle becomes obscure, and light alone is thrown by observations on the life-cycle of a similar parasite to be subsequently described. If dot-like forms are released from the female cell, as recently seen in *Trypanosoma gambiense*, on examination of infected salivary glands in the intermediate host, the tsetse, these elemental forms might well be the minute bodies occasionally seen in infected mononuclears.

Here then is possibly another rôle for that infective granule which I (A. B.) am convinced will be found to play an important part in many forms of protozoal infection.

Carter then passes on to describe a very similar parasite which he has found in the crop of *Erthesina fullo*, a species of Pentatomid bug common in the Himalayas and in many countries throughout the East. It is a blood-sucker, is attracted by light at night, and enters houses freely. He found the parasite which it harbours has a selective preference for human blood, and while we cannot follow him throughout his interesting description of its life-cycle and the experiments he conducted, the following paragraphs may be quoted :—

To review the points of similarity between the parasite causing non-ulcerating Oriental sore and that infesting the intestinal tract of *Erthesina fullo*.

They both multiply and develop pyriform forms, monadine and circular or oval flagellated forms, in a culture of human blood acidulated with sodium citrate. Neither parasite will develop in an alkaline medium. They both live and develop symbiotically with masses of cocci and bacteria.

Bodies like giant cocci and bluish homogeneous bodies are found in cultures of both parasites.

Pairs of dissimilarly shaped and staining flagellated parasites are seen in both cases, whilst in the parasite of *Erthesina fullo* cyst-like bodies have been found suggestive of the formation of multiple early forms from a fertilised female.

It is probable that these researches will throw fresh light on an interesting and important problem. Hitherto *L. tropica* had only been grown in liquid media or in the liquid portion of solid media, *i.e.* the blood-stained water of condensation in blood-agar tubes. Nicolle and Manceaux [1] have now succeeded in growing it on the solid part of the modified Novy-MacNeal medium (NNN). They cite two precautions which are necessary if this is to succeed—*i.e.*, do not use an old tube where the surface of the medium is dry; and before inseminating remove the water of condensation with a sterile pipette. One advantage of this method is that much better stained preparations are obtained. These authors [2] also furnish one of the most important recent papers on the subject, dealing as it does with inoculation and immunisation experiments. It is advisable to give a brief translation of their seventeen conclusions, omitting points already noted in this review :—

(1) *L. tropica* in Africa Minor is the same as elsewhere, and produces the same kind of lesion.

(2) The best time for making subcultures appears to be from the tenth to the fifteenth day of the culture. They can be carried on indefinitely.

(3) In culture *L. tropica* is identical with *L. infantum*. The only apparent difference is that the former is more active.

(4) The virus is pathogenic for man, the lower monkeys and the dog. With the monkey virus they obtained serial infection in monkeys (three passages) and once with that of man. With the dog virus they obtained serial infection in dogs (three passages).

(5) The first cultures of *L. tropica*, those made direct from the lesions of human origin, have given the same results in man and monkey.

(6) In all susceptible animals the lesions are identical. After an incubation period of from 16 to 166 days, usually long and always without any symptoms, hard papular tubercles appear, sometimes tender and involving the skin, which takes on a violet-red hue. The further development varies. They may disappear or pass on to ulceration. Cure results after a longer or shorter period, the longest noted being 90 days. Relapse was observed in two cases.

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[1] Nicolle, C., and Manceaux, L. (May 12, 1911), "Culture de *Leishmania tropica* sur milieu solide." *C. R. Soc. Biol.*

[2] *Idem* (September, 1910), "Recherches sur le Bouton d'Orient." *Ann. de l'Inst. Past.*

Oriental Sore—*continued*

(7) Sections of the lesions show the same appearance as in Oriental sore in man.

(8) In order to obtain constant positive results with the experimental virus it is necessary to take the material from very young lesions.

(9) The virus is inactive for the goat, cat, sheep, white rat, horse and ass.

(10) Strong and repeated doses of culture, if injected into the peritoneal cavity, are deprived of all pathogenic power. In the case of susceptible animals it is therefore necessary to make the inoculation into the thickness of the skin or in its neighbourhood.

(11) The seat of election for inoculation in the monkey and dog is the nose; for monkeys, the eyelids or their proximity.

(12) A first attack of Oriental sore confers immunity against a virulent experimental inoculation if the primary lesions are wholly cured and a sufficient time has elapsed. If the second inoculation is practised early during the evolution of the primary lesion, or still more at the time of its appearance, there is, on the contrary, an increased susceptibility shown by a shortening of the incubation period.

The virus of an affected dog can be successfully re-inoculated into the same dog during the evolution of the lesion from which the virus is derived.

(13) A preliminary intraperitoneal inoculation of 100 cultures of *L. tropica* does not confer any immunity on a dog when the animal is afterwards properly inoculated on the skin.

(14) In kala-azar they have demonstrated a negative phase of hyper-sensibility to the virus before the refractory state is established.

(15) A first cured attack of kala-azar protects the dog against inoculation with the virus of Oriental sore. Immunity also exists in this animal against the latter during the whole period of infection with kala-azar.

(16) The strong analogies which exist between the Leishmania of Oriental sore and of kala-azar, especially their morphological resemblance and their common pathogenic action for the same three species of animals—man, the monkey, and the dog—in no way indicates that they are one and the same protozoon the degree of virulence of which communicates to the infections of susceptible animals a different character and development. The question can only be settled by a knowledge of the intermediate host which forms the natural reservoir of the virus. If it is shown that the same vector is operative in both cases one may conclude that the Leishmania are not identical. If, on the contrary, there are two different vectors, it will suffice to infect each of them with the ordinary virus of the other, and a conclusion can then easily be drawn according as the effects on the same vector with the two viruses are or are not identical.

It is already known that the virus of kala-azar introduced into the neighbourhood of the skin in susceptible animals does not produce lesions identical with those of Oriental sore.

(17) There is reason to suspect the dog as a natural reservoir of the virus of Oriental sore. If so, this animal plays a very important rôle in the etiology of Leishmania infections.

In a still later paper Nicolle and Manceaux [1] present some new facts, the result of further work. They describe a curious case wherein a man inoculated with *L. tropica* from a monkey strain showed an incubation period of seven months. They think this may be due to the fact that the appearance of the lesion followed closely on an attack of Malta fever, and that the latter had diminished the resistance to the parasites and permitted such as survived to develop.

Sections of organs of infected dogs show no parasites. Observations on dog and man seem to indicate that a first non-effective inoculation of the virus or culture confers resistance to the inoculation of an active virus in the latter. The immunity conferred by a first successful experimental inoculation, however, does not appear very stable or very durable.

The result of Wenyon's [2] recent investigations in Bagdad has been issued in the form of a report. A good deal of interesting work has been accomplished, but nothing very special has been elicited. The research was conducted with a view to clearing up the following points :—

(1) The characters and course of the disease in man.

(2) The examination of lower animals for signs of the disease and inoculation of these from man.

(3) Study of the various biting flies, ticks, etc., found in Bagdad.

(4) Experiments with the biting flies fed on date boil cases and dissection of flies.

(5) Examination of the date boil parasite as it occurs in the sore.

(6) Culture experiments with the date boil parasite.

As regards (1) Wenyon notes that the terms male and female sore are justified clinically. As the types of two extremes there exist the ulcerating and the non-ulcerating sores. The former is the so-called female sore, the latter the male. He describes their appearance, and indicates that the incubation period, about which it was difficult to obtain precise information,

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[1] Nicolle, C., and Manceaux, L. (March 8, 1911), "Données expérimentales nouvelles sur le Bouton d'Orient." *Bull. Soc. Path. Exot.*

[2] Wenyon, C. M. (April 1, 1911), "Report of Six Months Work of the Expedition to Bagdad on the Subject of Oriental Sore." *Journal Tropical Medicine and Hygiene.*

Oriental Sore—*continued*

may be as short as a fortnight. The disease usually lasts a year, and the male sore may never break down. In the ulcerating type he found streptococci, staphylococci, various bacilli, and frequently a diplococcus resembling very closely the gonococcus, in that it occurs in pairs within the pus cells. He mentions a subacute ulcer liable to be confounded with the true date boil in which this organism is present. One attack, provided the sore is completely healed, confers permanent immunity, but Wenyon records one fact which, in the light of the view held by Markham Carter, Thomson, and myself, may prove significant, namely, that persons who have suffered from Aleppo boil, coming to Bagdad, have been known to contract the Bagdad lesion.

The parasite was not found in the peripheral blood, and there are no constitutional symptoms.

As regards (2) the author states that dogs are supposed to suffer from date boil about the nose. He examined a few such sores, but failed to find *L. tropica* in them, nor did he find this parasite in a dog with an ulcerating condition of the legs which had been regarded as date boil even after repeated examinations. He examined cats and rats with a negative result, and inoculated rats, rabbits, birds, and even ticks, in vain. Camels are rare in Bagdad. There was no evidence that the horse, mule, donkey, or ox had anything to do with the disease. With respect to (3 and 4) Wenyon passes in review the possible rôle of house-flies, *Stomoxys*, *Hippoboscidæ*, *Tabanidæ* (not found in the town). Fleas, lice, ticks, bed-bugs, sand-flies (Phlebotomus), and mosquitoes. He finds that house-flies can readily take up the virus, and can undoubtedly act as mechanical vectors, carrying the parasite to a wound or sore, but he is unable to throw any further fresh light on the subject, save that he found a partial development of *L. tropica* in the bed-bug, due, he thinks, merely to the favouring influence of the large amount of blood ingested by this insect. Under (5) he describes the parasite in the sore, noting that forms without nuclei are frequently seen. He regards them as probably degeneration forms. Re (6), culture was successful. Rabbit blood-agar is a better medium than that prepared with dog's blood. It is unfortunate that Wenyon could not obtain animals susceptible to inoculation. Had he been able to work with monkeys he might have confirmed and extended the researches of Nicolle and Manceaux. The examination of the peripheral blood has been mentioned. The only observer who has found *L. tropica* in this situation is Neumann.[1] On two occasions, with six months interval between them, he has seen parasites free in the plasma of blood taken from the finger, and states that at these times the patient suffered from a feeling of fatigue and from a slight access of fever.

Billet[2] has described a case of Biskra button. Like others, he found that blood from the congested zone at the periphery of the lesion showed an increase of mononuclears which was not present in finger blood. Commenting on the case, Jeanselme pointed out that certain forms of Oriental sore resembled warty and vegetative tuberculous skin lesions, *i.e.* some varieties of lupus.

Gros,[3] who has published an account of four cases on the Algerian littoral, is of Carter's opinion as regards direct transmission from case to case. In no instance was infection transmitted from his cases to those in contact with them. How close this contact is likely to have been any one conversant with North African customs and usages knows. Gros concludes that "le bouton d'Orient parait donc peu contagieux."

Row[4] has described the changes the flagellate body undergoes in cultures *in vitro*. Coccal bodies appear amongst the disintegrating masses of flagellates, and the condition seems to be something like that described by Carter. He stated that—

> Compared with Nicolle's result, it would appear that the Tunisian (Nicolle's) parasite is distinct from the Indian species. Experiments on monkeys—*Macacus sinicus*—showed that after the contents of a sore from the human lesion were used to infect a monkey by cutaneous scarification, tiny nodules formed at the seat of the lesion, and in the fluid obtained parasites of a larger type than in the human lesion were found. This would seem as if the parasite had undergone the first stage of development. Further cultures and experiments with monkeys appeared to demonstrate that the sore in monkeys is distinct from Nicolle's observations in Tunis. There seems no proof that a biting insect is required for the production of the disease, but rather that the common house-fly is the transmitting agent. Patients with Oriental sores are often seen with swarms of flies around them, and it

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[1] Neumann, R. O. (1909), "*Leishmania tropica* im peripheren Blute bei der Dehlibeule." *Cent. f. Bakt.*, I. Orig., Vol. LII.

[2] Billet, A. (February 10, 1909), "Sur un cas de Clou de Biskra (avec présentation du malade)." *Bull. Soc. Path. Exot.*

[3] Gros, H. (June 9, 1909), "L'ulcère à Leishmania (Bouton d'Orient) sur le littoral algérien." *Bull. Soc. Path. Exot.*

[4] Row, R. (August 1, 1910), "Further Observations on *Leishmania tropica* of Oriental Sore of Cambay, India." *Journal Tropical Medicine and Hygiene.*

is not unlikely that the parasites from their sores could be transferred directly from person to person, either in the legs of the fly or through its excreta, and an accidental nail scratch, made owing to the tickling of the fly on the spot, would be all that is necessary for the infection. Oriental Sore—*continued*

Darling [1] has recorded a case of autochthonous Oriental sore from Panama, a new locality. One may say here that it has also been found in French Guiana, New Caledonia, and the region of the Zinder in Africa, where it forms one type of craw-craw. In Darling's case the histo-pathology of the ulcer was not unlike in certain particulars that of the Leishman nodules (*loc. cit.*). The author suggests Dermal Leishmaniasis or Ulcerating Leishmaniasis as a name for the condition, but, as already stated, Superficial Leishmaniasis would be better, for some cases show no ulceration, and quite recently Carini [2] has described and illustrated a case of Leishmania of the rhino-buccal-pharyngeal mucosa, occurring in Brazil. The disease began with ulcers of the legs, but a year after their appearance an erosion of the palate commenced. The disease followed a slow and painless course, eventually involving the nose and pharynx. Typical *L. tropica* were found in the lesions. Carini says that infections of the mucosa occur almost always in patients who have been suffering from the cutaneous form. Sometimes it is merely a question of spread from the skin to the neighbouring mucous membrane, but in other cases the lesion starts *de novo* in the latter, as, for example, the palate, and in such cases the condition is not likely to be due to auto-inoculation from the skin lesions. He believes mucous membrane infections are more common than is thought to be the case, and points out that the absence of giant cells in the lesions is important in distinguishing Leishmaniasis from blastomycosis. In the latter, giant cells, as a rule, are very numerous.

The natural immunity of mice to inoculations with cultures of *L. tropica* has been the subject of study by Delanoe,[3] but we can only give the reference and hurry on to the subject of treatment, about which there is little to be said, although recent work has made the outlook more hopeful.

Marzinowsky's method was mentioned in the First Review. Billet (*loc. cit.*) cites the plan adopted by Benoit, namely, (1) Cleanse the surface thoroughly and then dust it with finely powdered permanganate of potash. (2) At the end of 8 or 10 days, after removing the crust which has formed, paint the brawny elevations with a 1 in 10 solution of methylene blue. This method has been successfully used in twenty-one cases of the North African type. Bussière and Nattan-Larrier [4] mention the use of iodine, silver nitrate, carbolic acid, permanganate of potash and methylene blue, but think that in many cases excision is indicated. With this finding Laveran does not agree, believing it to be contra-indicated in all cases, and possibly also dangerous. References are given to methods described by Gueytat and Moty.[5] Aviss [6] mentions Lincoln's treatment as used in India. It consists in the application of "rausath," a dark green fluid prepared from a very dark green gummy exudation, dried in and mixed with the leaves of the tree from which it is obtained. This is painted over the sore and allowed to dry, no dressing being applied. Every day a fresh coat is painted over the old one. A scab comes away after about a fortnight, and the surface is found completely healed. This method deserves to be widely known, and should be fully tested.

Benoit-Gonin [7] gives more details regarding the permanganate treatment, which, it is maintained, leaves no brown pigmentation in the scar; but of greater interest is a paper by Nicolle and Manceaux [8] on the use of salvarsan in two cases, one multiple. They gave the drug by intramuscular injection. In the first and milder case the dose of 0·3 gramme was not sufficient, and the benefit was temporary; in the second case 0·6 gramme was given, the result being remarkable, the condition being nearly cured in five days, and wholly so in twenty. An interesting and recent development is the employment by Broome [9] of carbonic acid snow.

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[1] Darling, S. T. (December, 1910), "Autochthonous Oriental Sore in Panama." *Transactions Society Tropical Medicine and Hygiene.*

[2] Carini, A. (May 10, 1911), "Leishmaniose de la muqueuse rhino-bucco-pharyngée." *Bull. Soc. Path. Exot.*

[3] Delanoe, P. (March 17, 1911), "L'immunité naturelle de la souris à l'égard des cultures de Kala-azar et de Bouton d'Orient Tunisiens." *C. R. Soc. Biol.*

[4] Bussière, A., and Nattan-Larrier, L. (June 9, 1909), "Essais de Traitement du Bouton d'Orient." *Bull. Soc. Path. Exot.*

[5] Gueytat and Moty (November 10, 1909), "Note sur le Traitement du Clou de Biskra." *Ibid.*

[6] Aviss, W. G. (July, 1910), "The Treatment of Oriental Sore." *Journal Royal Army Medical Corps.*

[7] Benoit-Gonin (April 12, 1911), "Note sur le Traitement du Bouton d'Orient." *Bull. Soc. Path. Exot.*

[8] Nicolle, C., and Manceaux, L. (April 12, 1911) "Application de L'arsénobenzol au Traitement du Bouton d'Orient." *Ibid.*

[9] Broome, H. H. (April, 1911), "The Treatment of Oriental Sore." *Indian Medical Gazette.*

Oriental Sore—*continued*

It is applied with firm pressure for forty seconds to thick and dense portions, and twenty-five seconds to the edges. There is some burning pain at the time of application, which rapidly passes off, to be followed during the reaction stage by a more severe and prolonged burning sensation. A blister forms which may be punctured. Cotton wool is applied and healing takes place under a scab. A small sore will apparently heal up in ten days. There certainly seems a future for this simple and effective method.

Parasites. It is quite impossible in a review of this nature to deal with all the papers relating to the subject of parasites, and although it is somewhat difficult to draw any hard and fast line as to the papers that should be included, it is hoped that the references given will be found useful to the worker in the Tropics. As in the last Review, the article is limited almost wholly to the metazoa. Some grouping has been attempted but it is not easy to classify so many aspects of a large subject.

The rôle played by parasites in causing disease either directly or indirectly was considered in our first Review and scarcely requires further mention, but one may quote some remarks by Washburn [1] in a paper dealing with "Health in the Philippines."

> There appears to be a greater abatement among civilians than among soldiers of diseases due to intestinal parasites. Intestinal diseases due to parasites are positively known to be preventable by the exercise of sufficient care in eating and drinking. Fortunately, too, the great majority of cases yield to treatment. There is reason to believe that in the near future intestinal parasites, through the achievements of preventive medicine, may cease to be important factors in producing intestinal diseases. This accomplishment will be almost as much of a boon to the tropics as was the discovery of the means of preventing yellow fever.

In a note in the *Lancet* reference is made to a series of papers published by Stiles and Goldberger [2] relating to parasitic worms.

A peculiar case of parasitism in man was observed in Florida :—

> The worms, which live in the subcutaneous tissue and cause swelling resembling acne, have been determined as very closely related to, and perhaps identical with, *Sparganum proliferum*. This parasite has been reported on only one former occasion, when it was found in Japan, but its life history, source of infection, prevention, and treatment are still unknown. Its chief peculiarity is a reproduction in its larval stage by the formation of supernumerary heads, which may become independent and wander through the tissue.

Shipley [3] has an interesting paper entitled "A Cause of Appendicitis and other Intestinal Lesions in Man and other Vertebrates." The paper is too long to be fully referred to, but one notes that mention is made of the important part played by parasites as a cause of appendicitis. Shipley mentions in particular *Oxyuris vermicularis*, *Ascaris lumbricoides*, and *Trichocephalus trichiurus*, and gives various references to papers illustrating the part played by these nematodes in the causation of appendicitis and peritonitis.

The same author [4] has an interesting paper referring to the relation of certain cestode and nematode parasites to bacterial disease. In this paper a description is given of a fatal epidemic disease among rainbow trout caused by nematode worms, some of which had penetrated to the swim bladder of the fish, apparently from the intestine, through the intervening tissues. The swim bladder of infected fish showed extensive invasion by intestinal bacteria, while the same organ in healthy fish was entirely free from such organisms. Allusion is also made to the occurrence of a species of *Strongylus quadriradiatus* in the intestines of pigeons which had died from an unknown malady. The intestinal walls of the pigeons were in all probability pierced by the parasite, and thus permitted the passage of the bacteria from the interior of the bowel into the peritoneal cavity.

Manson and Sambon [5] describe a case of intestinal pseudo-parasitism due to *Chilodon uncinatus*, a ciliated infusorian. The patient infected with this parasite complained only of slight looseness of the bowels for several years. As *Chilodon uncinatus* is, as a rule, a free living organism inhabiting fresh-water bodies, its presence in the intestine of man must be looked upon rather in the light of a chance or pseudo-parasite.

Rather a useful paper by Royal [6] refers to the subject of pseudo-parasites, and will be

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[1] Washburn, W. S. (September, 1908), "Health Conditions in the Philippines." *Philippine Journal of Science*, B.

[2] Stiles, C. W., and Goldberger, J. (1908). *United States Public Health and Marine Hospital Service, Washington, Bulletin* No. 40. Quoted in *Lancet*, July 11, 1908.

[3] Shipley, A. E. (December, 1908), "A Cause of Appendicitis and other Intestinal Lesions in Man and other Vertebrates." *Parasitology.*

[4] *Idem* (1909), "On the Relationship of certain Cestode and Nematode Parasites to Bacterial Disease." *Journal of Economic Biology.*

[5] Manson, P., and Sambon, L. W. (March 20, 1909), "A Case of Intestinal Pseudo-Parasitism due to *Chilodon uncinatus* (Blochmann)." *Lancet.*

[6] Royal, M. A. (March, 1908), "Pseudo-Parasites." *Bulletin of the State University of Iowa*, No. 182.

found very useful by those who have to carry out examinations of fæces for intestinal parasites. Royal divides the pseudo-parasites into two classes :— Parasites —*continued*

First. Those which are actually free living animals introduced by accident, usually in food and drink, into the human alimentary canal, and exciting therein abnormal conditions which induce their more or less immediate forceful expulsion. Examples : Botkin found in the vomit of a Russian numbers of small nematodes, which he wrongly thought to be a human parasite. This nematode lives normally in the onion, and its introduction into the stomach with this vegetable excited the symptoms noted. Cases of gordius, the hair snake : about a dozen cases taken from a man after a supposed sojourn of a few hours to fourteen days have been reported. Some of these have been vomited, others passed per anum. This form has often been mistaken by the physician for a true parasite, and in one celebrated case, at least, as a guinea-worm. There are forty recorded cases where myriapodes were mistaken for pseudo-parasites. The ingestion of such forms is purely accidental. The symptoms are those of helminthiasis. They remain at longest a very short time, and never show adaptation to their new environment.

Second. This class is composed of parts of substances of both plant and animal origin, used as food, which have not been destroyed by the action of the digestive juices. Examples : The radulæ of the common limpet have on several occasions been reported as found in the stools. The seeds of the mulberry have been mistaken for a parvalin worm, and plant tissue and other similar undigested structures of peculiar shape, appearing periodically, as new helminthes. That a differentiation of such structures is not easy is proved by the account given by Stiles and Bierring and Albert of the similarity of appearance of the partially digested banana fibres to minute tape-worms. Some years ago Leuchart entrapped a group of students doing research work in helminthology with the pulp vesicles of an orange which were found in the field of examination.

Under the heading of "Pseudo-Parasites simulating Animal Parasites," Royal calls attention to the fact how very difficult it sometimes is to distinguish these pseudo-parasites, such as banana fibres, orange cells, celery fibres, etc., from animal parasites. He mentions points to aid the differential diagnosis. Reference, however, to this paper has already been made under another section (*vide* "Fæces").

A few papers relating to trichinosis will also bear reference. Among them is a good one by Albert and Norris [1] relating to a small epidemic of trichinosis due to the eating of boiled ham. These observers were unable to determine at what temperature the infected hams had been boiled before being issued for consumption. They consider that the temperature required to kill trichina will depend on the degree of encapsulation of the embryonic forms and the nature of the capsule, whether the latter is simply a fibrous one or whether it has become calcareous.

This is a subject which would be well worth investigation, inasmuch as trichina infection of hogs is of frequent occurrence (it has been estimated that about 2 per cent. are infected), and inasmuch as our Government no longer inspects meat for home consumption for the presence of these parasites. Cooking seems to be the only effective prophylactic measure against trichina infection. Thorough salting and hot smoking also generally kills the parasites. They have been found alive in pickled meat for fifteen months, and have been known to resist freezing for two months.

The paper has a special reference to the occurrence of eosinophilia in this epidemic. The conclusions of these observers are worth quoting :—

(1) Trichinosis is no doubt of far more frequent occurrence than is usually supposed. Many cases are no doubt diagnosed as cases of typhoid fever, rheumatism, ptomaine poisoning, cholera morbus, etc., or considered as obscure conditions.

(2) Trichinosis usually results from the eating of uncooked seasoned or smoked pork or sausage, but may result from the eating of boiled ham which has not been exposed to a sufficient temperature for a sufficient length of time to kill all of the parasites.

(3) A temperature of 170° to 200° F., maintained from one to six or more hours, depending upon the size of the ham, no doubt destroys the trichinæ in the vast majority of cases. Investigations made to determine exactly just what temperature maintained for what length of time is necessary to kill trichina should be made.

(4) The severity of the case varies with the number, and no doubt also the vitality of the parasites. In the outbreak which we reported, although the symptoms were in many cases quite severe, there were no deaths. The usual mortality ranges in different outbreaks from 1 to 30 per cent.

(5) Every means should be adopted to prevent infection of hogs by removing, if possible, the possibility of their eating dead rats.

(6) All pork consumed in any other form than boiled ham should have all parts raised to the boiling point.

(7) The diagnosis of trichinosis occurring in isolated cases is frequently a matter of difficulty, and often can be greatly assisted by means of an examination of the blood.

(8) So far as we know at the present time there is no condition in which the percentage of eosinophiles in the blood reaches such a high number, so constantly as in trichinosis.

(9) Eosinophilia occurs in practically every case of trichina infection. A few cases have been reported where there was no eosinophilia (Da Costa, Howard, Rosenberger). Some of these were cases of severe infection, and in others an examination was made too long after the time of acute symptoms to be certain whether or not eosinophilia was or was not present at some time.

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[1] Albert, H., and Norris, H. W. (March, 1908), "The Study of a Small Epidemic of Trichinosis due to the Eating of Boiled Ham. Special Reference to the Occurrence of Eosinophilia." *Bulletin of the State University of Iowa*, No. 182.

Parasites —*continued*

(10) The eosinophilia of trichinosis varies ordinarily from 10 per cent. to 60 per cent.

(11) The highest percentage known to us was in one of our own cases in which it reached 72 per cent. The next highest of the reported cases is 68·2 per cent. (Brown).

(12) Eosinophilia makes its appearance with the beginning of the acute muscular symptoms which represents about the seventh to twelfth day after infection. It is at its highest at the height of the acute muscular symptoms, which is ordinarily during the second or third week after infection. After this time it gradually disappears, so that at the end of the second or third month there is usually no increase in the number of these cells.

(13) The total leucocyte count is usually, but not invariably, increased in trichina infection. The number of neutrophiles is relatively and sometimes absolutely diminished during the period of eosinophilia.

Mention may be made of a simplified method of examination for trichinæ as described by Böhm,[1] who carried out some tests on swine infected with trichinosis. He also examined them according to the methods of Reissmann,[2] and drew the following conclusions :—

(1) That the pillars of the diaphragm are the position in which trichinæ can most certainly be found, even in cases where swine are only slightly infected.

(2) That when swine are severely infected with trichinæ the tongue test is only a little less valuable than that of the diaphragm. As an example of this, Böhm found in each six preparations of the pillars of the diaphragm eighty-five trichinæ, of the larynx thirty-two, and of the tongue eighty-one.

(3) Sometimes it appeared clear that six preparations from the pillars of the diaphragm were too few, as contrasted with the other tests. In twenty-four preparations made according to Reissmann's directions, only one trichina was found in one preparation from the tongue. In a fresh series of twenty-four preparations from the pillars of the diaphragm seven were discovered. In the first six, none ; in Nos. 7, 10, 11, 17 and 23, one in each ; in No. 15, two. According to Böhm's view the efficiency of the method would not be diminished if, in place of the system proposed, twelve preparations were taken from the pillars of the diaphragm and six from the muscular tissue of the tongue at some point where the muscular fibres are continuous with a tendon.

Paul Wachter, an optician in Friedenau, has introduced improvements in the microscope which would lessen the expenditure of time and simultaneously increase the reliability of the method. The optical field, which in the former instrument had a diameter of 2 to 3·5 mm., now extends to 6 mm., and, with the tube thrust home and a correspondingly lower magnification, to as much as 9 mm. It is therefore clear that the crushed fragment could be completely examined by passing it twice through the field of vision in the longitudinal direction of the fibres—that is, from above downwards and again upwards. By using this modern form of microscope a well-trained observer might examine eighteen preparations in from ten to twelve minutes without any loss of efficiency, as contrasted with the old method.

Gaisböek [3] has a paper on the blood condition in trichinosis occurring in two patients as the result of eating the uncooked flesh of a trichinous hog. The disease was of a different type in the two cases. In the one case it closely simulated typhoid, and in the other there was a remittent fever associated with pains in the muscles.

Examination of the blood showed in both cases a very decided increase of the eosinophile polynuclear cells —in the first patient up to 20·79 per cent., in the second 48·66 per cent. In both cases the number of eosinophiles quickly diminished from the first height only to again increase and finally gradually diminish as convalescence set in. The first rapid fall was coincident with an increase in the severity of the symptoms, and is to be explained either as the result of the severe damage to all the organs, including the blood-forming organs, or of the onset of a new illness, probably through a mixed infection. Other observers have noted a similar fall in the number of eosinophiles during a bacterial infection, and it may obviously in trichinosis lead to errors of diagnosis if the blood be only examined once at the height of the disease. The lymphocytes showed an absolute increase at first up to 10·5 per cent. and 12·36 per cent. in the two cases respectively ; in both cases a further rise followed and continued during the whole period of observation, in one case being still present after a year. In the early part of the illness the whole number of leucocytes showed a moderate increase, being 11,300 and 12,000 respectively. This increase of leucocytes would negative a diagnosis of typhoid fever, in which condition there is a diminution of the total number of white cells, together with a relative increase in lymphocytes. The similarity in the condition of the blood in the two cases described in the article supported the view that both sprang from the same cause. The author believes that trichinosis may be diagnosed simply from the examination of the blood. Among other noticeable clinical points was the falling of the diazo-reaction at the height of the illness ; in one case, with the onset of venous thrombosis, as the diazo-reaction had dropped almost to nil, there was an intense diminution of the urobilin reaction and aldehyde reaction of the urine. In one of the cases, but not in the other, the typical condition of the reflexes—presence of Kernig's sign with absence of patellar and Achilles reflex—was well marked.

Romanovitch [4] has carried out some researches in connection with trichinosis. He found that the serum of trichinosed guinea-pigs and rats contained iso- and hetero-toxic properties. This toxicity, however, was not present in animals that were very heavily infected, and although existing nine days after infection did not last longer than a period of five to six

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[1] Böhm, J. (1909), "Eine neue Trichinendemie in Bayern." *Zeit. f. Fleisch u. Milchhyg.* Quoted in *Journal Comparative Pathology and Therapeutics*, March 31, 1909.

[2] Reissmann, E. (1908), "Kann die Trichinenschau ohne sanitären Nachteil beschränkt und verbilligt werden ?" *Ibid.*

[3] Gaisböek, F. (1909), "Beobachtungen über Trichinose, zugleich ein Beitrag zur diagnostischen Bedeutung der Blutuntersuchung." *Wien. Klin. Woch.* Quoted in Epitome, *British Medical Journal*, November 27, 1909.

[4] Romanovitch, M. (March 3 and March 10, 1911), "Recherches sur la Trichinose." *C. R. Soc. Biol.*

weeks. The toxic substances due to the presence of the larvæ were excreted by the kidneys, for in his experiments he found that the urine contained very toxic properties when injected into guinea-pigs. Parasites —*continued*

In a more recent paper this observer describes the results of blood cultures carried out on trichinosed rats and guinea-pigs that were killed at various stages of the disease. Various kinds of organisms were isolated, including *B. coli*, streptococci, staphylococci, *B. subtilis*, *B. mesentericus*, etc. As a result of his researches he concludes that the fever, abscess formation, and the general septicæmia which is frequently present in man is due to the presence of organisms inoculated by the *trichina*.

Coriat [1] has reported a very interesting case of trichinosis in a man in which symptoms resembling myotonia occurred.

Eight years before the patient came under observation there had been a history of a severe gastro-intestinal attack. Shortly afterwards a stiffness was noticed in the right leg, followed by a weakness of the muscles of the right foot. Finally, the left leg and foot became affected. On examination the calf muscles were seen to be thin and flabby. At first the foot could be flexed and extended rapidly, but then the movements became slower and more difficult, and then almost ceased, the calf muscles becoming hard and rigid. Walking produced the same effect. The correct diagnosis was reached by excising and sectioning pieces of the muscle, the larvæ of the *trichina* being found.

For a complete description of the disease a text-book by Stäubli [2] entitled *Trichinosis* may be consulted. It contains an account of a number of researches carried out by the author.

Mention may be made of a paper by Ströbel [3] dealing with the serum diagnosis of trichinosis.

Broden and Rodhain [4] have two very valuable papers entitled "Contribution à l'étude de *Porocephalus moniliformis*." In the first paper mention is made of the finding of nymphal porocephali in the omentum of a Congo native soldier and in four monkeys (*Macacus* sp.) from the Upper Congo, and the larvæ are described as belonging to the species *Porocephalus moniliformis* (Diesing). Illustrations of the larvæ are given in this paper.

The second paper [5] records the finding of the same parasite in five more monkeys (*Macacus* sp.) and three snakes (a Gaboon puff-adder, *Bitis gabonica*, and two West African pythons, *Python sebæ*).

In the monkeys they were chiefly present in the omentum, while in the snakes they were found to be present in the pulmonary sacs; the young forms being present in the monkeys and the adults in the snakes. These observers describe a number of experiments with a view of elucidating the life history of the parasite and the methods of infection in man and animals. They conclude that men, monkeys, rats, and cats become accidentally infected by swallowing the eggs of the parasite, and that these animals constitute the intermediate hosts of the parasite; while snakes constitute the definite host, and become infected by swallowing the intermediate host.

Sambon [6] has some remarks on Broden and Rodhain's papers. He considers that the lingatulid found and described by these observers as occurring in the Congolese native and monkeys is the nymphal form of *Porocephalus armillatus*, and that *Porocephalus moniliformis* belongs really to the Oriental region, and in its adult form is a parasite of the Indian python (*Python molurus*), differing in the tapering shape of its body, the larger number of rings and other particulars from the closely allied Ethiopian species which spends its maturity in the throat of African snakes. He is also at variance with the remarks made by Broden and Rodhain concerning the rarity of porocephalus in man, for he considers that tongue-worm infection in man is more prevalent than is generally supposed, not only in Africa but in other tropical countries, and even in Europe.

Breinl and Hindle,[7] in a short paper, give a description of a new species of porocephalus

[1] Coriat, I. (December 29, 1910), "Trichinosis in Man." *Boston Medical and Surgical Journal.* Quoted in *Journal Tropical Medicine and Hygiene.*

[2] Stäubli, C. (1909), *Trichinosis.* Wiesbaden.

[3] Ströbel, H. (March 28, 1911), "Die Serodiagnostik der Trichinosis." *Münch. Med. Woch.*

[4] Broden, A., and Rodhain, J. (February, 1908), "Contribution à l'étude de *Porocephalus moniliformis.*" *Annals Tropical Medicine and Parasitology.*

[5] *Idem* (February, 1909), "Contribution à l'étude de *Porocephalus moniliformis.*" *Ibid.*

[6] Sambon, L. W. (March 15, 1909), "Remarks on Drs. Broden and Rodhain's Paper on *Porocephalus moniliformis.*" *Journal Tropical Medicine and Hygiene.*

[7] Breinl, A., and Hindle, E. (February 3, 1909), "A New Porocephalus. *Porocephalus cercopitheci.*" *Annals Tropical Medicine and Parasitology.*

Parasites —*continued*

found encysted in the lung of a monkey (*Cercopithecus callitrichus*). They name this parasite *Porocephalus cercopitheci* n. sp., but Sambon [1] in a more recent paper pointed out that this parasite had been previously described by Leuckhart in 1860 under the name of *Pentastomum subuliferum*. Sambon also mentions that this same species has been found by him in the Gaboon puff-adder (*Bitis gabonica*).

Sambon [2] has a long and interesting article entitled "Porocephaliasis in Man," in which a full description of the species of *Porocephalus* affecting man is given.

In a more recent paper by Broden and Rodhain [3] these observers remark that their original observations (*loc. cit.*) on the parasite they considered to be *Porocephalus moniliformis* really referred to *P. armillatus*, as pointed out to them in a private letter written by Professor Gedoelst, who has thereby confirmed some of Sambon's remarks (*loc. cit.*) on Broden and Rodhain's paper. They carried out some further experiments, an account of which is given in this paper, and they conclude (1) That the definite hosts of *P. armillatus* are the large serpents *Python sebæ* and *Bitis gabonica*. (2) The natural intermediate host is the monkey, but that all other animals or man may be accidental intermediate hosts. (3) That the intermediate host becomes infected by swallowing the eggs of the porocephalus. (4) That the definite host becomes infected by swallowing the naturally infected intermediate host. (5) That in the intermediate host the larvæ of the porocephalus develop very slowly, whereas in the definite host the larvæ develop very rapidly. (6) The porocephalus introduced into the stomach of the definite host bores its way through the wall of the stomach and reaches the pulmonary sacs *via* the cellular tissue. (7) In the intermediate host the larvæ of porocephalus do not bring about anatomical or inflammatory lesions unless under exceptional circumstances.

A paper by Shipley [4] gives a description of a new porocephalus, *P. pachugensis*, found encysted in the liver of a female *Kachuga lineata* (Gray), a representative of the family *Testudinidæ*. Other pentastomids, such as *Linguetula subtriguetra* (Diesing), *P. moniliformis* (Diesing), *P. claratus* (Lohrmann), and *P. bifurcatus* (Diesing), are also discussed in this paper.

Wolferstan Thomas [5] has an interesting and important paper entitled "Œsophagostomiasis in Man." The following are the features of the case mentioned by this observer :—

The history of this case of œsophagostomiasis is unknown. The patient, a man, aet. about thirty-six, a native of the Amazon State, came from the river Purus region. He was admitted to the public ward of the Santa Casa in Manaos as suffering from dysentery. He became delirious and died within three days of entrance. The autopsy was performed ten hours after death.

On opening the abdomen a chronic peritonitis was seen, involving the right side and matting the omentum and coils of the small intestine to the cæcum and ascending colon. The small intestine was distended with gas. The spleen was not enlarged, but there was a marked peri-splenitis. The capsule of the organ was thickened in places, and there was a cartilaginous area on the superior surface, the size of a florin. The diaphragm was free ; the liver, kidneys, etc., were partly decomposed, but showed cloudy swelling.

As the adhesions were very firm, the small intestine, cæcum, ascending and transverse colon, were taken out *en masse*, and placed in Kaiserling's fluid for later examination.

On examination of the bowel, nodular cystic masses were found involving the outside of the walls of the ileum, cæcum and colon. In separating the adhesions, one of these cysts was ruptured, and a small worm was easily pressed out.

Fifty-three cystic nodules were opened up ; sixteen were found to contain immature males and thirty-seven females.

This does not appear to coincide with Weinberg's results as in the monkeys and apes, the male œsophagostome was found in greater numbers. Only one worm was found to be empty. Two immature adult females were found free in the fæces of the colon. In the fæces no ova of œsophagostome were found—a few ankylostomes.

A description of Thomas's œsophagostome is given by Railliet and Henry [6] in a paper following that written by Thomas.

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[1] Sambon, L. W. (April 1, 1909), "Remarks on Drs. Breinl and Hindle's Paper on 'A New Porocephalus.'" *Journal Tropical Medicine and Hygiene.*

[2] *Idem* (January 15, July 15, and September 1, 1910), "Porocephaliasis in Man." *Ibid.*

[3] Broden, A., and Rodhain, J. (July 25, 1910), "Contribution à l'étude du *Porocephalus armillatus.*" *Annals Tropical Medicine and Parasitology.*

[4] Shipley, A. E. (September, 1910), "Report upon two small Collections of Pentastomids, with the Description of a New Species of Porocephalus." *Parasitology.*

[5] Thomas, H. W. (December, 1909), "Œsophagostomiasis in Man." *Transactions Society of Tropical Medicine and Hygiene.*

[6] Railliet, A., and Henry, A. (December, 1909), "Description of Thomas's Œsophagostome." *Ibid.*

Parasites —*continued*

A fuller description of *Œsophagostomum Stephanostomum var. Thomasi* is given in a beautifully illustrated paper [1] published more recently than the one quoted. An exhaustive account of the pathological lesions, which are illustrated by coloured plates, presents an excellent description of the lesions resulting from œsophagostomiasis in man.

Railliet and Henry's [2] zoological study of this œsophagostome is also given in this paper, and is likewise illustrated.

Romanovitch [3] has an article referring to a septicæmia occurring in a monkey suffering from œsophagostomiasis. Sections of the parasitic nodules present in the submucosa of the stomach showed a large number of organisms, chiefly large Gram-staining bacilli. Diplococci and other organisms were also found. From the blood of the monkey, Romanovitch isolated a bacillus presenting all the morphological and biological characters of *B. butyricus.*

This organism had pathogenic properties for guinea-pigs.

The author gives as an explanation for the septicæmia which occurred in this monkey the fact that the intestinal organisms are able to reach the blood stream *via* the lesions present in the intestinal mucosa.

A recent paper by Leiper [4] describes the occurrence of *Œsophagostomum apiostomum* as an intestinal parasite of man in Nigeria. The material examined by Leiper was obtained by Dr. Foy of the West African Medical Staff, who collected it from a patient suffering from ankylostomiasis.

According to Leiper, *O. apiostomum* resembles *N. americanus* closely in size and general appearance. On examining with a hand lens, however, *O. apiostomum* is found to differ from *N. americanus* by a lack of the slight but characteristic crook at the anterior end of the body. The mouth is quite terminal, and is surrounded by tiny setæ which protrude somewhat through its aperture. Leiper gives a description of this *O. apiostomum*, and considers that as it corresponds so closely to *O. apiostomum* of monkeys and *O. brumpti* of man these two species are one and the same.

Musgrave, Clegg, and Polk [5] have a lengthy paper on trichocephaliasis, giving a report of four cases, including a fatal one. They call attention to the fact that the belief in the harmless character of trichiurus is based largely upon two observations : first, the great general prevalence of the parasite without symptoms, and second, that no satisfactory explanation of the nature of its pathogenic action has been offered. In discussing the pathology of fatal trichocephaliasis the following points are mentioned :—

The general pathologic changes in fatal cases of trichocephaliasis are severe secondary anæmia. The special conditions are the presence of the worms and certain changes at their points of attachment to the mucous membrane of the bowel or appendix. Several changes have been described by different authors, which in the main are hyperæmia of the mucosa with hæmorrhagic points ; erosions and superficial ulceration of the mucous membrane, surrounded by areas of cell infiltration ; and in some instances deep ulceration or other inflammatory reactions extending to the muscular coat of the bowel. Several observers have shown that the worms are attached to the mucous membrane during the life of the patient. They attach themselves by transfixing a fold of mucous membrane, by penetrating the glandular follicles, and by direct perforation, the head being embedded in the deeper layers of the bowel wall. After the death of the patient the worms detach themselves, and at autopsy are usually found free in the bowel. Several authors have demonstrated this direct attachment to the intestine. Corroborative evidence is furnished by the fact that they do not appear in the discharges even after violent purgation. The worms were not passed in a number of cases of successful treatment, when the disappearance of eggs from the fæces showed that they had been destroyed. In these instances we can only assume that the parasites have been killed and remain attached to the mucous membrane of the intestine after death.

The symptoms affecting the various systems are all fully given, and with regard to treatment mention is made of the good results obtained by enemas of solutions of benzine.

Jamieson and Lauder [6] have reported a fatal case of trichocephaliasis occurring in a child. The blood had the characters of a secondary rather than of a primary anæmia.

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[1] Thomas, H. W. (June 1, 1910), "The Pathological Report of a Case of Œsophagostomiasis in Man." *Annals Tropical Medicine and Parasitology.*

[2] Railliet, A., and Henry, A. (June 1, 1910), "Étude zoologique de l'œsophagostome de Thomas." *Ibid.*

[3] Romanovitch (March 8, 1911), "Septicémie polymicrobienne chez un singe atteint d'œsophagostome." *Bull. Soc. Path. Exot.*

[4] Leiper, R. T. (April 15, 1911), "The Occurrence of *Œsophagostomum apiostomum* as an Intestinal Parasite of Man in Nigeria." *Journal Tropical Medicine and Hygiene.*

[5] Musgrave, W. E., Clegg, M. T., and Polk, M. (December, 1908). *Philippine Journal of Science*, B.

[6] Jamieson, J. G. S., and Lauder, J. M. (December 3, 1910), "Case of Fatal Trichocephaliasis in a Child." *British Medical Journal.*

Parasites —*continued*

Logan [1] has an interesting paper entitled "The little known atypical (unfertilised) egg of *Ascaris lumbricoides.*"

The peculiarity of the unfertilised egg is that, when taken from the uterus, it appears as a finely granular, elliptical mass enclosed in a very delicate membrane. The typical or fertilised egg taken from the uterus has the same thick shell that is found when the egg is found in the fæces. In the fæces the appearance of the unfertilised egg is so different from that of the same egg taken from the uterus that one, who has not studied the matter thoroughly, would not suspect that he was examining the same egg; for, instead of finding the yolk finely granular, it is found to be coarsely globular in the fæcal specimen. The albuminous coating of the unfertilised egg is much less in volume than the coating of the typical egg, and projects from the shell somewhat like blunt saw teeth.

The unfertilised egg is considerably longer and somewhat narrower than the fertilised egg, and is generally markedly elliptical with a tendency to flatten at one or both ends under pressure. Occasionally it is oval in shape, but never round.

Hehir [2] brings forward some evidence to prove that a round worm fever exists in India. The fever produced resembles *Febricular* or *Simple Continued Fever.*

The onset is insidious and without rigors; the patient is indisposed for some days previously; there is usually a slightly coated tongue, loss of appetite, some constipation and headache, and there may be nausea and wandering pains or discomfort about the umbilical region. The temperature rises from 101° to 102·5°, reaching its maximum on the second or third day. After a dose of calomel, followed by a drachm of pulv. jalapæ co., or a Seidlitz powder, the fever disappears abruptly on the third or fourth day. If the nature of the condition is suspected on the first day, santonin followed by a purgative given, and the worms expelled, the fever abates on the second or beginning of the third day, and does not return. If the condition is not recognised, and no aperient is given, the fever, with slight constitutional symptoms, may continue for five or six days and then disappear by lysis, in some cases to return at irregular intervals of from five to six weeks to six months. An examination of the blood will usually reveal some eosinophilia (which may be up to 20 per cent. or more), leucocytosis and occasionally slight anæmia. When the nature of the case is at once suspected, a microscopical examination of a small particle of the fæces reveals the eggs of the *Ascaris lumbricoides.*

Hehir suggests that the term ascariasis be used to embrace the varied clinical phenomena associated with round worm manifestation.

In discussing the manner of infection he states :—

The soil everywhere in and around villages and towns in India contains the ova, and through it water and food, especially green vegetables, become contaminated. The conservancy arrangements of all villages and most towns is to a large extent responsible for the prevalence of these worms. I am disposed to believe that the use of ordinary earth for scouring the feeding and cooking utensils, as practised by the masses in India, is answerable for part at least of the prevalence of round worms. In one's own regiment one has the sand used for this purpose sterilised by dry heat in large iron dishes (*tawas*) or in metal *degchies*, collected and stored in covered boxes in the cook-rooms, to be used by the men as required. One is also convinced that the universal custom of *leeping* the floors, verandahs, and cooking places, with a layer of clay and cow-dung, is a prolific source of infestation by round worms. The moisture contained in this mixture provides the ova with the fillip they want to enable them to develop. The eggs are not infective until such time as the embryo has reached its maximum of development within the shell, which usually occupies a period of four or five months, but under favourable circumstances, as in warm water, or moist earth, this may be reduced to a month or less. This custom of coating floors, etc., with a layer of cow-dung and mud may be legitimately incriminated in connection with other diseases also, and should be condemned.

Landon,[3] in a reply to Hehir's paper, considers that there is a definite round worm fever, and mentions a constant clinical manifestation connected with the tongue :—

We have come to rely, for rapid diagnosis, almost entirely on the tongue, which resembles somewhat the "strawberry" tongue of scarlet fever. The dorsum is moderately coated, and pale, while large bright pink papillæ stand out in sharp contrast, and the tip is red and moist. When a child complains of being out of sorts, and presents a little fever, a distended abdomen, and the tongue as above described, we have no hesitation in diagnosing worms. Possibly the same appearance is presented in other parasitic infections of the alimentary canal.

Garrison [4] has a paper with illustrations of a new intestinal trematode found in man in Manila. A description of this trematode, *Fascioletta cliocana*, is given at some length.

At the meeting of the Zoological Society of London, on November 9, 1909, Leiper [5] gave a

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[1] Logan, O. T. (1908), "The little known Atypical (Unfertilised) Egg of Ascaris Lumbricoides." *American Society of Tropical Medicine.*

[2] Hehir, P. (August, 1910), "Remarks on Ascariasis. Is there a Round Worm Fever?" *Indian Medical Gazette.*

[3] Landon, E. (November, 1910), "Ascariasis." *Ibid.*

[4] Garrison, P. E. (November, 1908), "A New Intestinal Trematode of Man. *Fascioletta cliocana.*" *Philippine Journal of Science*, B.

[5] Leiper, R. T. (November 9, 1909), Meeting of Zoological Society, London. Quoted in *British Medical Journal*, November 27, 1909, p. 1546.

Parasites —*continued*

description of a new nematode worm found in abscesses in natives of Trinidad, namely *Lagochilascaris minor*. The account was as follows :—

An ascarid with three jaws split along their inner surfaces and separated from the body by a deep furrow. Small cuticular labia intermedia. Narrow keel of cuticle projecting from body in region of lateral bands. Œsophagus simple. Male 9 mm. in length, with over twenty-four pairs of pre-anal and with five pairs of post-anal papillæ. Spicules solid at tips, sickle-shaped, measuring 0·35 mm. and 0·4 mm. in length. Female 15 mm. long. Vulva 6 mm. from mouth. Ova round, with thick and pitted shell.

Garrison and Leynes [1] have an interesting paper entitled "The Development of the Miracidium of Paragonimus under various physical conditions."

After describing the methods for clearing the ova from the sputum and fæces, cultures of the ova were subjected to a temperature between 25° and 34° C., and kept uncovered out of direct sunlight on a laboratory shelf.

Since thoroughly washed ova kept under these conditions developed satisfactorily, and as under no variation from these conditions was development more constant, more rapid, or apparently more healthy, we have used the maximum development so obtained as the standard for comparison, and considered it, at least for the laboratory, as normal.

We have never found free-swimming miracidia in our cultures in less than twenty-five days from the time the sputum was expectorated, but in from twenty-five to thirty-five days they have frequently been noted. Therefore it is evident that the miracidia require, after they first acquire motility, a considerable period for further development before they are capable of leaving the shell.

A more striking observation is the length of time motile miracidia may remain in the shell before hatching. While as a rule practically all the shells in a culture thirty days old contained actively motile miracidia, active, unhatched organisms would persist in the same culture for one hundred and fifty days, and in one case we found shells containing motile miracidia in a culture one hundred and sixty days (twenty-three weeks) old. In cultures kept a longer time than this we were never able to find anything but empty shells or degenerated ova.

Therefore it would appear that while the ova develop comparatively uniformly until the miracidia are, to all appearances, fully mature, the escape of the miracidia from their shells is, for a given number of ova, a matter of considerable variation, and that the hatching of the ova thrown out in a single expectoration may be distributed throughout a considerable period of time—according to our experience, seventeen to eighteen weeks. This observation appears to explain the fact that we have never been able to find a great number of free-swimming miracidia in our cultures at any one time, even though the sediment was very heavily loaded with ova, and it is possible that the gradual hatching of the ova may prove to be not without significance when the complete life-cycle of the parasite is known.

Some experiments were then carried out to note the effect of various temperatures on the development of the ova. At body temperature cultures not only showed no development but rapidly degenerated. Cultures kept at room temperature till the miracidia developed, and then placed in an incubator at 37° C., gave similar results.

Cultures kept in cold storage at from 11° to 15° C., 10° to 12° C., and from 9° to 10° C., gave no signs of development after ten weeks, but likewise no degeneration, and when removed from the cold storage to room temperature never failed to develop motile miracidia in about the same length of time after leaving the cold chest as was required for its original control at room temperature.

It would appear, therefore, that while temperatures above 15° C. are required for the development of paragonimus ova, temperatures as low as 10° C. do not destroy or, apparently, even impair their vitality.

Under various conditions of light they found that direct sunlight is fatal to the life of the ovum, but that the presence of any light is not necessary to its development, at least to the free-swimming, miracidial stage.

Some experiments undertaken to note the effect of salt solutions on the ova resulted in demonstrating the fact—(1) That in sea-water the ova rapidly degenerate. (2) In 1·5 per cent. salt solution no development took place. (3) In 0·5 per cent. solutions the development was nearly as good as in tap water, but in neither the 0·5 per cent. nor in the 1 per cent. solutions were free-swimming miracidia seen.

In order to study the question of the possibility of the dissemination of the ova in dried sputum or dust, some desiccation experiments were carried out. As a result of these, Garrison and Leynes concluded that desiccation, even for a few moments, is fatal to the life of paragonimus eggs, and that the ova cannot be disseminated otherwise than in water.

The theory which has been broached that infection of man might occur by means of ova blown about in the air, even though there were no other objections to it, would appear to be absolutely excluded by the failure of the ova to withstand drying.

Goldberger and Crane [2] have discovered in the liver of the South American *Cebus cupucinus* a second species for the genus *Asthemia*. *A. foxi* n. sp. differs from *A. heterolecithodes* which occurs in the liver of a Madagascar bird, in that the body is more slender and the cæca do not extend so far backwards, failing to overshoot the vitelline zone.

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[1] Garrison, P. E., and Leynes, R. (June, 1909), "The Development of the Miracidium of Paragonimus under Various Physical Conditions." *Philippine Journal of Science*, B.

[2] Goldberger, G., and Crane, "A New Species of Trematode in Monkeys." *Hygienic Laboratory Bulletin, U.S.A.*, No. 71, *Public Health and Marine Hospital Service*. Quoted in *Journal Tropical Medicine and Hygiene*, April 1, 1911.

Parasites —*continued*

Reference may be made to a paper by Ward[1] entitled "*Fasciolopsis Buskii, F. Rathouisi*, and Related Species in China." A short historical description is given of the fasciolopsis found in man and the structural characters of *F. buskii* (Stiles), and *F. rathouisi* (Ward), compared.

There is a paper by Gage,[2] in which he describes the finding of the larvæ of *Strongyloides intestinalis* in the sputum of a case of pneumonia. At the autopsy made nine hours after death a large number of *Strongyloides intestinalis* was found in the duodenum and ileum. The duodenum showed numerous ulcers. The larvæ of this parasite were found in the submucosa and in the lymphatics. The broncho-pneumonic patches in the lungs also contained the larvæ.

Guiart and Garin [3] have carried out a number of observations on cases in which Weber's test for indican in the urine gave a positive result where it seemed to be connected with the existence of an intestinal parasite (trichocephalus).

They point out that if the mere existence of such a parasite is capable of giving rise to the condition in which a positive reaction is obtained, it is necessary, before drawing any deduction from the test, such as the probability of the existence of gastric or intestinal carcinoma, to examine the stools very carefully for the eggs of trichocephalus. They also think that even ascarides may cause the test to give a positive result. No similar observations seem to have been previously published, with the exception, perhaps, of some of Dr. Siccardi of Padua who examined the urine by this method in some cases of ankylostomiasis. The biology of the whip worm (*trichocephalus dispar*), which is said to be somewhat commonly found in the cæcum, especially in France, renders it very likely to be the cause of minute hæmorrhages in the intestine, which, though they may not of themselves be of any serious import, may very probably be sufficient to cause the test to succeed. In three cases of chorea examined by Dr. Guiart and Dr. Garin numbers of trichocephalus eggs were found and the test gave a positive result, whereas in all the other cases of chorea which were free from the eggs the result was negative. In one gastro-intestinal case with epileptic crises the stools were examined four times in three weeks, and trichocephalus eggs were always found, but the Weber test only twice succeeded. Dr. Guiart and Dr. Garin say that where trichocephalus eggs were present they never failed to find the Weber test give a positive result.

Gaiger,[4] in an extremely useful paper, gives a list of the ecto and endo parasites of the Indian domesticated animals. As a reference this paper will be found to be extremely useful, for the tabular arrangement of the list is an easy guide to any information required.

Weinberg and Moore Alexander [5] deal with eosinophilia in helminth infections. These observers consider that—

(1) The reaction of the organism in the production of an eosinophilia depends on the individual.

(2) This reaction is by no means proportionate to the number of intestinal parasites that are present.

(3) It is impossible to say after an examination of the blood whether the parasites are present in small or large numbers, as a small number of parasites leads very often to a marked eosinophilia, while a heavy parasitic infection is often accompanied by a small amount of eosinophilia.

(4) The eosinophilia may be diminished or disappear if the parasites in the intestine are dead or broken up.

Weinberg and Mello [6] carried out some researches on the production of eosinophilia in helminthiasis. They found that—

(1) A marked eosinophilia could be produced in a guinea-pig if this animal was injected with an extract of various parasites (Sclerostomes, Ascarids, Tæniæ, Botriocephalæ, and Distoma, etc.). The eosinophilia produced varied from 20 to 30 per cent.

(2) The eosinophilia sometimes appeared on the day following the first injection.

(3) The injection of large doses of the extract did not produce an eosinophilia.

(4) The toxins act directly on the bone-marrow, causing it to produce a larger number of eosinophiles than it normally does. The spleen of a guinea-pig with a marked eosinophilia shows in its substance a heavy infiltration with eosinophile cells.

Whyte [7] has a paper entitled "Helminthic Infection and its relation to Eosinophilia."

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[1] Ward, H. B. (1910), "*Fasciolopsis Buskii, F. Rathouisi*, and Related Species in China." *American Society of Tropical Medicine.* Collected Papers.

[2] Gage, J. (August, 1910), "Larvæ of *Strongyloides intestinalis* in Human lung." *Journal of Medical Research.* Quoted in *Bull. de l'Inst. Past.*, February 28, 1911.

[3] Guiart, J., and Garin, C. (September 1, 1909), *Semaine Médicale.* Quoted in *Lancet*, September 18, 1909, under the title "Weber's Test and Intestinal Parasites."

[4] Gaiger, S. H. (1910), "A Preliminary Check List of the Parasites of Indian Domesticated Animals." *Journal Tropical Veterinary Science*, Vol. V., No. 1.

[5] Weinberg, M., and Alexander, M. (October 14, 1908), "Quelques données sur l'éosinophilie dans les helminthiases." *Bull. Soc. Path. Exot.*

[6] Weinberg, M., and Mello, U. (October 14, 1908), "Recherches expérimentales sur l'origine de l'éosinophilie dans les helminthiases." *Ibid.*

[7] Whyte, G. D. (July 30, 1910), "Helminthic Infection and its Relation to Eosinophilia." *British Medical Journal.*

Parasites —*continued*

This observer carried out an examination of the blood and fæces of a number of cases to ascertain whether *Clonorchis sinensis* (syn. *Opistorchis sinensis*) infection was capable of producing an eosinophilia. His work was rendered somewhat difficult owing to many of the cases showing a mixed infection. Two series of groups of cases were compared; the one series only differing from the other by the *Clonorchis sinensis* being present in the former and absent in the latter. By this means Whyte was able to prove that this parasite had little if any influence on the degree of eosinophilia. A number of tables are submitted illustrating the effects of various helminths on the numbers of eosinophiles in the blood, and Whyte concludes that—

The more varieties of parasite that infest a man, and the more numerous the individuals of each variety, the greater degree of eosinophilia he is likely to show. This will be especially marked if he is between twenty and forty years of age, and will be less noticeable if he is older or is suffering from some form of tuberculosis.

Theobald Smith [1] has a note on the influence of infectious diseases upon a pre-existing parasitism.

A 3½-year-old cow was previously inoculated with a killed culture of tubercle bacilli. At the post mortem an unusual, small, sessile, pinkish tumour, 1 in. in diameter, was found on the omentum. In the centre of this was found, coiled up, the *Filaria labiopapillosa*, buried in lymphoid tissue, which took the circular, ringed form of the worm. In the right lung a like tumour was found. Another calf similarly vaccinated showed the same kind of tumour. In this was found an unrecognised worm. Both it and the surrounding lymphoid tissue showed stages of degeneration. In the lymphoid tissue no other suspicion of tubercle was found, except a few giant cells.

A third calf was twice vaccinated with cow-pox. Small yellowish nodules were found on the Peyer's patches. These consisted of follicles which were invaded by a minute dead nematode, showing *débris* and ova. Frequently nodules containing nematodes are found on the normal intestinal wall, but these contain only *débris* or the worm in a living condition, prior to migration to mucosa where the ova are deposited.

The author thus supposes that the viruses injected have disturbed the normal mutual relationship existing between the host and the parasite. The diseases, artificially produced, have therefore forced the development, killed, and fixed the parasites in sites not previously observed, on account of early migration.

By these means, therefore, the author suggests one might be able to observe parasites in stages not previously known, and even finds parasites hitherto not observed at all. Again, in tropical countries, many natives show filariasis without clinical signs, others suffer from lymph stasis of various parts of the body, and the author suggests that these latter conditions may be due to intercurrent infections of the body which fix the parasites in the lymph vessels of the parts affected.

Hall [2] recommends the following treatment for tape-worm infection :—

(1) 1½ pints of milk and 1½ pints of beef-tea daily for three days.

(2) Sodii bicarb. grains 20; sodii sulph. one drachm; sp. chloroform, minims 20; aq. menth. pip, add to one ounce; thrice daily for three days.

(3) On evening of day before the male fern is to be administered give a purge: mag. sulph. half an ounce; tinct. jalap one drachm; tinct. chloroform, minims 20; aqua add to one ounce, repeated on following morning if bowels not cleared.

(4) At 8 a.m. fourth day give ext. filicis liq. one drachm; mucil. tragacanth. one drachm; syrup. zingib. one drachm; aq. chloroform add to one ounce; repeat dose at 9 a.m.

(5) At 11 a.m. ol. ricini half an ounce; tinct. jalap one drachm. If bowels do not act within one hour administer an enema, 1½ pints soap and water.

(6) Examine motions for head.

(7) Keep patient in bed after giving the male fern in case faintness comes on.

Useful information will be found in a paper by Brüning [3] referring to the treatment of helminthiasis in the Tropics. Among other remedies mentioned this observer recommends the use of eucalyptus oil, chloroform, and castor oil in the treatment of agchylostomiasis, and oleum chenopodii anthelmintici and menthol in the treatment of ascariasis.

Railliet, Moussu, and Henry [4] have tried various remedies in the treatment of distoma. Among those employed may be mentioned aloes, calomel, salicylate of soda, phosphorus oil, and arsenical salts. The results, however, were disappointing, for in no case did a cure result.

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[1] Smith, T. (November, 1910), "Note on the Influence of Infectious Diseases upon a Pre-existing Parasitism." *Journal of Medical Research.* Quoted in *Journal of Royal Institute of Public Health*, January, 1911.

[2] Hall, F. de H. (August 6, 1908), "Treatment of Tape-Worm." *Clinical Journal.* Quoted in *Journal Tropical Medicine and Hygiene*, April 15, 1909.

[3] Brüning, H. (1910), "Zur Frage der Helminthiasistherapie in den Tropen." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIV., No. 23.

[4] Railliet, A., Moussu, and Henry, A. (March 24, 1911), "Essais de Traitement de la Distomatose." *C. R. Soc. Biol.*

Parasites —*continued*

Flynn [1] advocates doses of 9 grains of sulphur daily for a week as a cure for thread worms. Children may be given 1½ grains thrice daily for a week.

Telemann [2] describes his method for the detection of eggs in fæces as follows :—

(1) Select small portions about the size of a pea from different parts of the fæces ; (2) mix them in a reagent glass filled with equal parts ether and hydrochloric acid ; (3) shake the mixture ; (4) filter through a hair sieve ; (5) centrifugalise the filtrate for one minute. The eggs will be found at the distal end of the centrifugal tubes.

Mink and Ebeling [3] give the technique for the preparation of flat worms for purposes of study :—

The specimens are best obtained in a clean condition by mixing the fæcal material with an amount of warm (37–40) normal salt solution sufficient to make a thin broth. If the material is obtained at autopsy, as is usually the case with the parasites of animals used in experimental work, the intestinal contents may be washed or scraped off into the salt solution. In this warm solution the worms move about freely, and are more easily seen and transferred—especially small worms such as the *Hymenolepis nana*. With a pair of fine-point forceps the worms are picked up and transferred to a second dish of warm salt solution. In this dish the worms will be found to be in a clean condition, free from mucus and fæcal material. Material for sections and for the preparation of mounted segments should be taken from the salt solution and treated with the proper fixatives. The remainder of the gross material may be placed in 50–70 per cent. alcohol, with or without glycerin, Zenker's solution, or a 2 per cent. solution of formalin. Zenker's solution causes considerable shrinking and a rather marked yellowish discoloration. We considered the formalin mixture much better—the natural whiteness being preserved with little or no shrinkage.

Preparation and Sectioning of Material

Here it is of great importance to prevent curling or distortion of the worm or segment. This is best prevented by a fixative which kills rapidly, and for this we found Zenker's best. About three or four inches of the live tape-worm were taken from the salt solution and stretched out on an ordinary glass slide. By means of a pipette the slide is rapidly covered with Zenker's solution. The section of the worm straightens out, hardens, and floats on the solution. It may then be transferred to a flat dish filled with Zenker's and allowed to remain here from two to twenty-four hours, according to the convenience of the worker. By cutting a little beyond the part actually desired for work, little end pieces are left which may be grasped with the forceps in subsequent manipulations. Thus the actual segments desired for study need not be touched by the forceps. The subsequent steps include the alcohol-iodine solution, graded alcohols for dehydrating and other steps up to the melted paraffin. In blocking the specimen it seems better to place the longest and broadest surface downward, and later to orient by trimming and mounting as desired. Specimens may be cut in planes (1) parallel with the long broad surface, (2) parallel with the long and perpendicular to the broad surface, (3) perpendicular to the long axis. The first and last methods give a sufficient opportunity to study all parts of the worm. There is no object in cutting sections less than 15 microns, and much time in preparation and examining will be saved if sections 25 to 30 microns are used. If too hard a paraffin is used, it will be found that the ribbons of thick sections break very easily. For 10 to 15 microns sections a 52° paraffin may be used, but for the thicker sections it is better to use a 45° paraffin. We found the most convenient stain to be a rapidly acting purely nuclear hæmatoxylon.

Preparation of Segments for Mounting

The specimens are washed in normal salt solution (0·85 per cent.) and fixed in 2 per cent. formalin for a certain time, preferably fourteen to sixteen hours. It is better not to allow the formalin to act over sixteen hours. After this the specimens are transferred to the following glucose medium, which is a slight modification of the Fabre-Domerque medium :—

Syrup (glucose 48 parts, water 52 parts)	1000 c.c. (one thousand).
Methyl alcohol	200 c.c. (two hundred).
Glycerin	100 c.c. (one hundred).
Camphor (q. s. to keep)	100 c.c. (one hundred).

The specimens may be left in this medium indefinitely, although it was found that they cleared sufficiently within four or five hours. In mounting, a sufficient amount of Keisser's glycerin jelly is dropped on a slide and the specimen transferred to this, care being taken not to introduce air bubbles. A flamed cover-glass finishes the mount. After the glycerin jelly hardens a few coats of gold size applied consecutively around the cover-glass furnishes rigidity and improves the general appearance of the preparation. Concave slides are more desirable when the specimen is of uneven thickness or rather thick throughout.

Hall [4] has a most useful paper discussing the various methods of examining fæces for evidence of parasitism. He concludes that—

the attainment of successful results depends mainly upon proper concentration, and that this is accomplished by careful comminution of the fæces, the uses of sieves, sedimentation, centrifuging, and washing in water.

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[1] Flynn, T. P. (April 24, 1909), "Treatment of Thread Worms." *Hospital.*

[2] Telemann, W. (August 27, 1908), "Eine Methode zur Erleichterung der Auffindung von Parasiteneiern in den Fäces." *Deutsch. Med. Woch.*, Leipz. u. Berl. Quoted in *Journal Tropical Medicine and Hygiene*, April 15, 1909.

[3] Mink, O. J., and Ebeling, A. H. (1909), "A Method for the Preparation of Flat Worms for Study." *American Society of Tropical Medicine.*

[4] Hall, M. C., "A Comparative Study of Methods of Examining Fæces for Evidences of Parasitism." *United States Department of Agriculture, Bureau of Animal Industry, Bulletin* No. 135. Quoted in *Journal Tropical Medicine and Hygiene*, June 1, 1911.

Hall has elaborated a new method which in his experience appears to be the best for routine examinations of various kinds of fæces. Its description is too long to be quoted here. Parasites —*continued*

Paratyphoid Fever. Ruge and Rogge [1] describe an outbreak of this fever on board a ship. There were eleven cases, and their predominant symptoms consisted of vomiting, diarrhœa, abdominal cramps, and general weakness and depression. The temperature in these cases was between 39° and 39·5°. The fever lasted two to three days, after which the patients became convalescent. During the fever the tongue presented a very dry appearance, and the conjunctiva and kidneys were congested.

Paratyphoid bacilli were present in the stools of four of the cases that were examined. The agglutinating power of the serum from these cases did not exceed a dilution of 1 to 50.

Ruge and Rogge were struck with the fact that the stools represented almost a pure culture of paratyphoid bacilli.

Konrich [2] gives an account of an epidemic in a children's hospital. The diagnosis was established by means of blood culture carried out at the end of the first or at the beginning of the second week. The serum taken from these cases all agglutinated *B. paratyphosus* B, but the highest agglutination was not reached till the second or third week. At the commencement of the disease the serum more readily agglutinated *B. paratyphosus* A than *B. paratyphosus* B. The latter was found in the fæces, but its presence there was somewhat inconstant, as it was found in large numbers one day and was entirely absent the following day.

Subcutaneous and intraperitoneal inoculations of the organism isolated were carried out on guinea-pigs and mice, the bacillus proving very virulent for these animals, whereas feeding experiments *per os* gave negative results.

Schmitt [3] has a paper discussing the pathogenicity of *B. paratyphosus* B in the calf. He considers that this organism is capable of producing diarrhœa, septicæmia, and pleuro-pneumonia in the calf, and that it invades first of all the blood, and then the muscles, where it can be found.

Mayer [4] carried out some work to show the powers of resistance of *B. paratyphosus* B in dried human excreta. He found in three specimens of fæces rich in *B. paratyphosus* B that this organism was capable of living for a period of six months, whereas the *B. typhosus* retained its vitality for only three months. A knowledge of these facts enabled Mayer to trace the origin of certain paratyphoid infections in the course of an epidemic, the particulars of which he details in this paper.

Gaehtgens [5] on two occasions has isolated *B. paratyphosus* B from water. After precipitation of the water with oxychloride of iron he isolated the organism in malachite green media.

Mayer [6] has a note to the effect that cases of paratyphoid fever often show no agglutinating power for the *B. paratyphosus* B. In seven cases of gastro-enteritis in which he isolated this organism the serums of these cases tested on the tenth and thirtieth days failed to agglutinate it. He attributes this to the fact that in all probability the infection in the alimentary tract is a local one, and does not produce a sufficiently marked intoxication to bring about the development of agglutinins.

Weinberg and Mello [7] have an interesting paper describing a paratyphoid infection in a chimpanzee. At the autopsy the small intestine contained a large number of ulcers affecting the Peyer's patches. These ulcers resembled those met with in typhoid fever. A large

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[1] Ruge, R., and Rogge, M. (September 8, 1908), "Die Paratyphuserkrankungen an Bord S.M.S. 'Blitz.'" *Cent. f. Bakt.*, I. Orig., Vol. XLVII.

[2] Konrich, "Eine Paratyphusepidemie in einem Krankenhause." *Klin. Jahrb.*, Vol. XIX. Quoted in *Bull. de l'Inst. Past.*, January 15, 1909.

[3] Schmitt, F. M. (November 28, 1908), "Der *Bacillus paratyphosus* B als Krankheitserreger bei Kälbern." *Deutsche Tierärzt. Woch.*

[4] Mayer, O. (October 27, 1908), "Über die Resistenz von Bazillen des Typhus-Paratyphus B in ausgetrockneten menschlichen Darmentleerungen." *Münch. Med. Woch.*, Vol. LV.

[5] Gaehtgens, W. (May 3, 1909), "Über das Vorkommen der Paratyphusbazillen (Typhus B) im Wasser." *Arb. a. d. Kais. Gesundheitsamt*, Vol. XXX. Quoted in *Bull. de l'Inst. Past.*, October 15, 1909.

[6] Mayer, O., "Über die Bewertung des Befundes von Paratyphus B-Bazillen in menschlichen Darmentleerungen bei akuter Gastroenteritis ohne Gruber-Widalsche Reaktion." *Klin. Jahrb.*, Vol. XXI., Fasc. 2. Quoted in *Bull. de l'Inst. Past.*, December 15, 1909.

[7] Weinberg, M., and Mello, U. (January 13, 1909), "Un cas de paratyphoïde avec lésions d'aspect typhique chez le chimpanzé." *Bull. Soc. Path. Exot.*

Para-typhoid Fever—*continued*

number of punctiform hæmorrhages was present in the large intestine. The spleen was very congested and enlarged. A bacillus was isolated from the heart's blood and spleen which gave all the characters of the paratyphoid group of bacilli.

Loghem [1] records a case of a paratyphoid B occurring as a secondary infection. The case was a peculiar one which clinically resembled that of typhoid fever, but during the pyrexial stage *B. paratyphosus* B was cultivated from the blood. Typical typhoid lesions were found to be present at the post mortem, and typhoid bacilli were alone present in the organs. Cultivations from the spleen and bile gave no evidence of *B. paratyphosus* B being present.

Gerrard [2] refers to the fevers of Malta, considering chiefly those pyrexias of uncertain origin which are included in the three-day, seven-day, and ten-day fevers. Their signs and symptoms justified them being included in the enteric group, and Gerrard considers the possibility of many of them being due to paratyphoid infection.

Samut [3] has an interesting paper on paratyphoid fever in Malta. He classifies the symptoms present under four types :—

(1) In the mildest form the patient may pass through the disease with no more than a feeling of indisposition for a few days, with symptoms of gastric derangement and malaise. Constipation is often well pronounced.

(2) The second type is that which reproduces the clinical picture of enteric fever. In this form of the disease we generally meet with the usual premonitory signs, malaise, depression, headache, and, above all, loss of appetite, and even nausea, the tongue being usually white and glossy. The patient may go about and struggle to do his work, but soon he feels too weak and realises that he is seriously ill. A high temperature develops, which runs an enteric-like course. Rose spots make their appearance on the abdomen. Diarrhœa may be present, but constipation seems commoner. Enlargement of the spleen and sometimes of the liver with jaundice are met with. Epistaxis is extremely common. The urine is highly concentrated with an increase of urea and uric acid, but a diminution of sodium chloride; albumin may be present, and a positive diazo reaction is not unusual. Complications are not so common in paratyphoid as compared with true enteric, yet hæmorrhage from the bowel is, according to Klemperer, met with in 3 per cent. of cases; pulmonary complications such as congestion and pneumonia are among the commonest.

(3) The next form is one which is characterised by those symptoms usually met with in Malta fever. Now, while the close resemblance between paratyphoid fever and true enterica is firmly established, it is not usually accepted that paratyphoid may simulate Malta fever so closely as to be identical with it in all its clinical manifestations. Yet many cases have come to my notice, and during the present epidemic of the disease in Malta a large number have been returned to hospital in which symptomatology was as far removed from the usual picture of infections by the paratyphoid group as it was closely related to that of Malta fever, and which on careful bacteriological examination yielded undeniable proof of paratyphoid infection. I attach particular interest to these cases.

(4) The last form is paratyphoid fever as a complicating infection during the course of other fevers, notably Malta fever. That such a mixed infection exists was proved by me in the September number of the *Journal of the Royal Army Medical Corps*, and by other cases since. What I consider most conclusive, however, is the fact that some years ago, before the paratyphoid bacilli were well understood and cultivated, hæmorrhage from the bowel had been met with in several cases of Mediterranean fever in which the blood had given absolutely negative results to the Gruber-Widal test with *B. typhosus*. Hence ulceration of the intestine was considered to be one of the complications of Mediterranean fever, while the fact was apparently proved beyond doubt in the post-mortem room, when the ulcerated Peyer's patches were held up for demonstration as proof conclusive of the destructive changes of the bowel brought about by the *Micrococcus melitensis*.

Grattan [4] carried out some useful researches for the purpose of ascertaining what proportion of cases of enteric are due to (1) *B. typhosus*, (2) paratyphoid group, (3) other members of the typho-colon group. This observer made a large number of blood cultures and obtained the best results by using Kayser's plain sterile ox-bile as a medium for blood inoculation. Among other interesting points he noted that two of the strains of *B. typhosus* when first isolated resisted the agglutinating properties of an anti-typhoid serum, but at a later date, after several subcultures had been made, these two non-agglutinating strains were eventually agglutinated by the specific serum. Grattan summarises the results of his researches as follows :—

(1) Cultures were made from the blood of sixty suspected cases of enteric fever; twelve of these proved not to be enteric (tubercle, appendicitis, influenza, middle-ear disease, etc.). The blood cultures were positive in twenty-six out of the forty-eight cases of enteric.

(2) The *B. typhosus* was the only member of the typho-colon group which was recovered from the blood of the twenty-six positive cases.

(3) A diagnosis of paratyphoid fever based on an examination of the stool only is unreliable.

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[1] Loghem, J. J. V. (1909), "Paratyphoid-B as Secondary Infection." *Transactions Bombay Medical Congress.*

[2] Gerrard, J. J. (October, 1909), "Further Notes on Fevers in Malta." *Journal Royal Army Medical Corps.*

[3] Samut, R. (October, 1909), "Paratyphoid Fever in Malta." *Ibid.*

[4] Grattan, H. W. (April, 1910), "A Preliminary Enquiry into the Prevalence of Paratyphoid Fever in London, with Remarks on Blood Culture in forty-eight Cases of Enteric Fever." *Ibid.*

Para-typhoid Fever—*continued*

(4) Plain sterile bile (Kayser's method) gave the best results.

(5) The action of the *B. typhosus* on dulcite is variable; a recently isolated true typhoid bacillus may ferment dulcite.

(6) A strain of *B. typhosus* when first isolated fermented raffinose in thirteen days, and in forty-eight hours after subculture.

(7) A recently isolated true typhoid bacillus may fail to be agglutinated by an anti-typhoid serum.

Grattan and Harvey [1] have an interesting paper referring to an epidemic of paratyphoid fever in an Indian camp. In seven out of the eight cases *B. paratyphosus* A was isolated from the blood.

The symptoms and signs which presented themselves were as follows :—

All the patients suffered from sore throat; this varied much in severity. The first two men had severe congestion of the fauces with tonsillar abscess; the milder cases showed only congestion. Constipation was the rule in all. Spots were only noted in one case. All suffered from headache and severe pain in the back. *B. paratyphosus* A was recovered from the blood of seven out of the eight cases. The fæces and urine were examined frequently throughout the fever and during convalescence.

The source of the epidemic was traced to a soldier who was employed as a cook orderly. The first two cases of paratyphoid fever in this epidemic occurred in men who occupied the same tent as the cook orderly, who had some months previously apparently suffered from an attack of paratyphoid A fever followed by cholecystitis. Although no paratyphoid A bacilli were found in this man's fæces or urine, his serum reaction gave a high agglutination with *B. paratyphosus* A (up to 1–200). Grattan and Harvey noted that the blood serum taken from the eight cases in the epidemic gave a positive agglutinatin to *B. paratyphosus* A, but in low dilutions (20–40) and always incomplete. Six out of the eight agglutinated the *B. typhosus*, and, but for the fact that *B. paratyphosus* A had been cultivated from the blood, these cases would in all probability have been diagnosed as mild cases of true enteric fever, the agglutination for paratyphoid A being so slight that it might have been considered a group reaction.

Schöne [2] also has a paper referring to a *B. paratyphosus* A infection which is of some interest.

Sacquépée and Bellot [3] describe an epidemic of paratyphoid fever which was apparently due to contamination of food by a paratyphoid carrier.

In a corps of 250 soldiers which formed part of a garrison an outbreak of paratyphoid fever occurred. On June 14th one man was attacked, on the 15th two men were attacked, on the 16th five, on the 18th five, on the 19th three, on the 20th two, and on the 21st one, making a total of 19 cases in eight days. Most of the cases ran a benign course; a few were severe, and none were fatal. The duration of the disease was from 15 to 22 days. In three cases meningeal symptoms—intense headache, rigidity of the neck, and Kernig's sign—were prominent. The diagnosis was soon made by bacteriological examination. In seven out of eight cases cultures made from the blood showed the paratyphoid bacillus of the type B. In twelve cases the stools and urine were examined. The bacillus was found ten times in the stools and twice in the urine. Finally, a positive serum reaction for the paratyphoid bacillus of the type B was obtained in all cases. In investigating the outbreak attention was drawn to the fact that the " epidemic curve " corresponded to the manifestations of a water-borne or food-borne disease; the cases at first were numerous; the outbreak lasted some days and then ceased. The drinking water was exculpated; its examination before, during, and after the outbreak revealed nothing abnormal. The men in the other corps of the garrison, who consumed the same water, were free from infection. The source of infection must therefore have been the food. The cooking arrangements for the affected corps were special to it. The source of infection could not have been raw food, for although salads, strawberries and the like, were distributed, they were not consumed by all the patients or even by a majority of them. The source must therefore have been cooked food. Properly cooked food has never been known to convey typhoid fever unless it was contaminated after cooking, and such contamination by typhoid carriers is now well known. This outbreak must therefore have been due to someone employed in the kitchen who was infected with the paratyphoid bacillus. It was found that a cook had an illness for some days before June 10th, characterised by lassitude, headache, anorexia, and pains in the limbs. He was so ill that he sought medical advice, but he remained at work. Examination of his stools revealed the paratyphoid bacillus of the type B in notable quantity, and the same result was obtained many times in August, September, and October. He also gave the serum reaction for the bacillus. Evidently his illness was a mild attack of paratyphoid fever, and after recovery he remained a paratyphoid carrier.

Reference may be made to a paper by M'Naught [4] on paratyphoid fevers in South Africa. In the course of his remarks M'Naught mentions the fact that there are various

[1] Grattan, H. W., and Harvey, D. (January, 1911), " Inquiry into an Epidemic of Paratyphoid Fever." *Journal Royal Army Medical Corps.*

[2] Schöne, C. (1910), " Über Infektionen mit Paratyphusbazillen des Typhus A und Befunde von verwandten Bakterien." *Zeit. f. Hyg. u. Infekt.*

[3] Sacquépée, E., and Bellot (January 15, 1910), " Sur la recherche des bacilles typhiques et paratyphiques dans les excreta." *Progrès Méd.* Quoted in *Lancet*, March 5, 1910.

[4] M'Naught, J. G. (May, 1911), " Paratyphoid Fevers in South Africa." *Journal Royal Army Medical Corps.*

Para-typhoid Fever—*continued*

continued fevers in South Africa which are somewhat similar to paratyphoid, but appear to be associated with other bacilli of the coli-typhoid group. He considers these anomalous fevers to be distinct entities, and that they can be differentiated clinically from enteric fever or the recognised forms of paratyphoid fever. Their chief characters are as follows :—

(1) The onset is sudden, and is accompanied by particularly severe headache, pains in the back and limbs, dark flush on cheeks, injected conjunctivæ, and suffused eyes. Sometimes the patient has been out of sorts for a few days before the onset of distinct symptoms, but usually the disease sets in quite suddenly.

(2) A characteristic dark red maculo-papular rash, not unlike the rash of German measles, appears all over the trunk and limbs. I have found this rash present on the soles and palms in all cases in which I had an opportunity of looking for it. Interspersed with the characteristic rash are sometimes found lighter red spots like rose spots. The rash leaves brown stains when it fades. It appears earlier than the rash of typhoid fever, sometimes coming out on the second or third day of illness.

(3) The tongue is coated, but not usually dry or brown. Constipation is usual; the motions have a dark brown colour. The spleen is generally enlarged. There may be some abdominal fulness but not marked distension.

(4) The fever lasts from ten to fourteen days as a rule. It usually comes down by rapid lysis, but may do so by crisis. Convalescence is rapid, and there are no relapses.

(5) Though the patient often appears to be extremely ill during the first week of the disease, yet I do not know of it ever proving fatal.

Bainbridge [1] has an excellent paper dealing with the differentiation of the paratyphoid and food-poisoning bacilli, and makes special reference to the absorption and agglutination tests as useful methods in distinguishing the food-poisoning group.

Reference to this paper has already been made in another section (*vide* "Food Poisoning").

A paper by Mandelbaum [2] deals with a method of diagnosing enteric and paratyphoid fever. As this paper is quoted in another section (*vide* "Enteric Fever"), no further mention of it is necessary.

Petrie and O'Brien [3] carried out some experiments dealing with the experimental production of the carrier-state by feeding. Guinea-pigs were fed on cultures of an organism of the paratyphoid group. They found that—

(1) Healthy intestinal carriers (guinea-pigs) of a bacillus of the "paratyphoid" group (*Bacillus aertryck, or Bacillus suipestifer*) can readily be produced experimentally.

(2) Some of the carriers gave evidence of an intermittent excretion of the bacilli in the fæces.

(3) The agglutinin content of the carriers' sera was in excess of that of normal control animals, although, so far as the experiments go, there was no evidence of a somatic infection.

The question of the mechanism of agglutinin production is discussed in this paper. In their experiments specific agglutinins were produced in the serum of the guinea-pigs in the apparent absence of even a mild infection, a point which is difficult of explanation.

It is possible, of course, that a transitory invasion of the organs by the bacilli from the intestinal canal had occurred, and that the agglutinins were called forth in response thereto; but there is also the possibility that no such migration had taken place and that the agglutinins were evoked by a reaction on the part of the intestinal epithelium to the bacilli present in the intestinal contents. In this connection it is known that killed cultures of bacteria given by the mouth may stimulate the production of specific agglutinin, but in a very irregular and inconstant fashion. It must be confessed that the whole question is at present obscure.

Reference may be made to an article by Rolly [4] dealing with paratyphoid infection. A number of temperature charts are shown in this paper, which is chiefly of clinical interest.

Bainbridge and O'Brien [5] present a useful contribution on the paratyphoid group of bacilli. Its distribution in man, animals and food, is discussed. Their conclusions are as follows :—

(1) The term "paratyphoid group of bacilli" has been confined in the present inquiry to those strains which in their cultural characters and agglutination reactions are indistinguishable from *B. suipestifer* and *B. paratyphosus* (B). *B. enteritidis* Gærtner and *B. paratyphosus* (A) are excluded.

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[1] Bainbridge, F. A. (April, 1909), "On the Paratyphoid and Food-poisoning Bacilli, and on the Nature and Efficiency of Certain Rat Viruses." *Journal Pathology and Bacteriology*, Vol. XIII.

[2] Mandelbaum, M. (January 25, 1910), "Eine neue einfache Methode zur Typhusdiagnose." *Münch. Med. Woch.* Quoted in *Journal Royal Army Medical Corps.*

[3] Petrie, G. F., and O'Brien, R. A. (December, 1910), "The Experimental Production of the Carrier-state by Feeding." *Proceedings of the Royal Society of Medicine.*

[4] Rolly, Fr. (March 14, 1911), "Über Paratyphusinfektionen." *Münch. Med. Woch.*

[5] Bainbridge, F. A., and O'Brien, R. A. (March, 1911), "On the Paratyphoid Group of Bacilli." *Journal of Hygiene.*

Para-typhoid Fever—*continued*

(2) The strains of bacilli belonging to the "paratyphoid" group can be separated into two classes by means of the absorption method, namely one group identical with recognised standard strains of *B. suipestifer*, and one identical with standard strains of *B. paratyphosus* (B); and we regard these two bacilli as separate organisms.

(3) In our experience, *B. suipestifer* has been found only in food or in outbreaks of acute illness attributable to food-poisoning, whereas *B. paratyphosus* (B) has been found in cases of paratyphoid fever or in persistent paratyphoid "carriers."

(4) We are disposed to put forward the suggestion indicated by these observations, that these two organisms have a different distribution in nature, the normal habitat of *B. suipestifer* being the alimentary canal of the pig (and other animals) and of food derived from such animals, whereas the normal habitat of *B. paratyphosus* (B) is the human alimentary tract (including the gall-bladder).

(5) The examination of cultures from the fæces and urine of 300 typhoid convalescents was completely negative, neither *B. suipestifer* nor *B. paratyphosus* (B) being obtained. These observations confirm those of other writers, and, apart from carrier cases, the occurrence of *B. paratyphosus* (B) in healthy human beings appears to be unknown in this country.

Bainbridge and Dudfield [1] have a report on an outbreak of acute gastro-enteritis caused by *B. paratyphosus* B. It would thus appear that this organism is not only capable of giving rise to paratyphoid fever, but also to acute gastro-enteritis simulating food-poisoning.

Mention may be made of another excellent paper by Bainbridge [2] entitled "The Etiology and Epidemiology of Paratyphoid Fever and Food-poisoning." As there is a reference to it under another section (*vide* "Food Poisoning"), there is no necessity to call attention here to the important points brought out by this observer.

Firth [3] puts in a plea for clear thinking as to the use of the term "paratyphoid fever." His vast experience of fevers of this type had led him to suggest that the somewhat loosely applied name of paratyphoid fever should only be given to fevers due to *B. paratyphosus* A infection, and that the term "food poisoning" should be given to conditions in which the causative micro-organism is either the *B. paratyphosus* B, or *B. suipestifer*, or the other closely allied organism, *B. enteritidis* (Gærtner).

Without going into the question of what is meant by a *Bacillus paratyphosus* B, or discussing how confusion has arisen, or the methods by which confusion can be avoided as to whether a given micro-organism is *Bacillus paratyphosus* B, or *Bacillus suipestifer*, it appears desirable to recognise that infections by these micro-organisms are really not "fevers" as ordinarily understood, but rather explosive infections of the nature of an acute enteritis commonly the outcome of what is called "food poisoning." As explained, the infection by the "A" bacillus conforms to quite a different type, and is best described as "paratyphoid fever."

Pellagra. Pellagra in all probability existed for many years in Europe before it was recognised as a distinct disease, as it was for a long time considered as an unusual manifestation of some other condition such as scurvy or leprosy. Indeed, Gaspard Casal, a physician of the Asturias, described pellagra under the name *lepra Asturiensis*. Frapolli in 1771 gave it the name of pellagra, derived from pelle, skin; and agra, rough.

A good historical account of the disease is given by Wood.[4]

It is found to be present in Europe, Africa, Asia, and America. In Europe at the present time the chief seats of the disease are Northern and Central Italy and Roumania, while it is also to be found in Southern France, Portugal, Spain, Austria, and Turkey. In Africa it is known in Egypt, Algeria, Tunisia, and South Africa. Of recent years pellagra has extended with great rapidity in America, chiefly in the Southern States.

The precise etiology of this disease has yet to be solved, for the actual knowledge of the cause of pellagra remains still in the realms of hypothesis, although of recent years many important points in connection with it have been elucidated.

Lavinder,[5] in an interesting paper, discusses the etiology of pellagra, and mentions the general grounds upon which are based the etiological relations between maize and pellagra.

(1) It is declared that history and observation show clearly that the first appearance of pellagra, and its later dissemination, followed, more or less closely, the introduction of maize culture into Spain, and its gradual spread to France, Italy, and other countries of southern Europe.

(2) It is declared that pellagra is found as an endemic disease only in those countries where maize is grown and extensively used as an article of diet by the poorer rural classes. It is of importance to note, on the other

[1] Bainbridge, F. A., and Dudfield, R. (March, 1911), "An Outbreak of Acute Gastro-enteritis Caused by *B. paratyphosus* (B)." *Journal of Hygiene.*

[2] Bainbridge, F. A. (February, 1911), "The Etiology and Epidemiology of Paratyphoid Fever and Food-poisoning." *Proceedings of the Royal Society of Medicine.*

[3] Firth, R. H. (May 27, 1911), "Paratyphoid Fever." *Lancet.*

[4] Wood, E. J. (1908), "The Appearance of Pellagra in the United States." *Transactions of the College of Physicians, Philadelphia.*

[5] Lavinder, C. H. (July 10, 1909), "The Etiology of Pellagra." *New York Medical Journal.* Quoted in *American Society of Tropical Medicine*, Collected Papers, 1909.

Pellagra—*continued*

hand, that the area in which pellagra is found endemic is but as a spot on the extensive area over which maize is found under cultivation. There are vast tracts where maize is, and has been, grown and used as food for many years, and yet no pellagra has appeared. This is a matter of much import with regard to the etiological rôle which spoiled maize is supposed to play.

(3) It is declared that countries in which maize is not grown or used as food, or only exceptionally so used, even though contiguous to pellagrous sections, or actually surrounded by them, are free of pellagra. There are numerous striking instances of this kind reported in the literature of pellagra (*see* Lombroso, Procopiu, Babes and Sion, and others).

(4) It is declared that a change of food, either among individuals or groups of individuals, brings constantly a diminution or disappearance of pellagra, or *vice versa*. There are also many reported instances of this kind. Most writers allege that recovery may take place, or amelioration occur in the condition of pellagrins by removing from their diet all maize and maize products. The case of Corfu in this connection is regarded as such a notable instance that it may bear quoting. Typaldos states that pellagra was unknown in this island previous to 1857, and that up to that time the inhabitants grew their own maize, which was of a fine quality, but, for economic reasons, the culture of grapes became almost universal, and they began to subsist on an imported maize of very poor quality—that is, spoiled maize. Pellagra followed and became endemic, and he found, in 1866, eighty-one cases there.

Lavinder in this paper then discusses the various modifications of the maize theory under the following headings—(1) That maize as a foodstuff is wanting in proper nutritive value. (2) That good sound maize contains certain toxic substances that cause pellagra. (3) The toxico-chemical idea that, under the influence of parasitic growths, maize may undergo certain changes with the formation of one or more toxic substances of a chemical nature. (4) The toxico-infective idea that from spoiled maize there is formed within the body certain toxic substances. (5) The idea that pellagra is a specific infection derived from maize, either a mould or a bacterium. Lavinder then discusses the views held by those who are against the maize theory ("antizeists"), and makes a reference to Sambon's protozoan theory. The paper is concluded by a brief description of the main predisposing causes of pellagra.

At the conference on pellagra held in Columbia, South Carolina, in 1909, Sandwith[1] stated that the following axioms held good in Italy and Egypt :—

(1) In districts where no maize is cultivated or habitually eaten, pellagra does not exist. (2) Maize may be cultivated in many districts and yet there be no pellagra. (3) The disease requires for its production the habitual use of damaged maize.

At the British Medical Association Meeting held in 1905, Sambon,[2] however, pointed out that pellagra did not appear to be a food disease due to unsound maize, but in all probability was due to the presence of a protozoon. His reasons for this view were as follows :—

(1) The total absence or extreme rarity of pellagra in certain places where maize forms the staple food of the population.

(2) The presence of the disease in places outside the area of maize culture, and in people who have never partaken of this cereal as food.

(3) The utter failure of numerous investigators to reproduce the disease (true pellagra) in either man or the lower animals by means of maize itself, by the toxins obtained from decomposing maize or the cultures of any of the numerous bacteria and fungi found on maize which have been at one time or another incriminated as its causative agents.

(4) The striking recurrence of symptoms each spring, even after removal of the patient from the endemic area, and after the entire suppression of maize from the diet.

(5) The similarity of symptoms (early skin eruption, late nervous manifestations) and anatomical lesions (perivascular small-cell infiltration), with other protozoal diseases such as syphilis and trypanosomiasis.

(6) The marked increase of large mononuclear leucocytes.

(7) The favourable action of arsenic in the treatment of the disease, as in trypanosomiasis, kala-azar, and other protozoal infections.

Sambon [3] about a year ago published a progress report on his investigations connected with pellagra in Italy. He states he has been able to establish the following points :—

(1) That pellagra is not due to the eating of maize, either sound or deteriorated, as hitherto almost universally believed.

(2) That it has a striking, peculiar, and well-defined topographical distribution.

(3) That its endemic foci or "stations" have remained exactly the same in many places for at least a century.

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[1] Sandwith, F. M. (November 13, 1909), *Journal American Medical Association.* Quoted in *Medical Annual*, 1911.

[2] Sambon, L. W. (November 11, 1905), "Pellagra." *British Medical Journal.*

[3] *Idem* (September 15, October 1, October 15, November 1, 1910), "Progress Report on the Investigation of Pellagra." *Journal Tropical Medicine and Hygiene.*

Pellagra—*continued*

(4) That its stations are closely associated with streams of running water.

(5) That a minute blood-sucking fly, of the genus *Simulium*, is, in all probability, the agent by which pellagra is conveyed.

He enumerates the various Italian theories concerning the etiology of pellagra, all of which, with the exception of one, agree in making maize responsible for the incidence of the disease. Alessandrini's parasitism theory of a nematode worm (*Filaria* ?), as yet undetermined, is the one exception. Alessandrini claims to have found this worm in the skin of pellagrins and in the drinking-water of affected districts.

The objections to the maize theory are stated as follows, and these are discussed.

All theories making maize the direct causative factor of the disease are opposed by the following facts :—

(1) There is no foundation whatever for the belief that pellagra broke out in Europe soon after the introduction of maize from America.

(2) The topographical distribution of pellagra does not coincide either with the distribution of maize cultivation or with that of maize consumption.

(3) The disease occurs frequently in persons who have seldom or never partaken of maize as an article of food.

(4) All preventive measures based on the maize theory have failed.

(5) The characteristic skin eruption and other symptoms of the disease may recur each spring for several successive years in patients who are far removed from the endemic districts and who abstain from maize.

Sambon's reasons for considering that pellagra is a parasitic insect-borne disease are as follows :—

(1) *Pellagra is a parasitic disease*, because—

(*a*) The characteristic eruption and other symptoms of the disease may recur each spring for a number of years, notwithstanding the removal of the patient from the endemic districts and the strict elimination of maize from his diet. The peculiar periodicity of symptoms can be explained only by the agency of a parasitic organism presenting definite alternating periods of latency and activity. Analogous periodicities are met with in other parasitic diseases—as, for example, in tertian fever, in which the periods of activity of the parasite (*Plasmodium vivax*) recur each summer in correlation with the activity period of its anophelic definitive host. No toxic substance could account for it.

(*b*) It presents the peculiarities of distribution and seasonal incidence found in all parasitic diseases.

(*c*) Its symptoms, course, duration, morbid lesions are analogous to those of other parasitic diseases.

(2) *It is an insect-borne disease*, because—

(*a*) It is not directly contagious.

(*b*) Neither food nor drinking-water account for its peculiar epidemiology.

(*c*) It is limited to certain rural districts only, towns and villages almost invariably escaping.

(*d*) It presents a definite and peculiar seasonal incidence—viz. spring and autumn.

(*e*) It is practically restricted to only one class of people—viz. the field labourer, owing to greater exposure to infection.

(3) *It is conveyed by a Simulium*, because—

(*a*) Simulium, so far as known, appears to affect the same topographical conditions as pellagra.

(*b*) In its imago stage it seems to present the same seasonal incidence.

(*c*) It is found only in rural districts, and, as a rule, does not enter towns, villages, or houses.

(*d*) It explains most admirably the peculiar limitation of the disease to agricultural labourers, a limitation which nothing else can explain in a satisfactory manner.

(*e*) It has a wide geographical distribution which seems to cover that of pellagra, although certainly exceeding it, in the same way that the distributional area of the *Anophelinæ* exceeds that of malaria, and the range of *Stegomyia calopus* that of yellow fever.

(*f*) It is known to cause severe epizootics in Europe and America.

(*g*) Other similarly minute blood-sucking diptera such as *Phlebotomus papatasii* and *Dilophus febrilis* are strongly suspected of being propagators of human diseases.

Sambon then calls attention to the chief points considered by the Italian physicians in the diagnosis of pellagra, and mentions that they do not lay any stress on the erythema, which, in their experience, is frequently absent, or easily confounded with a strikingly similar eruption due to ethyl alcohol, and accordingly called "ethylic erythema." Sambon, however, found that those who held the erythema to be frequently missing had either overlooked it or confounded other diseases with pellagra, and that the so-called "ethylic erythema" is nothing more nor less than the pellagra dermatitis in alcoholics. His experience leads him to consider the pellagrous eruption as the earliest, most distinctive, and essential manifestation of the disease.

Its features are characteristic and striking. It occurs in spring or early summer, rarely also in autumn, and is limited, almost exclusively, to the agricultural population of certain well-defined endemic areas. It appears suddenly under the action of the sun's rays, and affects those parts of the body which are ordinarily bare and

Pellagra—*continued*

exposed to the sun, such as the back of the hands, the face, the neck, and, when bare, the extensor surfaces of the feet and legs, the forearms, the upper part of the chest and back. It appears in the form of more or less symmetrical patches of a bright red, or deep red, colour, with sharply defined margin. The affected parts are more or less swollen, and the patient experiences a painful sensation of burning or tingling, which becomes particularly acute under exposure to the action of the solar rays. The rash stands out for some days, and is followed by marked and persisting desquamation, leaving the skin pigmented, thinned, and parchment-like.

In cases of a mild type, especially in young children, the pellagrous rash may very easily escape observation, being not infrequently scarcely perceptible, and soon disappearing without leaving any trace. In such cases it may be mistaken for an ordinary sunburn, as Strambio pointed out over a century ago. I have no reason to doubt that pellagra may exceptionally occur without any cutaneous manifestation, and that we may speak of a *pellagra sine pellagra* as we do of *morbilli sine morbillis*, of *scarlatina sine scarlatina*, and even of *variolæ sine variolis*. But I am inclined to believe that the majority of cases of pellagra without eruption are to be accounted for by evanescent undiscovered rashes, and this is all the more probable when the actual presence of desquamation obviously suggests an antecedent cutaneous inflammation.

In children, I have frequently noticed the extreme mildness, brief duration, and complete disappearance of the cutaneous marks, and I believe this to be one of the reasons why so many authors have wrongly stated that pellagra is a rare disease in young children.

Sambon then discusses the complication of pellagra with other infections which may lead to confusion of the diagnosis. Such infections as scurvy, ankylostomiasis, and syphilis are mentioned. With regard to ankylostomiasis he considers "that a specially severe form of infection with this condition plays a decided part in the development of pellagra, as it certainly does in kala-azar, beri-beri, and other diseases."

A long description is given of the topographical distribution of pellagra, and the permanency of endemic areas and exemption of towns is considered. With regard to the latter Sambon notes that—

The exemption of towns cannot be explained by the maize theory, and, indeed, is a very important fact against it. The poor townfolk eat as much maize as the peasants. The zeists say that the townfolk escape because they eat other things besides ; but so do the peasants. A further reason submitted is that in towns the grain is of better quality, but the peasants eat their grain in these very same towns.

The absence of pellagra from towns struck me from the first as analogous to the absence of malaria from large towns. Rome, placed in the very heart of an intensely malarious region, escapes the disease. However, in pellagra the limitation is far more definite, because whilst mosquitoes enter houses the sand-flies do not. Therefore, while the smaller inhabited centres of malarial regions often suffer very heavily from the disease, pellagra never attacks them.

Sambon, during his investigations, found that the greater liability of those engaged in agrarian occupations was due to the fact that they were tormented by the sand-flies which swarmed about the neighbouring streams.

The seasonal incidence of pellagra in Italy was either in spring or autumn, but more frequently in spring, and Sambon noticed that the date of appearance of the eruption varied from year to year according to the prevailing meteorological conditions. With regard to the contagiousness of pellagra, Sambon considers that as pellagra is an insect-borne disease, the contagion theory is untenable, and quotes instances to prove this. Likewise he does not hold that pellagra is a hereditary disease. The hæmatology of pellagra is considered, and although Sambon noticed that there was a relative increase of the mononuclear leucocytes, it is not quite clear whether he refers to the large or the small mononuclears, more especially when the results of Low's observations are considered, for in differential leucocyte counts made by Low there was a definite relative increase of lymphocytes.

No parasites were found in the blood of pellagra patients, and Sambon suggests that the causal germ may be ultra-microscopical. The suspected insect carrier of pellagra is discussed at some length, together with other points, but lack of space prevents any further reference being made to what is an extremely suggestive report, written by an observer who has certainly made out as strong a case as possible in support of his views without the help of experimental evidence.

Long [1] brings forward what he calls a working hypothesis regarding the nature of pellagra, viz., that it is a disease resulting from an injury to the intestinal mucous membrane produced by an amœba. He states that—

As a result of the ulceration there is an inflammatory process extending throughout the alimentary tract which interferes with the absorptive power of the intestine and the manufacture of the digestive ferments normally produced in the intestines. Later, owing to the long-continued inflammation the pancreas and liver undergo inflammatory changes which interfere with the quality of the digestive juices that they produce, with the result

[1] Long, J. D. (August 27, 1910), "Pellagra." *Journal American Medical Association.* Quoted in *Journal Tropical Medicine and Hygiene*, October 15, 1910.

that the food ingested is improperly digested. The presence in the intestine of undigested food favours fermentation and putrefaction of its elements, with the production of certain toxins, ptomaines, and intermediate products of digestion which are harmful to the body. Pellagra—*continued*

Long's view, however, is too hypothetical to call for further remarks.

Raubitschek [1] has subjected various specimens of maize flour, sound and unsound, to a bacteriological examination for the purpose of testing the various theories—the bacterial, the autotoxic, and toxic—of the causation of pellagra. All his experiments gave negative results. Cultural examination of the diarrhœa-like pellagra stools, bacteriological examination of the organs of patients after death, serum precipitation and complement fixation tests all gave negative results.

Raubitschek refers to "jago pyrismus," a condition which has been recognised amongst white or partially white animals fed on buck-wheat, and at the same time exposed to sunlight; the animals become emaciated or suffer from paralysis, and die in a short time. The similarity of the condition to pellagra is striking. Some experiments were carried out on animals, white and coloured rabbits, guinea-pigs, and mice

The animals were confined in cages, some of them in the dark, others in sunlight, and were differently fed on mixed diet, on raw or cooked maize, both sound and unsound, and on cooked rice.

The light-coloured animals fed only on maize or rice and, kept in the light, lost weight and suffered from paralysis, and eventually died in eight to twenty-one days. The dark-coloured animals, however, escaped, and the others, if the cage was removed into the dark after the symptoms had begun to show themselves, recovered, even without change of diet.

Raubitschek's theory is that on a preponderating maize diet, under the influence of sunlight, a poison is formed from the lipoids of the maize on the parts of the skin exposed to sunlight, and this poison acts not only locally on the skin but also in the organism as a whole.

Sambon [2] has referred to the work of Raubitschek and Hausmann, and states that their experiments do not explain the definite topographical distribution of the disease or its peculiar double seasonal incidence. Moreover, he points out that the skin lesions in pellagra are evanescent phenomena of only a few days duration, notwithstanding continued consumption of maize and persistent exposure to sunlight.

Reference may be made to a note by Dudgeon on pellagra in Egypt. This observer, from his experience of the disease in Egypt, is not inclined to coincide with Sambon's view as to the sand-fly being the transmitter of pellagra, but considers that certain forms of maize, and those particularly under certain conditions of decay, are implicated in the cause of the disease.

Dudgeon [3] considers that pellagra is undoubtedly confined entirely to people whose staple diet is maize.

It is very uncommon amongst the rich agricultural class whose diet is not maize, although it does occur; and, as bearing on the theory of fly-bite, I would point out that the poorer class when they sleep at night are more protected, for they wrap themselves entirely, including their heads, in their cloaks, whereas the richer class sleep under mosquito nets, which are practically no protection against the small sand-fly. If, therefore, Dr. Sambon's theory were correct, the disease ought to be more prevalent among the well-to-do agriculturists than the fellaheen. Amongst the town dwellers where wheat-bread is eaten, pellagra is almost unknown, and, in the few cases I have come across, it has always been found on inquiry that maize has been eaten in some form or other at some time.

Hodson [4] thinks that pellagra in Egypt is only a rash arising in patients who have been the subjects of prolonged anæmia, that it is, in most cases, due to persistent worm infections, and occurs in the worst cases of these infections in association with poverty and malnutrition. Hodson gives a few facts to support his views.

Enough has perhaps been said as regards the views held with relation to the etiology of pellagra. From the various papers referred to, it is apparent that the whole subject is still more or less *sub judice*, though Sambon's theory is undoubtedly gaining ground and may yet be proved correct. Recent observations in Georgia and elsewhere in the United States tend to confirm his interesting hypothesis.

Tucker [5] has a paper on pellagra, in which he bases his remarks on the analytical

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[1] Raubitschek, H. (June 30, 1910), "Zur Kenntnis der Pathogenese der Pellagra." *Wien. Klin. Woch.* Quoted in Epitome, *British Medical Journal*, December 3, 1910.

[2] Sambon, L. W. (November 16, 1910), "Pellagra Investigation Committee." Quoted in *Journal Tropical Medicine and Hygiene*, December 1, 1910.

[3] Dudgeon, H. W. (September 15, 1910), "Pellagra." *Journal Tropical Medicine and Hygiene.*

[4] Hodson, V. S. (October 1, 1910), "Pellagra in Egypt." *Lancet.*

[5] Tucker, B. G. (January 28, 1911), "Pellagra." *Journal American Medical Association.* Quoted in *Journal Tropical Medicine and Hygiene*, February 15, 1911.

Pellagra— *continued*

study of fifty-five non-institutional or sporadic cases. He concludes from his statistics that—

(1) Pellagra may occur at any age from childhood to old age.

(2) In the Southern States, although the negro forms the majority of the lower class, yet pellagra is most common in the white.

(3) The disease, while affecting chiefly the lower classes, is occasionally seen among those of good hygienic and social surroundings.

(4) The disease is widely spread, and does not occur in local epidemics.

(5) The disease in the cases reported is more common in rural districts than in the cities.

(6) The majority of cases occur in the spring and early summer.

(7) The gastro-intestinal symptoms, especially the diarrhœa, are usually the first manifestations of the disease.

(8) The ingestion of maize or maize products, whether spoiled or not, is not alone the cause of pellagra.

(9) Patients whose constitutions are depleted by pernicious habits or chronic diseases are not rendered thereby more susceptible to pellagra than those not so affected.

(10) The backs of the hands are always affected in the cutaneous lesions of pellagra, and the lesions are always symmetrical.

(11) Exposure to the sun cannot account for the cutaneous lesions.

(12) Stomatitis is almost a constant symptom.

(13) The nervous and mental symptoms conform to known nervous disease or forms of insanity.

(14) The nervous and mental symptoms form no distinct clinical entity.

(15) The eye symptoms are not pathognomonic.

(16) Emaciation is practically constant.

(17) The special senses are only occasionally affected.

(18) Pellagra is not *per se* a febrile disease, and when an elevation of temperature occurs, it may frequently be accounted for by a complication.

(19) A moderate anæmia is found in most of the cases.

(20) The heart, lungs, and genito-urinary organs do not seem to be particularly affected by pellagra.

(21) Examinations of the urine, fæces, and blood show nothing pathognomonic of pellagra.

(22) The cause of pellagra is unknown, and the study of these cases throws no positive light on the etiology. Patients may have pellagra, who do not eat corn products. Sunlight does not account for the condition. In these cases no parasite, toxin, bacteria, nor insect has been isolated as being the causative factor.

(23) The disease is not communicable by ordinary contact.

(24) Three great systems are affected: the digestive tract, the cutaneous surface and the cerebro-spinal and peripheral nervous systems, and their involvement seems to be in the order named.

(25) Remissions occur in over half of the cases.

(26) Death frequently occurs in the first attack.

(27) It is too early in the study of the disease in this country (America) to estimate the mortality. Probably 50 per cent. die during the first two years.

(28) In these cases it cannot be said that any patient is more than apparently cured, as it may simply be a remission.

(29) No specific cure for the disease has been found, and the remedies in general use are of doubtful value. Hexamethylenamin may possibly have curative properties.

Gurd [1] has contributed an interesting paper on the histology of the skin lesions in pellagra:—

The cutaneous lesions in pellagra, he states, consist of an early erythema, or, in some cases, of vesicles or bullous formations which are followed by hyperkeratosis and pigmentation, resulting in a dry, dark brown scaliness. The various lesions resemble those produced by the sun, but much more marked. The histological phenomena of the erythematous and bullous stage are those of a mild acute inflammatory reaction, plus a degeneration in the superficial layers of the corium. Following this degeneration, which involves not only the general connective tissue but the connective tissue of the blood-vessels, there is reparative change evidenced histologically by an increased cellularity of the corium and the presence of fibroplasts. There is an increase also in the number of the capillaries, which become dilated, and the epidermis becomes thickened, this increase being specially marked in the prickle cells and the stratum granulosum.

In the later stages the epithelium dips down deeply into the rarefied connective tissue. Round the blood-vessels during the reactionary process are found collections of lymphoid cells, a few plasma cells, but no mast cells or eosinophiles. The irritant producing the degeneration in the corium is sunlight, in the presence of some predisposing factor. This is suggested by the enormous increase in pigment formation in the epithelial cells and by the large number of chromatophores in the superficial layers of the corium. The pigmentation is autochthonous in both types of cell. There is no reason for believing that the pigment is formed in the cells of the corium and thence discharged into the epithelium, or that the reverse process takes place.

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[1] Gurd, F. B. (January 5, 1911), "A Study of the Histological Skin Lesions in Pellagra." *Journal of Experimental Medicine*. Quoted in *Journal Tropical Medicine and Hygiene*.

Pellagra—*continued*

The predisposing factor inducing the changes in the corium is apparently due to a lessened resistance of the epithelium to the violet or ultra-violet rays, due to some metabolic insufficiency on the part of the epithelial cells.

Gurd is of the opinion that more extended observations may justify the conclusion that pellagra throughout the body is a disease essentially of the epithelium, including the nervous system, this pathological condition manifesting itself by an insufficient or altered function.

Welton,[1] in a report of the examination of the eyes of fifty-five pellagra patients in the Illinois State Hospital, states that—

(1) Paralysis of the eye muscles is found in the later stage of the disease in a small percentage of cases; conjunctivitis is not an uncommon symptom. Early-forming cataracts are frequently noted, and the theory of the metabolic nature of pellagra is supported, because cataract is generally considered as an altered state of the nutrition of the lens when occurring in normal individuals. Inflammation of the optic nerve and retina is observed in a relatively large percentage of cases. Common and most pronounced of all the eye changes is involvement of the choroid.

(2) In none of the cases presenting eye symptoms could the character of the eye changes be regarded as pathognomonic of pellagra.

(3) The severity of the eye symptoms runs parallel with the severity of the general manifestations of the disease, and the finding of marked eye changes adds to the gravity of the prognosis in pellagra, and indicates, in a large percentage of cases, an early fatal termination.

Dods Brown and Low [2] describe a case of apparently true pellagra in a woman who had lived all her days in Shetland. The typical nervous, gastro-intestinal, and cutaneous symptoms were present. The patient had never eaten maize, but had been in the habit of eating raw oatmeal and rice.

Reference may be made to a paper by Willets,[3] entitled "A General Discussion of Pellagra." The clinical manifestations and pathological findings in this disease are discussed, and an illustrated report of a probable case of pellagra in the Philippine Islands is given.

Bass [4] recorded an interesting case of pellagra in which the patient, a female, had been an exclusive starch eater for a few months, or a year, before recognisable symptoms of pellagra had developed. Further, she also suffered from a severe uncinariasis.

Cole,[5] recognising that recovery from an attack of pellagra might produce a certain degree of immunity in a patient, utilised the blood of such a case for transfusion into a patient dying from the disease. The result obtained was remarkable, for the patient eventually recovered.

Encouraged by this method of treatment Cole,[6] in collaboration with Gillman and Winthrop, has since transfused nineteen additional patients in the terminal stages of the disease. The recoveries (60 per cent.) following transfusion in the grave type of cases compared most favourably with the recoveries (10 to 20 per cent.) in the same type of cases in which other therapeutic measures were employed. In several cases there was an astonishing improvement in the patients' mental condition, following operation. In all cases there was a rapid increase in the patients' hæmoglobin index, a rapid return of body strength, a return of digestive faculties, and an increase of body weight.

As regards drug treatment in pellagra, no specific has yet been found.

Willets (*loc. cit.*) considers that the best results have been obtained by

excluding corn from the diet, giving a liberal allowance, including meats, and treating the cases symptomatically. Tonics are often administered. The skin lesions do not respond well to local treatment. The exhibition of common salt is thought to be beneficial. Arsenic in the form of Fowler's solution, arsenic trioxide, atoxyl and soamin has been used, but reports of the results are very conflicting, some men apparently obtaining good results, while others believe that no beneficial effects are secured from its use. However, the balance of evidence tends to show that Fowler's solution is of importance, especially in non-asylum cases.

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[1] Welton, C. B. (November 13, 1909), "Eye Symptoms of Pellagra." *Journal American Medical Association.* Quoted in *Journal Tropical Medicine and Hygiene,* February 1, 1910.

[2] Brown, R. D., and Low, R. C. (September, 1909), "Pellagra in Shetland." *Edinburgh Medical Journal.*

[3] Willets, D. G. (November, 1910), "A General Discussion of Pellagra, with Report of a Probable Case in the Philippine Islands." *Philippine Journal of Science,* B.

[4] Bass, C. C. (1910), "A Case of Pellagra caused by Amylophagy resulting from Uncinariasis." *American Society of Tropical Medicine,* Collected Papers.

[5] Cole, H. P. (November 12, 1908), "Transfusion of Blood in a Case of Pellagra." A paper read before Southern Medical Association at Atlanta. Quoted in *Journal Tropical Medicine and Hygiene,* August 16, 1909.

[6] *Idem* (February 11, 1911), "Transfusion in Pellagra." *Journal American Medical Association.* Quoted in *Journal Tropical Medicine and Hygiene,* April 15, 1911.

Pellagra—*continued*

Babes, Vasilin, and Georghus [1] recommend as a further step in the atoxyl treatment of pellagra the combination of arsenious acid both internally and externally. They report a series of fourteen cases in which this treatment gave very good results. The treatment consists in one injection of 5 centigrammes atoxyl; simultaneously from 1 to 4 mgms. of arsenious acid is given in pill form, and 5 grammes of a 1 to 50 arsenious acid ointment is rubbed on the sound part of the skin. In slight cases a single treatment was sufficient, but in severe cases the same treatment was repeated the next day, and in very severe cases again after a week's interval on two successive days. These doses were well borne even by children weighing only 8 to 20 kilogrammes. The treatment apparently affects all the manifestations of the disease.

Marie,[2] in an excellent text-book on Pellagra, cites Lombroso's views as regards treatment, and states that in great part the present therapy of pellagra is founded on Lombroso's teaching. Referring to Lombroso, Marie says :—

> He recommends as a rule a liberal diet, including meats especially, but points out that this alone is insufficient. He also remarks that in well-nourished pellagrins this is of course not so much indicated, and adds that such cases are rebellious to treatment. He speaks of baths and cold douches, which he thinks benefit especially paretic states, the skin manifestations and the painful burning sensations so common in pellagrins; and further says that, while they do not cure, they at least prolong existence or render it more tolerable. In some patients, however, there is a true aversion to baths, and in such they should not be tried.

Lombroso's method of giving Fowler's solution is also quoted. Marie's book is full of useful information, and is recommended for the perusal of those interested in pellagra.

Phlebotomus Fever. This fever has of recent years attracted a considerable amount of attention and research, and has finally been accepted as a definite entity.

One has only to refer to an interesting historical summary given by Birt [3] to see that this fever was described as far back as 1804 by Pym of the Army Medical Service. Since then it has been honoured by an extensive nomenclature till the year 1908 when Doerr,[4] who had an opportunity of studying an epidemic of it in Herzegovina named it "Das Pappatacifieber," as he definitely proved its transmission to human beings by a species of gnat—*Phlebotomus papatasii*—belonging to the family of the *Psychodidæ*. This same observer, after much research, failed to find the causal parasite of the fever, and came to the conclusion that it was due to an invisible virus, as he was able to communicate the fever in a typical form by inoculating the filtrates obtained when blood taken from cases during the course of the fever was passed through Berkefeld-Nordtmeyer and Reichel filters.

Birt,[5] in an excellent paper on phlebotomus fever in Malta and Crete, describes the clinical signs and symptoms of the disease, and by an interesting series of experiments has confirmed Doerr's results. Birt showed—

(1) That the blood of a person suffering from phlebotomus fever is virulent during the first day;

(2) That the virus can pass through a Pasteur Chamberland candle "F";

(3) That the *P. papatasii* can convey the infection;

(4) That the incubation period varied from three days sixteen hours to seven days;

(5) That *P. papatasii* are infective seven to ten days after sucking virulent blood;

(6) That the virus retains its activity for a week *in vitro*.

Birt states that phlebotomus fever is an infection distinct from dengue, which has well-marked clinical signs in the rashes and joint pains, and these are of a much more severe type than the aches of phlebotomus fever.

The phlebotomus fever of Malta and Crete is evidently a milder ailment than the type occurring in Herzegovina. As in Malta, the fever is prevalent in Herzegovina during the summer months only, after the *P. papatasii* has made its appearance. Ophthalmo and skin reactions and precipitin tests gave negative results, and so far no specific test for diagnosing the infection, except human inoculation, has been discovered. The typical clinical picture of a case of phlebotomus fever is given in Birt's paper.

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[1] Babes, V., Vasilin, A., and Georghus, N. (February 8, 1909), "Über kombinierte Behandlung der Pellagra mittels Atoxyls und arseniger Säure." *Berl. Klin. Woch.* Quoted in *The Medical Annual*, 1910.

[2] Marie, A. (1910), *Pellagra*. Translated by Lavinder, C. H., and Babcock, J. W.

[3] Birt, C. (February, 1910), "Phlebotomus Fever in Malta and Crete." *Journal Royal Army Medical Corps.*

[4] Doerr, R., Franz, K., and Taussig, S. (1908), "Das Pappatacifieber, ein epidemisches Drei-Tage-Fieber im Adriatischen Küstengebiete Österreich-Ungarns." *Berl. Klin. Woch.*, XXII. Quoted in *British Medical Journal*, December 5, 1908.

[5] Birt, C. (March, 1910), "Phlebotomus Fever in Malta and Crete." *Journal Royal Army Medical Corps.*

Phlebotomus Fever —*continued*

Chilliness, nausea, headache, heaviness and discomfort about the eyes; lumbar pain and stiffness of the muscles of the lower extremities, and somnolence, induce the patient to take early to his bed. He finds himself unfit for his duty next morning, and comes for relief. His temperature will then be 101° to 102° F., and pulse slow, 70 to 80. His face will be flushed, eyes suffused and heavy, the tongue rather large, and coated with a thin white fur, except at the tip and edges. There is no rash except from the effects of biting insects. The same evening the temperature may rise to 103° F., though without a corresponding increase in the frequency of the pulse. A fall of two degrees takes place next morning, which often is continued without a further rise until the normal standard is attained. Convalescence is rapid. The suffused appearance of the conjunctiva caused the condition to be popularly termed "pink eye." In Austria, for the same reason, it was at first known as "the dog disease."

The blood changes show a moderate degree of leucopenia, which may continue into convalescence. The polynuclear leucocytes are diminished, numbering as a rule about 56 per cent., while there is an increase of the large and medium-sized mononuclears; the lymphocytes and eosinophiles are decreased. There is apparently no splenic enlargement. Franz, in Doerr's monograph (*loc. cit.*), notes the occurrence of cases of phlebotomus fever in which the intestinal symptoms are pronounced with little or no elevation of temperature. According to Birt second attacks occurred in 6 per cent. of cases. In Birt's paper, a short description of the habits and life history of *P. papatasii* is given.

Marett [1] continued Birt's observations on the *P. papatasii* in Malta, and in a more recent paper gives an account of the likely breeding-places of the sand-fly, together with a descriptive account of its larva and pupa. In a still more recent article [2] he again returns to the subject.

Newstead [3] has an excellent monograph on the pappataci flies of the Maltese Islands. He confirmed the observations of Birt and Marett with regard to the habits of the sand-flies of these islands; and states "that as far as our present knowledge is concerned the only conclusion which can be drawn from the investigations in Malta is that the chief breeding-places of the pappataci flies (*P. papatasii*, and *P. perniciosus*) are the crevices between the loose rocks in caves, stone walls, bastions, and similar situations."

Although there was no evidence that pappataci flies breed in the cellars and drains in Malta, one must remember that Grassi [4] found *P. papatasii* breeding in such places. Newstead's remarks concerning prophylactic measures for dealing with the phlebotomus fly are referred to under another section (Flies).

In India, explosive summer outbreaks occur in many parts, notably in Peshawar and the Punjab. The epidemics in Chitral and Kila Drosh were closely studied by M'Carrison [5] in 1903–4, who suspected that the sand-fly might be the agency by which the fever was spread.

Wimberley [6] gives a description of an epidemic of fever which occurred in the autumn among troops in Nowshera. The clinical signs and symptoms certainly simulated phlebotomus fever, but this observer noted that in 8 per cent. of the cases a rash appeared either in the form of a mere mottling of the skin, or a well-marked maculo-papular eruption. The diagnosis rested between dengue or phlebotomus fever. Wimberley states that the phlebotomus is common in the Peshawar valley, especially in the months of April and May. During the very hot months the flies diminish in number, and reappear in large numbers in the autumn.

In a later note [7] Wimberley considers that the epidemic described by him was in reality due to phlebotomus fever.

Doerr and Russ [8] carried out some further researches on pappataci fever, and stated that in the majority of their cases the incubation period was four days. The virus was eliminated very quickly from the blood, for although the latter was infective for the first day it was avirulent at the end of the second day.

These observers carried out some experiments with the virus. *In vitro*, they found that saponin and trypan red exerted no action, but that atoxyl in strong solution completely destroyed the virus. They proved that if the virus contained in the serum was mixed with

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[1] Marett, P. J. (September, 1910), "Preliminary Report on the Investigation into the Breeding-Places of the Sand-Fly in Malta." *Journal Royal Army Medical Corps.*

[2] *Idem* (July 1911), "The Life-history of the Phlebotomus." *Ibid.*

[3] Newstead, R. (May, 1911), "The Pappataci Flies (Phlebotomus) of the Maltese Islands." *Bulletin of Entomological Research.*

[4] Grassi, B. (1907), "Richerche sui Flebotomi." *Memorie della Società Italiana delle Scienze*, Ser. 3a, XIV.

[5] M'Carrison, R. (January, 1906), "The Three-Day Fever of Chitral." *Indian Medical Gazette.*

[6] Wimberley, C. N. C. (August, 1910), "Dengue, or Phlebotomus Fever? Notes on an Epidemic at Nowshera." *Ibid.*

[7] *Idem* (December, 1910), "Sand-fly Fever." *Ibid.*

[8] Doerr, D., and Russ, V. K. (1909), "Weitere Untersuchungen über das Pappataci-Fieber." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIII., No. 22.

Phlebotomus Fever —*continued*

the serum of a patient who had recovered from the disease two years previously the virus lost its toxic properties. The virus was unaffected by the serum of animals.

Doerr and Russ consider that the virus, in all probability, is transmitted by the female pappataci to its larvæ, and these, being infected through hereditary transmission, when adults, convey infection through their bites, causing a mild form of phlebotomus fever.

Franz and Kolár [1] have a paper referring to the pathology and treatment of pappataci fever. The pathological changes in the blood are discussed, and mention is made of septicæmia occurring as a secondary infection. In these septicæmia cases, electrargol injected hypodermically appears to have given good results. Among other drugs pyramidon is mentioned as being useful in relieving pain, and arsenical preparations are indicated in cases showing prolonged convalescence. Balfour found a full dose of Batley's solution of opium useful in relieving distressing symptoms in what was almost certainly an attack of phlebotomus fever.

Reference may be made to a paper by Tiraboschi [2] describing phlebotomus fever in South America.

Phillips,[3] at the British Medical Association Meeting in 1910, described the three-day fever of Egypt, which exactly corresponds to the phlebotomus fever of Malta.

Piroplasmosis. The whole subject of piroplasmosis has attained such great dimensions that it will not be possible to refer to all the work that has been carried out in recent years in connection with it. References, therefore, will be made only to the more important papers, and the latter will be grouped under the headings of Bovine, Canine, and Equine piroplasmosis. The subject of anaplasmosis is also considered.

Bovine Piroplasmosis. Soulié and Roig [4] have described bovine piroplasmosis affecting cattle in the neighbourhood of Algiers. Piroplasms were present in 15 per cent. of their cases. The bacillary forms were observed in the blood of latent cases, while in the acute infections, ring and ovoid forms were in evidence. There was, as a rule, a marked basophilia. Inoculation of the infected blood into healthy bovines produced the disease.

These observers consider that the parasites found represented *P. mutans* (Theiler) and *P. annulatum* (Dschunkowsky and Luhs).

Schein [5] has carried out some observations on the blood of infected bovines in Indo-China.

The ovoid and bacillary forms were more frequently seen than those of the *P. bigeminum* type. In the repeated examinations that were made, the twin pear-shaped form, when present, rarely existed for longer than three days, and its appearance was only noted in animals suffering from rinderpest.

Mention may be made of a paper by Stockman,[6] in which he discusses Redwater fever in England, and the possibility of *Ixodes ricinus* and *Hæmaphysalis punctata* being the transmitting agents. A few experiments carried out with the *Ixodes ricinus* failed to show that infection passes through the eggs to the young ticks. Experiments on similar lines were carried out with *Hæmaphysalis punctata*. Stockman found that adult ticks (*Hæmaphysalis punctata*) which had fed as nymphæ on infected blood were able to transmit the disease, whereas the nymphs of ticks which had sucked as larvæ infective material failed to do so. Similar negative results were obtained with the larvæ from mothers that had fed on infective material.

Stockman concludes his paper by some remarks on the prevention of Redwater, which may well be quoted :—

> There are three methods under the head of prevention which one may attempt to carry out.
>
> (1) By inoculating with virulent blood all new animals going on to the infected pastures and nursing them, if necessary, through the attack, one may give them a degree of immunity to start with which will prevent them

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[1] Franz, K., and Kolár, H. (April, 1910), "Zur Pathologie und Therapie des Pappatacifiebers." *Arch. f. Schiffs-u. Tropen-Hyg.*, Beihefte II.

[2] Tiraboschi, C. (October 30, 1910), "*Le Phlebotomus pappatasii* et la fièvre à Pappataci dans l'Amerique du Sud." *Arch. de Paras.*

[3] Phillips, L. (October 1, 1910), "Sand-fly Fever (Phlebotomus Fever or Pappatacifieber) in Cairo." *British Medical Journal.*

[4] Soulié, H., and Roig, G. (April 5, 1909), "Piroplasmose Bovine des environs d'Alger." *C. R. Soc. Biol.*

[5] Schein, H. (December, 1908), "Observations sur la piroplasmose des bovidés d'Indo-Chine et constatation de piroplasmose chez les buffles." *Ann. de l'Inst. Past.*

[6] Stockman, S. (September, 1908), "Redwater in England, and its Carriers." *Journal Comparative Pathology and Therapeutics.*

suffering severely from the infection conveyed by the ticks. The infected ticks themselves will keep up the degree of immunity as long as the animals are on the pastures. Piroplasmosis—*continued*

(2) One may attempt to eradicate the ticks from the pastures and so dispose of the natural carriers, the only agents which convey the disease naturally. One attempts to get rid of ticks by fully stocking the pastures and periodically dipping or spraying their hosts; that is to say, one tempts the ticks on to their hosts in order to kill the former.

(3) One may leave the infected ticks to purify themselves by keeping cattle off the pasture.

Theiler [1] has carried out some experiments to show the influence of cold on ticks and *P. parvum*. He found that—

(1) A temperature of 0° C. retards the hatching of *Rh. appendiculatus* nymphæ into adults.

(2) A temperature of 0° C. does not interfere with the development of the parasite within the engorged nymphæ.

(3) A temperature of 0° C. does not kill the virus contained in engorged nymphæ of *Rh. appendiculatus*.

(4) Larval ticks of *Rh. decoloratus* die within thirty minutes when exposed to a temperature of 18° C.

(5) Larval ticks of *Rh. decoloratus* do not die when exposed to a temperature of 18° C. for fifteen minutes.

(6) Larval ticks of *Rh. decoloratus* do not die when exposed to a temperature of 5° C. for twenty-four hours.

(7) The majority of larval ticks of *Rh. decoloratus* die when exposed to a temperature of 5° C. for forty-eight hours.

Bouet [2] has a short paper on bovine piroplasmosis on the Gold Coast. *P. parvum*, *P. mutans*, and *P. bigeminum* were found in the blood of different cattle. The ticks infesting these cattle were *Margaropus annulatus* (Say), *decoloratus* (Koch), and *Amblyomma variegatum* (Fab).

Broden and Rodhain [3] have also noted the presence of *P. mutans* and *P. bigeminum* among the cattle at Stanley Pool in the Congo.

Theiler [4] carried out some experiments to test the immunity of cattle inoculated with *P. mutans*. As a result of these he proved the following facts :—

(1) The exposure of animals immune against redwater in the low veld proved that this immunity protected against the redwater of that veld.

(2) Animals immune against heartwater were protected against that disease in the low veld.

(3) Animals which were only immune against redwater contracted a *Piroplasma mutans* infection when exposed in the low veld.

(4) All the animals which were not immune against *Piroplasma mutans* contracted this infection when exposed in the low veld, but none died.

(5) Of the two control animals which were not immune against any of the diseases both died; *Piroplasma mutans* was present in both cases, but the deaths were due to heartwater, and in one case complicated with redwater.

(6) All the exposed animals showed reactions, due either to heartwater or to some other agency, and this reaction, in the majority of cases, caused an increase in the number of *Piroplasma mutans* present in the blood.

(7) The animals which were immune against heartwater, *Piroplasma mutans* and *Piroplasma bigeminum*, showed a slight *Piroplasma mutans* infection, and also a slight reaction.

With the co-operation of Stockman, Theiler [5] carried out some experiments with English and South African redwater, in order to prove (1) whether English and South African redwater are identical; (2) if English cattle immunised against English redwater would thereby acquire any immunity against the ordinary redwater of South Africa; and (3) if English heifers inoculated in England with South African redwater would be immune against South African redwater when exposed to natural infection in South Africa. As a result of these experiments Theiler found that (1) English redwater is not always inoculable, and therefore differs in this respect from South African redwater; (2) English heifers when inoculated with English redwater do not acquire any immunity against South African redwater; (3) the inoculation of English cattle with South African redwater did not give a complete guarantee against a natural infection of ordinary redwater.

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[1] Theiler, A. (October 14, 1908), "The Influence of Cold on Ticks and *Piroplasma parvum*." *Bull. Soc. Path. Exot.*

[2] Bouet, G. (April 8, 1908), "Piroplasmose bovine observée à la côte d'Ivoire." *Ibid.*

[3] Broden, A., and Rodhain, G. (March 10, 1909), "Piroplasmoses des bovidés observées au Stanley-Pool." *Ibid.*

[4] Theiler, A. (1907–8), "The Immunity of Cattle Inoculated with *Piroplasma mutans*." *Report of the Government Veterinary Bacteriologist, Transvaal Department of Agriculture.*

[5] *Idem* (January, 1909), "Experiments with English and South African Redwater." *Journal Tropical Veterinary Science.*

Piroplasmosis—*continued*

In another paper entitled "Further Inoculation Experiments with South African Redwater," Theiler [1] gives the result of his experiments :—

(1) The inoculation of the ten Sussex heifers in England with a South African strain of redwater produced in all a more or less severe attack of this disease, followed by immunity, which protected them against a second attack of redwater in the Transvaal after an injection of an immune blood. This immunity was pronounced in all animals. In no instance was there any severe reaction. In some animals fever reactions were noted, but the animals were never noticed to be ill.

(2) Five of the animals, or 50 per cent., died of a disease of which the pathological blood lesions resembled those of redwater, but it differed from this disease through the absence of hæmoglobinuria and through the presence of peculiar chromatic bodies, the so-called "marginal points."

(3) The appearance of these marginal points corresponds to an incubation time, varying from twenty-seven to thirty-two days, with the exception of one animal injected with sick blood containing visible marginal points, in which instance it was shorter.

(4) The appearance of the marginal points coincided with the onset of a severe fever reaction. The number of these points increased with the progress of the fever reaction, and the temperature fell when the number of the chromatic bodies decreased or disappeared.

(5) The severe pathological lesions of the blood in the form of oligocythæmia, anisocytosis, poikilocytosis, polychromasia, basophilia, micro- and macro-cytosis, normo- and megalo-blasts were preceded by the appearance of marginal points.

(6) These observations point to the fact that the so-called marginal points play the rôle of a pathogenic organism acting in a similar way, but not so acutely on the red corpuscles as *Piroplasma bigeminum*.

Theiler, in 1906, published a paper [2] in which he brought forward a certain amount of evidence to prove the duality of *P. bigeminum* and *P. mutans*. In a later article [3] he gave further proof of this, and more recently published another paper [4] with final proofs showing that *P. mutans is* a distinct species. He was successful in obtaining an animal infected with *P. mutans* alone; later, however, this animal eventually contracted redwater and succumbed to the effects of *P. bigeminum*. During the stage that it showed a *P. mutans* infection, blood was collected and used for inoculation experiments, by means of which he was able to determine the following important facts :—

(1) The incubation period after a pure *Piroplasma mutans* infection varies between thirteen and forty-two days.

(2) The blood lesions are those of anæmia, principally indicated by poikilocytosis, and accompanied by all the other lesions described as occurring in various animals—anisocytosis, polychromasia, metachromasia, basophile granulations, and macrocytes.

(3) In some animals the presence of marginal points has been noted. I am not yet in the position to explain the nature of these "points" or to state the relation in which they stand to *Piroplasma mutans*.

(4) The tests to prove the absence of immunity against the *Piroplasma bigeminum* infection succeeded in every instance. *Piroplasma mutans* does not protect against a subsequent inoculation of *Piroplasma bigeminum*, and this fact should give the final proof that *Piroplasma mutans* has to be considered as a distinct species.

(5) No mortality occurred amongst twenty-five animals injected with *Piroplasma mutans* pure.

(6) In some recent publications mention has been made of small piroplasma—usually found in connection with other diseases—which have been identified as *Piroplasma parvum*. This is decidedly incorrect, as these small piroplasms are described as inoculable, whereas, as has been frequently proved, *Piroplasma parvum* is not. It has therefore to be concluded that these piroplasms are probably *Piroplasma mutans*, or, in any case, belong to the same species.

Another paper [5] by the same observer deals with the transmission of piroplasmosis by means of different species of ticks. Mention is made of the part played by *Boophilus decoloratus*, which is the principal host of *P. bigeminum*, and in a more recent paper [6] reference is made to the possibility of the eggs and further developmental stages of this tick being able to transmit *P. bigeminum* from one generation to another. Transmission experiments carried out with adults, nymphs and larvæ of *Rhipicephalus appendiculatus* gave positive results as regards *P. bigeminum*. Adult *Rhipicephalus appendiculatus* and adult *Rhipicephalus evertsi* were also found capable of transmitting *P. mutans*.

A considerable amount of work has been carried out with *Theileria parva*, the parasite of East Coast fever of cattle.

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[1] Theiler, A. (1908–9), "Further Inoculation Experiments with South African Redwater." *Journal Tropical Veterinary Science.*

[2] *Idem* (December 31, 1906), "*Piroplasma mutans* (n. spec.) of South African Cattle." *Journal Comparative Pathology and Therapeutics.*

[3] *Idem* (March 30, 1907), "Further Notes on *Piroplasma mutans.*" *Ibid.*

[4] *Idem* (June 30, 1909), "Further Notes on *Piroplasma mutans.*" *Ibid.*

[5] *Idem* (June 9, 1909), "Transmission des spirilles et des piroplasmes par différentes espèces de tique." *Bull. Soc. Path. Exot.*

[6] *Idem* (July 21, 1909), "Quelques observations concernant la transmission du *Piroplasma bigeminum* par des tiques." *Ibid.*

Piroplasmosis—*continued*

Many attempts were made by Koch,[1] Theiler [2] and others to transmit the disease by inoculation of large quantities of infected blood, portions of spleen pulp, and material from lymphatic glands, but all were attended with negative results. Meyer,[3] however, was successful in transmitting this disease to healthy cattle by intraperitoneal inoculation of the spleen, or portions of the spleen, of a sick animal. Theiler [4] then carried out an extensive series of transmission experiments and established a number of important conclusions which may well be quoted :—

(1) East Coast fever was not transmitted by means of blood of a sick animal either by infusion into the blood system or injection into the peritoneal cavity, the spleen, or the lymphatic glands of five healthy animals.

(2) The insertion of the spleen, pieces of the spleen, and injection of spleen pulp into the peritoneal cavity, the spleen, lymphatic glands, thorax, under the skin and into the jugular vein, produced the disease in twelve out of seventeen animals—71 per cent.

(3) The insertion of lymphatic glands and injection of lymphatic gland juice by the above-mentioned six methods, and, in addition, intracutaneously, produced the disease in fifteen out of sixty-six animals—23 per cent.

(4) The intraperitoneal injection of the whole spleen, pieces of spleen, spleen pulp, lymphatic glands, and lymphatic gland juice, succeeded in seven out of fifteen instances—41 per cent.

(5) The intrasplenic injection of spleen pulp and lymphatic gland juice succeeded in six out of six instances—100 per cent.

(6) The intralymphal injection of spleen pulp, lymphatic glands, and lymphatic gland juice succeeded in eight out of forty instances—20 per cent.

(7) The subcutaneous injection of spleen pulp, lymphatic glands, and lymphatic gland juice succeeded in two out of four instances—50 per cent.

(8) The intrathoracal injection of spleen pulp, lymphatic glands, and lymphatic gland juice succeeded in two out of four instances—50 per cent.

(9) The intrajugular injection of spleen pulp and lymphatic gland juice succeeded in two out of thirteen instances—15 per cent.

(10) The intracutaneous injection of lymphatic gland juice did not transmit the disease in one instance.

(11) The material used for these experiments can be classified as follows :—

(*a*) From animals which contracted the disease in a natural way from ticks.

(*b*) From animals which contracted the disease by inoculation.

(*c*) From animals which contracted the disease from ticks, these ticks having been infected by biting animals which contracted the disease by inoculation.

The results were :—

(*a*) The disease was produced in 41 per cent.

(*b*) The disease was produced in 88 per cent. (origin).
The disease was produced in 66 per cent. (first generation).

(*c*) The disease was produced in nil (first generation).
The disease was produced in 10 per cent. (second generation).

From this it appears that the disease can be most successfully transmitted with material obtained from experimentally inoculated animals of the original and first generation.

(12) As indicated by the statistics, the disease was not so fatal from artificial transmission as it is under natural conditions. In the transmission experiments by inoculation, the mortality amongst the animals which contracted the disease was sixteen out of twenty-nine—59 per cent.

(13) Out of eighty-three animals treated—

16 contracted the disease and died ;
11 recovered and proved immune ;
11 gave atypical or no reactions, and died to the test ;
3 gave atypical or no reaction, but recovered when tested ;
42 were not tested and should be considered not to be immune, the test not being carried out on account of the absence of any symptoms indicating a typical East Coast fever reaction.

The disease transmitted by inoculation did not always resemble the disease contracted by ticks ; it was either of a longer or shorter duration.

Piroplasms were not present in every instance, and even the plasma bodies were not found in one instance. The reactions were not always typical, and from the fever reactions in some instances no diagnosis as to the presence of East Coast fever could be made.

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[1] Koch, R. (1903), *Reports on Rhodesian Redwater, or African Coast Fever.*

[2] Theiler, A. (1903–4 and 1907–8), *Annual Report of the Government Veterinary Bacteriologist, Transvaal Department of Agriculture.*

[3] Meyer, K. F. (September 30, 1909), "Preliminary Note on the Transmission of East Coast Fever to Cattle by Intraperitoneal Inoculation of the Spleen or Portions of the Spleen of a Sick Animal." *Journal Comparative Pathology and Therapeutics.*

[4] Theiler, A. (1909–10), "The Artificial Transmission of East Coast Fever." *Report of the Government Veterinary Bacteriologist, Department of Agriculture, Union of South Africa.*

Piroplasmosis—*continued*

(14) Immunity was followed in several instances where no definite diagnosis of a previous East Coast fever reaction could be made. Accordingly the absence of piroplasma in the blood, or of the gamogonous or agamogonous forms in the glands, does not of necessity mean that the animal has not become immune against East Coast fever through the inoculation.

Although Koch was the first to describe the parasite of East Coast fever in cattle in German East Africa, Hutcheon was the first to distinguish the disease from Texas fever or Redwater. At a later date Theiler [1] proved the following facts :—

Cattle which are immune to Redwater are susceptible to East Coast fever. East Coast fever is not communicable by blood inoculations (thirty experiments, wherein 5 to 2000 c.c. of East Coast fever blood were inoculated). He noted the absence of hæmoglobinuria in the majority of animals affected with East Coast fever, its presence in the majority of the animals affected with redwater. He found that in most cases of East Coast fever there was no appreciable decrease in the number of red blood corpuscles, this being in marked contrast to what is observed in redwater. Theiler noted that cattle might harbour both the parasites of redwater (*P. bovis*) and those of East Coast fever (bacillary forms—*T. parva*).

Nuttall, Fantham and Porter,[2] in an interesting paper with diagrams, record some of their observations on *T. parva*.

These observers consider that as East Coast fever is not communicable by blood inoculation, the infection does not therefore occur through the escape of parasites from infected corpuscles and their entry into fresh corpuscles as in true piroplasmosis.

Summarising our observations on the living parasite, we would state that they show active movements within the corpuscles, and at times undergo alterations of form. No structural details can be made out in living parasites. We have not obtained any conclusive evidence that the parasites multiply within the infected corpuscles, but at times appearances were observed suggesting this possibility. In several cases the parasites seemed to grow slightly in size during the period of observation. When infected corpuscles lost the hæmoglobin the parasites were distinctly seen for a time, after which they degenerated and died. The escape of parasites from infected corpuscles was witnessed on six occasions ; it was accomplished without injury to the corpuscle. On two occasions the escaped parasites appeared to re-enter fresh corpuscles.

In a later paper, Nuttall and Fantham [3] give an account of their observations on *T. parva* in stained preparations. This paper is illustrated, and contains a complete account of the morphological characters of this piroplasm. In staining these preparations these observers obtained the best results by the ordinary method of drying the blood films, fixing them in absolute alcohol, and then staining them according to Giemsa's method. Wet fixation methods gave poor results as the corpuscles did not become flattened, the consequence being that the hæmoglobin clouded the image of the parasites. Nuttall and Fantham arrived at the following conclusions :—

The percentage of infected corpuscles in the peripheral circulation rises steadily as the disease progresses, and at the same time there is a progressive increase in the proportion of infected corpuscles which contain two, three, and four or more parasites.

The percentage of infected corpuscles observed in smears from various internal organs immediately after death, and the percentage of corpuscles containing more than one parasite, coincide with those obtained in the case of the peripheral blood. In other words, there does not appear to be a heavier infection of the corpuscles in any of the internal organs than there is in the general circulation.

Free parasites are rarely encountered in the blood.

Whilst the parasite is very pleomorphic, the commonest forms seen in stained preparations are ovoid or rounded, and comma-shaped or clubbed. The proportion of bacilliform parasites is also fairly large, and increases as the disease advances, but may fall toward the end of the malady. Parasites having a pyriform shape are rare, and observations on living parasites indicate that they simply arise in the course of transitory or amœboid movements ; consequently such parasites are not to be compared with the common and typical pyriforms in piroplasma, the latter, when formed, maintaining their shape for a considerable time. In other words, the pyriforms in piroplasma represent a definite stage in the life history of the parasite, whereas in theileria they do not. The study of stained and living theileria confirms us in the opinion already expressed that this parasite deserves generic rank, since it differs in essential characters from piroplasma.

Judging from the study of stained specimens, the observer is tempted to conclude that the prevalent type of small ovoid parasite grows in size and becomes pleomorphic. The chromatin mass in ovoid parasites may become elongated or horse-shoe-shaped, and divides directly into two masses by a median constriction, the masses subsequently moving to opposite poles of the parasite. In bacilliform parasites the chromatin mass simply divides and the two masses wander to opposite poles of the parasite ; in many cases the long parasite shows a marked bend at the point where the final division of the cytoplasm of the daughter cells is to follow. Finally, in certain parasites which are rich in chromatin, the mass may undergo division into four, giving rise to "cross-forms,"

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[1] Theiler, A. (1904), "Rhodesian Tick Fever." *Report of South African Association for the Advancement of Science.*

[2] Nuttall, G., Fantham, H., and Porter, A. (December, 1909), "Observations on *Theileria parva*, the Parasite of East Coast Fever of Cattle." *Parasitology.*

[3] Nuttall, G., and Fantham, H. (July, 1910), "*Theileria parva*, the Parasite of East Coast Fever in Cattle." *Ibid.*

the subsequent separation of the cytoplasm then liberating the daughter organisms. We have not observed more than eight parasites within an infected corpuscle. Piroplasmosis—*continued*

Observations on living parasites have established the fact that oval parasites may, when active, protrude processes, become constricted, or assume a pyriform shape. In some cases we observed the formation of bent dumb-bell-shaped parasites from ovoid or short rodlike forms. We were never able, however, to observe actual division in living parasites. Therefore we were led to doubt if multiplication of intracorpuscular parasites actually takes place, and assumed that if it takes place the process "must be very slow." The careful study of stained films suggests that intracorpuscular division may take place, consequently further observations on the living parasite will have to be made before reaching a final conclusion. We may note, however, that observations on theileria are fraught with considerable difficulty owing to the minuteness of the parasite.

Nuttall and Graham-Smith [1] carried out some attempts to cultivate *Theileria parva* with the object of confirming the results obtained by Miyajima.[2] According to this last mentioned observer, he found no difficulty in cultivating this parasite when he added the blood of cattle (containing theileria) to ordinary bouillon in the proportion of 1:5 to 1:10, the cultures being maintained at 20–30° C. He stated that trypanosomes appeared in these cultures after an interval of three days, and underwent vigorous multiplication, reaching the maximum after the tenth to the fourteenth day.

Nuttall and Graham-Smith give an account of two carefully conducted experiments in which they failed to confirm Miyajima's results. No development of *Th. parva* was observed, and they conclude that the flagellates described by Miyajima as occurring in cultures of cattle blood containing *Th. parva* were probably cultural forms of a trypanosome which he failed to detect in blood smears taken from animals because of their small numbers in the circulating blood.

Mention may be made of a paper by Deseler [3] referring to his attempts to cultivate piroplasma in artificial culture media. An illustration accompanying this paper shows the changes in shape and size attained by the piroplasma within the blood corpuscle when grown on artificial media.

Meyer [4] has a paper entitled "Notes on the Nature of Koch's Granules and their rôle in the Pathogenesis of East Coast Fever." Koch [5] was the first to describe these bodies, which he found in the different organs of an animal that had died of this disease. These bodies are known as "Koch's granules," "Blue bodies," or "Koch's plasmakugeln," and were illustrated in his reports. When stained with the usual protozoal stains they assumed a bluish colour, and showed a number of chromatin nuclei apparently resembling small piroplasms.

Theiler [6] has noted the absence of these Koch's granules in an infection with *Piroplasma mutans*, although they are invariably present in the spleens of animals infected with East Coast fever, a point which is of diagnostic importance in assisting in the differentiation between an infection with *P. mutans* and *P. parvum*. Meyer in his paper gives a detailed description of the method of puncturing the lymphatic glands and spleen for the purpose of detecting the presence or absence of Koch's granules. Of the lymphatic glands that should be punctured he advocates the prescapular and the precrural. Smears are then made for microscopical examination.

All smears made by the different methods were fixed by either the moist or dry method, the first in sublimate alcohol and the latter in methyl-alcohol. They were stained after Giemsa, Leishman, or May-Grunwald Giemsa (Pappenheim) for panoptic stains, with hæmotoxylin (Delafield or Heidenhain). In several cases, also, sections were used. Generally the well-known facts of a morphological nature were confirmed in all smears taken from animals which died of East Coast fever. Koch's granules in an unstained preparation are round or oval bodies which contain in their plasma a few or several strongly refractile granules, which become enlarged under the influence of alkali, and which are never dissolved by sodium taurocholate, but often become slightly enlarged. In a stained smear they are light blue or dark violet discs or spheres, which contain a variable number of round or irregular light reddish or more bluish violet granules, which microchemically are pure chromatin. Generally these spheres are not only found free in the lymph, of different sizes (from 1 to 10 μ in diameter), but also are very frequent in the plasma of cells which have the character of lymphoid elements, generally mononuclear

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[1] Nuttall, G., and Graham-Smith, G. (September, 1909), "*Theileria parva*: Attempts at Cultivation." *Parasitology.*

[2] Miyajima, M. (May, 1907), "On the Cultivation of a Bovine Piroplasma." *Philippine Journal of Science*, B.

[3] Deseler, B. (October 28, 1910), "Ein Beitrag zur Züchtung von Piroplasmen in künstlichen Nährböden." *Zeit. f. Hyg. u. Infekt.*

[4] Meyer, K. F. (1909–10), "Notes on the Nature of Koch's Granules and their rôle in the Pathogenesis of East Coast Fever." *Report of the Government Veterinary Bacteriologist, Department of Agriculture, Union of South Africa.*

[5] Koch, R. (1906), "Beiträge zur Entwicklungsgeschichte der Piroplasmen." *Zeit. f. Hyg. u. Infekt.*

[6] Theiler, A. (1907–8), "Further Investigations into the Disease Caused by *Piroplasma mutans*." *Report of the Government Veterinary Bacteriologist, Transvaal Department of Agriculture.*

Piroplasmosis—*continued*

leucocytes. Shortly before death, cells of the same character are often found in the circulating blood, as in East Coast fever a leucopenia is followed by a lymphocytosis. These leucocytes with the granules, when found in blood smears, can be used in doubtful cases for diagnosis. If one of these elements is found in a blood smear where small piroplasma are fairly frequent, *P. mutans* can be excluded. In one case I observed free Koch's granules on the fifth day after the rise of temperature. The Koch's granules were always present when the post mortem examination revealed East Coast fever. In all cases where Koch's granules can be detected only in rare numbers in the hæmatopoietic organs, spleen, and lymphatic glands, every organ should be examined for these bodies. I know of one case where the temperature reaction, as a sequel to infection with ticks, was so typical of East Coast fever that I was astonished to find only a few Koch's granules in the lymphatic glands and the spleen. I therefore trepanned one of the ribs and found Koch's granules in considerable numbers. In all atypical cases of East Coast fever, the Koch's granules are always found in the first stages of development, and are comparatively rare in number.

The paper concludes by disproving Martin Mayer's theory that Koch's granules are the results of products of reaction to an ultra-visible virus. In a paper written by Martin Mayer [1] on the subject of *Spirochæta duttoni*, he stated that Koch's bodies were present in other diseases, and were also to be found, although rarely, in healthy animals.

Mayer sums up his paper by stating that—

Koch's granules are a developmental stage of the blood parasite *P. parvum*. They are, therefore, specific for East Coast fever. These granules are engaged in the formation of the secondary metastasis in the liver, kidney, lungs, heart (ulceration in stomach, etc.). The endothelial cells of the small capillaries become affected under the influence of Koch's granules. The secondary endarteritis gives rise to hæmorrhages, invasion of cells, and proliferation of lymphoid elements with increase of Koch's granules.

Bruce and others [2] demonstrated the existence of "Koch's plasmakugeln" in a disease of calves in Uganda called "Amakebe." The presence of these Koch's bodies led to the identification of the disease, which was doubtless East Coast fever.

Gonder,[3] in a very interesting paper, describes the life-cycle of *Theileria parva*. This observer divides the development of the parasite in the organs into two generations distinguishable by their morphology, *i.e.* agamogonous and gamogonous: the former representing certain forms which multiply agametically and which are not capable of performing a sexual function. It is only after the elimination of nuclear substance (reduction of nucleus) that parasites resulting from these agamogonous stages develop into the gamogonous generation. The gamogonous generation supplies the sexual forms, which copulate when they obtain access to the stomach of the transmitting host.

Referring to the transmitting host of *Th. parva*, Gonder says :—

In South Africa the tick, which is of chief importance, and with which I have experimented in the latter part of my investigations exclusively, is *Rhipicephalus appendiculatus*. *Rhipicephalus evertsi*, which is also a transmitter of East Coast fever, was only used at the commencement of my investigations.

It is well known that the parasite of East Coast fever does not pass through the egg, but the tick can only transmit the disease in the nymphal or imago stage. For the completion of its cycle the tick requires three changes of host. If a larval tick attaches itself on an animal suffering from East Coast fever it leaves the host as soon as it is replete, the length of time it remains on the host depending chiefly on the external temperature, a fact which is the cause of many difficulties in the study of the East Coast fever parasite in the tick itself. After having dropped off the animal, the larval tick moults sooner or later, according to external favourable or unfavourable climatic conditions. Warmth undoubtedly influences the rapid development of ticks. It is only after the tick has moulted into the nymphal stage that it seeks a new host, where it again becomes replete. It leaves this second host to moult again for the second time, in order to finally arrive at the imago stage on the third host. It leaves this third host either as a male, which has no other task than to mature and to fertilise the female, or as a female to become fertilised and to replete itself with the great quantity of blood necessary for the formation of eggs. If the tick has been infected as a larva it can only transmit the disease in the nymphal stage; if it has become infected as a nympha it can only transmit the disease as an imago.

An infected tick purifies itself completely from all infection once it has bitten an animal. If infected as a larva it can only become re-infected as a nympha, but never as an adult tick. It only transmits the disease in the last stage if it has infected itself in the previous stage as a nympha. Its purification can be effected by biting on any mammal; an ox is not exclusively necessary. As far as is known *Theileria parva* is only pathogenic for cattle. The biological peculiarity of the cleansing of the ticks from infection has been made use of in South Africa for combating East Coast fever.

Gonder then describes the development of the agamont stage in the animal.

With the bite of an infected tick small uninuclear forms arrive in the blood circulation of cattle and undergo further development in the organs, more especially in the lymphatic and hæmo-lymphatic glands, in the bone-

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[1] Mayer, M. (1908), "Beiträge zur Morphologie der Spirochäten (*Sp. duttoni*) nebst anhängender Plasmakugeln." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XII., No. 1.

[2] Bruce, D., Hamerton, A. E., Bateman, H. R., and Mackie, F. (1910), "Amakebe: A Disease of Calves in Uganda." *Reports of the Sleeping Sickness Commission of the Royal Society*, B., Vol. LXXXII.

[3] Gonder, R. (December 31, 1910), "The Life-cycle of *Theileria parva*: The Cause of East Coast Fever in Cattle in South Africa." *Journal Comparative Pathology and Therapeutics.*

Piroplasmosis—*continued*

marrow, and in the spleen. These small parasites represent the sporozoites, or, according to Hartmann's nomenclature, the agametes of the first or metagametic generation. They are only found after the ticks have moulted, that is, at the time when the tick is ready to seek a new host. I have not yet been able to trace these forms in cattle, and I have not found them in clean ticks or in ticks which have become purified by biting.

If we carry out a systematic puncture of the glands and an occasional puncture of the spleen, commencing on the first day of the disease—that is to say, from the day on which the tick attaches itself—we are able to trace the further development of the parasite. The superficial cervical and precrural glands are the most convenient for puncturing purposes. The first forms of the parasites are occasionally found on the twelfth or thirteenth days, but it is difficult to state the exact date, as the period of incubation varies in the different experiments. These parasites reach the size of about ·8 to 1 micron, and at first are found free. During the following days they are seen intracellularly, *i.e.* in the large mononuclear lymphocytes, and very rarely in leucocytes. They grow in size rapidly within the next few days. These agametes increase in size, and after multiplication of the nuclei grow into agamonts, which finally divide into as many segments as there are nuclei. On an avcrage the agamont measures about 10 to 12 microns, rarely, 12 to 15 microns.

Naturally the larger ones contain the greater number of nuclei. In the intracellular forms a considerable number of segments—agametes of the second generation—are frequently found, caused by double infection. As a result of this parasitism the lymphocyte is destroyed, and, accordingly, it is not surprising to meet irregular forms if the infected lymphocyte dies off before the agamont has divided into its daughter cells.

Division of the nuclei takes place by amitosis; in exceptional cases we meet indications of primitive mitosis in moist fixed smears or sections. The number of nuclei increases very considerably by successive fission processes, and may amount to more than forty or fifty. The form of the nuclei and their structure is characteristic for the process of agamogony. The nuclei do not possess an envelope; they have an irregular, rugged form and no compact structure. During life they do not appear very refractile; they do not show much affinity for the various stains. In differentiation preparations stained with hæmatoxylin and Giemsa, fixed and treated by the moist method, the stain easily escapes from the nuclei. The development of the agametes, from the youngest to the full-grown agamonts, and the succeeding schizogony into agametes, can repeat itself.

In the animal the disease commences with the appearance of these agamogonous forms. The temperature begins to rise, and reaches the maximum with the formation of the gamogonous forms.

The agamont, which does not produce any more agametes, divides into gamonts after its nuclei have been liberated from the vegetative substance by the formation of chromidia and the process of reduction.

These gamonts increase both in size and in the number of nuclei and finally divide up into gametocytes, which invade the red corpuscles, and now represent the parasite of East Coast fever known under the name of *Theileria parva*.

The gamogonous forms are clearly distinguishable from the agamogonous forms by their nuclei. The youngest gamonts measure about 0·8 μ, and possess a strongly refractile nucleus which takes the various stains intensively. In advanced stages the nuclei possess distinct karyosomes, and occasionally in the youngest forms, along with the main nucleus, a second smaller nucleus is found, which may be compared with the blepharoplast of the flagellates, and is of importance for the systematic position of our parasite.

The multiplication of the nuclei in the gamonts takes place by a primitive mitosis in such a way that the karyosome splits the two fragments of the nucleus. Finally, the gamont divides into gametocytes after leaving a residual body staining blue with Giemsa. As already stated, the nuclei are characterised during life by strong refraction, and accordingly are easily distinguishable from the granules of the lymphocytes, although, contrary to the agamogonous forms, their shape is more regular, being almost oval.

Usually the intracellular gamonts supply a far greater number of gametocytes than those that are free. This is partly due to double infections, similar to what is found in intracellular agamogonous forms. The schizogony of these agamonts within the lymphocytes may take place at the same time, so that, naturally, there are a great number of gametocytes present; in many cases I could count 150 to 200 gametocytes, the products of the gamonts of one single lymphocyte.

The evolution forms of *Theileria parva* of the gamogonous stages as described above have been known for some time under the name of "Koch's bodies" or "plasma bodies."

Gonder considers that the failure to transmit the disease by blood inoculation is due to the fact that the gametocytes do not develop any further and do not undergo parthenogenesis. In the transmission experiments with organs, as undertaken at the laboratory, agamonts are inoculated—that is, forms which are capable of further development.

As regards the cycle in the tick, Gonder points out that—

The parasite in the red corpuscle can only undergo further developments after it has entered into the tick. The gametocytes contained in the blood then grow out. When copulation occurs in the tick, micro- and macro-gametocytes can be distinguished in the blood. The gametocyte, which is ring-shaped or pear-shaped, takes on either the elongated, so-called bacillary form, or it grows into a broad ring or more pear-shaped form. The former represent the microgametocytes, the latter the macrogametocytes.

After the infected blood corpuscles have reached the stomach of the tick the parasites emigrate within the first half-hour. A great number perish. Only the mature gametocytes grow into gametes and fuse with each other. The microgametes contain a distinct small nucleus similar to the centrosome or blepharoplast of other organisms, which acts as the stimulating agency for the development.

The fertilised macrogamete "rounds-off" after karyomyxis, from which the ookinete results, and, as in other blood parasites, takes the shape of a retort, changing into that of a gregarine, and finally growing into the elongated ookinete. The ookinetes can be recognised by their activity; they double back and stretch out rapidly, and show contracting movements like gregarines.

Piroplasmosis—*continued*

During the moulting process I was unable to trace any intermediate forms which would lead from the ookinetes to the agametes of the first generation. With the formation of the agametes the evolution of *Theileria parva* is complete, and when these agametes find their way into a beast the described cycle commences afresh.

In cattle that recover from the disease a general decrease of the parasites is noted in the blood after the crisis. The agamogonous forms disappear and the fever subsides. The gamogonous stages do not develop beyond the formation of gametocytes, and these are the endoglobular parasites. As parthenogenesis does not occur, the animal is completely protected against relapses, and recovery apparently leaves a complete sterile immunity. No tick can infect itself on this animal, and no infected tick can infect such a beast.

Gonder's excellent paper contains a plate illustrating the various stages in the life-cycle of *Th. parva*. A more detailed account of his work is given in two other papers, one [1] in English and the other [2] in German, both being illustrated by coloured plates.

Mention must be made of a recent paper by Theiler,[3] in which he describes the successful transmission of Amakebe by means of *Rhipicephalus appendiculatus*. The ticks were removed, in the nymphal stage, off Uganda calves suffering from acute Amakebe, and sent to Pretoria. By the time these nymphal ticks had reached Pretoria they had developed into adults and were used by Theiler in transmission experiments. Theiler was successful in producing typical East Coast fever in two calves that he used. He has therefore given additional proof that Amakebe of Uganda is identical with East Coast fever and is transmitted by the brown tick *Rhipicephalus appendiculatus*. This conclusion corroborates that obtained by the Royal Society Sleeping Sickness Commission of 1909.

Attention is directed to a paper by Gonder[4] dealing with *Theileria parva* and *Babesia mutans*. It is accompanied by coloured illustrations and micro-photographs, which represent in an excellent manner the comparative morphological differences between these parasites.

With regard to the transmission of East Coast fever by means of ticks, reference may be made to Theiler's [5] work. He carried out a large number of experiments, as a result of which he concluded that—

Rhipicephalus decoloratus and *Amblyomma hebræum* must not be considered as hosts of *Piroplasma parvum.*

Rhipicephalus appendiculatus, evertsi, capensis, simus, and, according to Lounsbury, also *nitens,* must be considered to be hosts of *Piroplasma parvum.* It may safely be concluded that *Piroplasma parvum* in its life-cycle of development does not pass through the egg, and finally it is evident that immune animals do not carry the infection.

Rather a useful paper by the same author [6] deals with the prevention and eradication of East Coast fever. It is written as a guide chiefly for the layman, and more particularly for the farmer. After describing the cause and the transmitting agents of the disease, Theiler considers the preventive measures under two headings: (1) Measures to be adopted by the farmer; (2) Measures to be adopted by the State. Under the first-mentioned heading the question of "dipping and spraying" all animals stocked on a farm is considered.

When it was demonstrated that the red-legged and brown ticks were the carriers of the disease, dipping, to be of any use to combat East Coast fever, had to be applied at different intervals in order to attack these particular ticks, on account of the short time they spend on their host. In the case of the red-legged tick, which remains as an adult about eight days on a host, and in the larval and nymphal stage about a fortnight, at least one dipping every eighth day would be required. In the case of the brown ticks, which remain only three to five days on the animal, dipping would have to be repeated every fourth or fifth day at least. When put to the test, it was demonstrated that dipping every fourth or fifth day interfered too much with the condition and the health of the animals, and at one time it was thought to be absolutely impracticable to dip every fifth day. In Natal, however, when the disease spread on to farms on which dipping at intervals of one month had been carried out for a number of years, dipping at shorter intervals became imperative, and finally a dip was prepared which could be used at an interval of five days without interfering too much with the condition of the animal.

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[1] Gonder, R. (1909–10), "The Development of *Theileria parva*, etc." *Report of the Government Veterinary Bacteriologist, Department of Agriculture, Union of South Africa.*

[2] *Idem* (1910), "Die Entwicklung von *Theileria parva*, dem Erreger des Küstenfiebers der Rinder in Afrika." *Arch. f. Protist.*, Vol. XXI., No. 2.

[3] Theiler, A. (July, 1911), "Transmission of Amakebe by means of *Rhipicephalus appendiculatus*, the Brown Tick." *Proceedings of the Royal Society Series*, B., Vol. LXXXIV.

[4] Gonder, R. (1911), "*Theileria parva* and *Babesia mutans.*" *Arch. f. Protist.*, Vol. XXI., No. 3.

[5] Theiler, A. (1906–7), "Further Transmission Experiments with East Coast Fever." *Report of the Government Veterinary Bacteriologist, Transvaal Department of Agriculture.*

[6] *Idem* (October, 1910), "The Prevention and Eradication of East Coast Fever." *Transvaal Agricultural Journal.*

As regards the dips to be employed, those containing arsenic are recommended. The formula of the Laboratory Dip prepared by Pitchford in Natal is quoted :— Piroplasmosis—*continued*

5½ lb. soft soap.
2 gallons paraffin.
8½ lb. arsenite of soda.
400 gallons of water.

Theiler also recommends that the ears of all the animals be syringed, as also the sheath in oxen and the region of the anus and tail, and other parts where the dip does not gain easy access.

According to Theiler, "dipping" is only of use when it has been commenced some time previous to the appearance of the disease on a farm, and is of little value once the farm has become infected.

As a second measure, Theiler recommends the transference of cattle from an infected paddock to a clean one.

The precaution must, therefore, be taken that the sick animals are left behind. For this purpose, the cattle should be transferred into clean ground (quarantine camp) where there is sufficient grazing for about three weeks. As pointed out before, within three weeks animals which are infected will show signs of the disease, and can be easily detected by means of the thermometer. They must be sent back into the infected paddock or slaughtered. After that time all animals in the quarantine camp which have passed the thermometer test can be considered free from the disease. They are then passed on to the third and clean paddock, the quarantine and original camp being closed for cattle. Perhaps for a farmer it will be more practical to use two quarantine camps instead of one, keeping the animals in each paddock for about fifteen days. The reason for this is that two quarantine camps are safer than one when inexperienced farmers have to handle thermometers. In the quarantine paddocks all ticks on the animals will drop off. We know that the brown tick requires at least sixteen days to moult, and is not able to attach itself for the next few days ; therefore, when the cattle are removed after this period there is no longer danger of them picking up infected ticks. When two quarantine camps are used, the sick animals can be detected without the use of the thermometer, as within a month the animals either die out or are visibly sick.

From the State point of view the preventive measures should include the prevention of the importation of cattle from an infected area, and early notification of the disease when it once has broken out. A period of six weeks elapses as a rule between the first and the second outbreaks. Blood smears should be sent for microscopical examination, and immediately the disease is diagnosed the farm should be placed in quarantine, which should be maintained for fifteen months after the last death from East Coast fever.

Lichtenheld [1] carried out some preliminary experiments on the fixation of complement in East Coast fever and in horse sickness. For the manufacture of the East Coast fever "antigen" he obtained the best results with extracts from infarcts in the kidneys of animals that had suffered from the disease. Extracts of *Theileria parva* in the corpuscles were also satisfactory for providing the antigen. Unfortunately the small quantity of antigen obtained in this way did not permit of a large number of experiments; accordingly an extract of the lymphatic glands was used instead as the antigen.

As a result of his experiments Lichtenheld found that the serum of normal cattle did not deviate the complement when pure or mixed with antigen, but that the serum of animals suffering from East Coast fever, or which were immune against it, with few exceptions gave a distinct deviation in the dose of 1 c.c.

Nuttall [2] has a short note on the mode of multiplication of *Piroplasma bovis*, as observed in the living parasites.

In a previous paper,[3] in conjunction with Graham-Smith, he described the appearances of this piroplasma in stained films, and showed that they agreed with those of *P. canis* and *P. pitheci* with regard to the presence of the budding or multiplication forms. In a more recent paper by Nuttall and Hadwen [4] dealing with drug treatment in piroplasmosis, reference was made to the large single ovoid or pyriform forms of *P. bovis*, which differed from those observed in *P. canis*. Further, *P. bovis* showed less active movement than *P. canis*, and contained a higher percentage of dividing forms than is encountered in blood containing the canine parasite.

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[1] Lichtenheld, G. (1909–10), "Preliminary Communication on the Fixing of Complement in Horse Sickness and East Coast Fever." *Report of the Government Veterinary Bacteriologist, Department of Agriculture, Union of South Africa.*

[2] Nuttall, G. (December, 1909), "Note on the Multiplication of *Piroplasma bovis*, as observed in the Living Parasite." *Parasitology.*

[3] Nuttall, G., and Graham-Smith, G. (June, 1908), "The Mode of Multiplication of *P. bovis*." *Ibid.*

[4] Nuttall, G., and Hadwen, S. (September, 1909), "The Drug Treatment of Piroplasmosis in Cattle." *Ibid.*

Piroplasmosis—*continued*

Mention may be made of an illustrated paper by Holmes [1] which furnishes a number of references dealing with the flagellate forms of *P. bovis*. Holmes notes that in the majority of instances these flagellate forms have chiefly been met with in the blood of animals in the last stage of the disease. Definite proof, however, is apparently still lacking as to the nature of these flagellate bodies.

Lichtenheld, [2] in a paper dealing with the diagnosis of the small piroplasma causing cattle sickness in Africa, refers to the different effects produced by infection with *P. mutans* and *P. parvum*. It is pointed out that antelopes show piroplasmic infection similar to *P. mutans*.

Dodd [3] has rather an interesting paper entitled "Piroplasmosis of Queensland Cattle." In this paper he gives a list of the piroplasms, arranged according to Bettencourt.

(1) Piroplasms presenting in one of their phases the form of a pear, and often arranged in pairs in a corpuscle—

(*a*) *Piroplasma bovis* (Babes).

(*b*) *Piroplasma bigeminum* (Smith and Kilborne).

Geographical distribution—Europe, America, Australia, Asia, and Africa.

(2) Piroplasms always presenting at one phase of their life history the rod or bacillary form—

(*a*) *Inoculable.—Piroplasma annulatum* (Dschunkowsky); *Piroplasma mutans* (Theiler); *Piroplasma bicilliforme* (Miyajima and Shibayama).

Geographical distribution—Transcaucasia, Japan, South Africa, Madras, Annam, Portugal, Gold Coast, Dutch Indies, China, German East Africa, Sudan, Congo, New Guinea, and Australia.

(*b*) *Non-inoculable.—Piroplasma parvum* (Theiler); piroplasma of Egypt and Tunis.

Geographical distribution—South Africa, East Africa, Egypt, and Tunis.

Dodd carried out a series of inoculation and other experiments, and concluded that two distinct protozoan diseases caused by piroplasmata existed among the cattle in Australia. One was due to *Piroplasma bigeminum*, and the other was due to small parasites whose prevailing form was that of a rod. Previously these small parasites were considered to be phases in the life-cycle of *P. bigeminum*, but Dodd proved that these views were erroneous, and that the one species of piroplasm was quite distinct from the other.

Stannus [4] has a paper giving an account of piroplasmosis among cattle in Nyasaland. The peripheral blood showed rod-shaped and comma-shaped piroplasms. "Koch's granules" were present in splenic smears. Stannus considered that the type of piroplasm present did not correspond to *Th. parva* or *P. mutans*. Nuttall, however, in a footnote to this paper, states that the parasites figured were identical with *Th. parva*. The presence of Koch's granules in the spleen would appear to confirm Nuttall's statement.

Hutchinson and White [5] have recorded an outbreak of piroplasmosis among the calves at a vaccine depot in India. The blood of the sick animals showed the presence of piroplasms occurring in various forms—bacillary, oval, etc. The disease occasioned a high mortality. The paper contains an account of the clinical and pathological conditions that were present in the animals. Among the prominent symptoms observed was diarrhœa, which occurred in 78 per cent. of the cases. The pyrexia was of an intermittent type, and it was noted that there was generally an absence of ulcerative changes in the alimentary canal.

Stockman [6] has carried out a number of experiments in order to test the efficacy of trypanblue in the treatment of redwater in cattle. The treated animals received 1 to 1½ grammes of the drug in 100–150 c.c. of water. The result of his experiments showed that the drug confined the piroplasms to the internal organs for varying periods, but that it did not completely clear them out of the system.

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[1] Holmes, J. (1908–9), "Flagellate Forms of *Piroplasma bovis*." *Indian Civil Veterinary Department Memoirs*, No. 1.

[2] Lichtenheld, G. (1910), "Beiträge zur Diagnose der durch kleine Piroplasmen verursachten Krankheiten beim Rinde mit Berücksichtigung ihrer Verbreitung." *Zeit. f. Hyg. u. Infekt.*, Vol. LXV.

[3] Dodd, S. (June 30, 1910), "Piroplasmosis of Cattle in Queensland." *Journal Comparative Pathology and Therapeutics.*

[4] Stannus, H. (September, 1910), "Piroplasmosis among Cattle in the Mombera District, Nyasaland." *Parasitology.*

[5] Hutchinson, F., and White, N. (1909), "Preliminary Report on an Outbreak of Piroplasmosis, etc." *Transactions Bombay Medical Congress.*

[6] Stockman, S. (December 31, 1909), "The Treatment of Redwater in Cattle with Trypanblue." *Journal Comparative Pathology and Therapeutics.*

Piroplasmosis—*continued*

Mention may be made of some experiments carried out by Dschunkowsky[1] to test the effect of "606" (Salvarsan) as a curative drug in the treatment of animals affected with Texas fever.

The dose employed was ·01 gramme per kilogramme of body weight, and was administered intravenously at the height of the disease. This drug brought about the prompt destruction of the piroplasms, but by doing so caused large quantities of endotoxin to be liberated, and produced acute intoxication in the animals.

Nuttall and Hadwen[2] describe the drug treatment of piroplasmosis in cattle. Their efforts were directed towards the treatment of Redwater by means of trypanblau. As a result of their experiments they arrived at the following conclusions :—

(1) Trypanblau promises to be an efficient remedy for bovine piroplasmosis, since it exerts a direct and obvious effect upon the parasites.

(2) The effect of the drug upon *Piroplasma bovis* is similar to that which it produces upon the canine parasite. The dividing forms are the first to disappear, and after a few hours the pyriform parasites also disappear from the peripheral circulation ; the parasites which are detected in the blood after a few hours appear degenerated and rounded or irregular ; within nine to forty-five hours, or less, all the parasites have disappeared from the blood.

(3) As in canine piroplasmosis, the disappearance of the parasites from the blood may be temporary. The parasites also disappear and reappear in small numbers (after two to eleven days) in animals undergoing natural recovery. In three treated animals the parasites reappeared in exceedingly small numbers after five to six days ; in two they had not reappeared after sixteen and eighteen days respectively. The animals show no symptoms, and progress towards recovery.

(4) It remains to be determined (1) how long the blood of treated cows may contain parasites after their apparent recovery ; (2) if the parasites in such recovered animals are altered in virulence ; (3) if the parasites are capable of infecting ticks.

(5) The experiments were conducted on nine cows, of which four served as controls and five were treated with trypanblau. Of the controls two suffered from hæmoglobinuria, and one of these died of piroplasmosis ; the two other controls had no hæmoglobinuria, and were very mild cases. All of the treated cows had hæmoglobinuria, and recovered. In four of the treated cows hæmoglobinuria occurred before treatment began.

(6) As might be expected, the drug exerts a more rapid effect when injected intravenously. The parasites disappear more slowly after subcutaneous injection of the drug.

(7) Although doses of 150–200 c.c. of a saturated watery solution of the dye were used, it is probable that smaller doses will prove efficient. The drug appears to produce no ill-effects upon cattle.

(8) The drug, being a dye, has the disadvantage of colouring the tissues, more especially the subcutaneous connective tissues. How long the coloration persists remains to be determined. In any case this disadvantage can scarcely weigh in the balance as against saving the life of the animal, especially when used for breeding purposes.

(9) We hope that experiments, which are about to be conducted in the field of Africa and elsewhere, will demonstrate the value of the remedy in practice.

(10) Trypanblau and similar drugs should be given a trial in the treatment of Carçeag in sheep and biliary fever in horses.

França[3] suggests the following classification for the piroplasma. He considers the piroplasma represent a family with five genera.

(1) *Piroplasma* (Patton), 1895 ; *Babesia* (Starcovici), 1893. The classical forms are twin pear-shaped. *P. bovis* (Babes), 1888 ; *P. bigeminum* (Smith and Kilborne), 1893 ; *P. ovis* (Starcovici), 1893 ; *P. canis* (Piana et Galli-Valerio), 1895 ; *P. pitheci* (P. H. Ross), 1905 ; *P. muris* (Fantham), 1905 ; *P. avicularis* (Wenyon), 1909.

(2) *Theileria* (Bettencourt, França, and Borges), 1907. Very small parasites, bacillary and oval in shape, dividing in the form of a cross. *Th. annulata* (Dschunkowsky), 1904 ; *Th. parva* (Theiler), 1904 ; *Th. mutans* (Theiler), 1907 ; *Th. dama* (B, F, and B), 1907.

(3) *Nicollia* (Nuttall), 1908. Nucleus shows dimorphism ; multiplies in fours. *N. quadrigemina* (Nicolle), 1907.

(4) *Nuttallia*, n. g., differs from *Theileria* by the absence of bacilliform parasites. *N. equi* (Laveran), 1899 ; *N. sp. ?* (Denier), 1907, of the *Cervus aristotelis*. *N. herpestidis* (França), 1908.

(5) *Smithia*, n. g. Pear-shaped swollen parasites occupying the whole breadth of the corpuscle ; are not arranged in pairs ; division occurs by fours into cross forms. *S. microti*, n. sp.

This classification is useful, especially as regards the genera, but is, of course, already somewhat out of date so far as species are concerned.

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[1] Dschunkowsky, E. (January 5, 1911), "Traitement de la Piroplasma Bovine par le '606.'" *Berl. Tierärztl. Woch.*, Vol. XXVII., No. 1. Quoted in *Journal Comparative Pathology and Therapeutics*, March, 1911.

[2] Nuttall, G., and Hadwen, S. (September, 1909), "The Drug Treatment of Piroplasmosis in Cattle." *Parasitology*.

[3] França, C. (March, 1909), "Sur la classification des Piroplasmes et description et deux formes de ces parasites." *Arch. Inst. Bact. Cam. Pest, Lisbon*, Vol. III., No. 1.

Piroplasmosis—*continued*

Anaplasmosis.—Strictly speaking this should not be considered under the subject of piroplasmosis, as recent work has proved it to be quite a distinct entity, due to the presence of the so-called "marginal points" in the blood. These marginal points were considered for a long time as a phase in the life-cycle of *P. bigeminum*. Theiler [1] referred to them in a paper in 1905, and in a later paper [2] entitled "Further Inoculation Experiments with South African Redwater," he proved certain facts which led him to consider that these "marginal points" represented a new genus of protozoa for which he proposed the name of *Anaplasma*, the species being *Anaplasma marginale*.

Theiler, in another paper,[3] gives a short review of the literature containing references to these marginal points by other observers such as Smith and Kilborne,[4] Knuth,[5] Lignières,[6] Dschunkowsky and Luhs.[7]

Kolle and Turner,[8] when carrying out some work on rinderpest in South Africa in 1897, noted the presence of these anaplasms in the erythrocytes of cattle. It is due, however, to the efforts of Theiler that the exact significance of these forms has been determined, for he has shown that they are the causal agents of the disease known as gall-sickness, a disease in which other parasites [9] had been found in the blood, among them being *Trypanosoma theileri*, *Babesia bigemina*, and *Babesia mutans*.

Theiler was successful in producing gall-sickness proper in freshly-imported heifers from England. The blood of these animals showed the presence of anaplasms without any of the above-mentioned parasites being present. In his report for 1908–9, Theiler [10] gives an excellent and full description of the disease and its pathology under the heading of "Anaplasmosis of Cattle." Another paper [11] in the same report gives an account of an experiment in which he proved that the blue tick (*Boophilus decoloratus*) could transmit the disease. In this experiment the incubation period was a long one. Theiler is of the opinion that *Anaplasma marginale* and *Piroplasma bigeminum* can be transmitted not only by the same species of ticks but by one and the same individual.

Sieber [12] has a good paper with coloured plates dealing chiefly with the morphology of the *Anaplasma marginale*. Various fixing and staining solutions are recommended for the study of the intricate morphology of the "marginal points," and Sieber concludes his paper by some remarks on their nature.

> Based on the results of my morphological experiments, I consider I am justified in comparing them with formations which Prowazek, under the name of "chlamydozoa," places in one group. These are micro-organisms, which in regard to their parasitism adapt themselves very easily, and whose attacks on the host cell result in formations of peculiar reaction products. By means of nuclear staining their existence is generally proved.

Spreull [13] gives a clinical account of two cases of anaplasmosis in cattle in East Griqualand. The blood showed a heavy infection with "marginal points," which he considered are parasitic in nature.

Balfour [14] has noted the existence of anaplasmosis and *Nuttallia equi* occurring together

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[1] Theiler, A. (1905–6), "*Piroplasma mutans* (n. spec.) and the Disease caused by it." *Report of the Government Veterinary Bacteriologist, Transvaal Department of Agriculture.*

[2] *Idem* (1908–9), "Further Inoculation Experiments with South African Redwater." *Ibid.*

[3] *Idem* (1908–9), "The Marginal Points in the Literature on Piroplasmosis." *Ibid.*

[4] Smith, T., and Kilborne, F. L. (1893), *Eighth Annual Report of the Bureau of Animal Industry, Washington.* Quoted in *Report of the Government Veterinary Bacteriologist, Transvaal Department of Agriculture*, 1905–1906.

[5] Knuth, P. (1905), "Studien über das Texasfieber (La Tristeza) der Rinder in den La Plata-Staaten." Berlin. Quoted in *Ibid.*

[6] Lignières (1900), "La Tristeza, or Malaria Bovine dans la République Argentine." Quoted in *Ibid.*

[7] Dschunkowsky, E., and Luhs, J. (1904), "Die Piroplasmosen der Rinder." *Cent. f. Bakt.*, I. Orig., Vol. XXXV., No. 4.

[8] Kolle, W., and Turner, G. (1898), "Über Schutzimpfungen u. Heilserum bei Rinderpest." *Zeit. f. Hyg. u. Infekt*, Vol. XXIX., No. 2.

[9] Theiler, A. (1908–9), "The association of *Piroplasma bigeminum*, *Anaplasma marginale*, and *Piroplasma mutans* in South African Cattle." *Report of the Government Veterinary Bacteriologist, Transvaal Department of Agriculture.*

[10] *Idem* (1908–9), "The Anaplasmosis of Cattle." *Ibid.*

[11] *Idem* (1908–9), "Transmission of *A. Marginale* by Ticks." *Ibid.*

[12] Sieber, H. (1909–10), "*Anaplasma marginale.*" *Report of the Government Veterinary Bacteriologist, Department of Agriculture, Union of South Africa.*

[13] Spreull, J. (December 31, 1909), "Note on the Occurrence of 'Marginal Points,' or a new intra-corpuscular Parasite in the Blood of Cattle in South Africa." *Journal Comparative Pathology and Therapeutics.*

[14] Balfour, A. (March, 1911), "Anaplasmosis in Donkeys." *Ibid.*

in the blood of donkeys in the Sudan. Some of the so-called "marginal points" were truly marginal, but the majority were a short distance from the edge, and quite a number were central. Balfour raises the question of the possibility of these bodies being of the nature of the Jolly Körper or Howell and Jolly bodies met with in embryonic blood, the blood of rodents, and in certain anæmic states; but from their position in the red cells, and from the fact that Jolly bodies have not been seen in the process of budding, he is inclined to agree with Theiler's views regarding the specificity of these marginal points. The transmitting agent of anaplasmosis in the Sudan has yet to be proved. *Boophilus decoloratus* does not exist in the country, but *Boophilus australis* has been found on cattle and dogs. Balfour is inclined to consider that *Rhipicephalus evertsi* is the tick implicated in transmitting this disease in the Sudan. Anaplasmosis does not appear to have been previously encountered in equines.

Piroplasmosis—*continued*

Jowett [1] has a paper entitled "Some Observations on the Subject of Marginal Points." It is of interest, inasmuch as he noted the presence of these marginal points in apparently healthy animals.

Canine Piroplasmosis.—Nuttall and Graham-Smith,[2] referring to the fact that all attempts to infect different species of animals with *P. canis* have failed, conclude that this parasite is only communicable to dogs, this conclusion being strengthened by their failure to transmit the disease to foxes in England, and by Lounsbury's experiments on jackals in Cape Colony, whose results were also negative.

This is discussed by them in a short, interesting paper, and they summarise the position by saying:—

> The experiments appear to indicate that *P. canis* is peculiarly specific in its pathogenicity, since it is not capable of producing disease in the fox and jackal, species closely allied to the dog. They also seem to show that neither of these species is concerned in the maintenance of the disease in nature. Experiments on the wolf would be extremely interesting.

In a paper [3] on immunity in *P. canis* the same observers give their results of a series of experiments. They do not consider that the results yielded have been promising, and say—

> We do not consider that further experiments of the kind are required, since there is little evidence that they will lead to a practical means of protecting dogs against piroplasmosis. On the other hand the drug treatment (trypanblau and trypanrot) gives us a means of curing the animals, and, combined with previous inoculation with virulent blood, affords us a practical means of "salting" animals without there being much risk attached to the procedure.

Nuttall and Graham-Smith [4] have contrasted the mode of multiplication of *P. bovis* and *P. pitheci* with that of *P. canis* as it takes place in the circulating blood. They also discuss other species of piroplasms. In their summary they give the points which they consider to be characteristic of the genus *Piroplasma*.

> In stained preparations *Piroplasma canis*, *P. bovis*, and *P. pitheci* may be distinguished from other intracorpuscular parasites by the presence of intracorpuscular pyriform bodies, usually occurring in pairs and less commonly in fours, eights and sixteens. These pyriform bodies show a dense mass of chromatin near the pointed end, and a loose mass, often connected with the dense mass, situated towards the blunt end. In suitable preparations peculiar dividing forms, most typically represented by trilobed forms or more or less pyriform bodies joined to a single smaller rounded or elongated mass of protoplasm, may be seen.
>
> In the absence of observations on the living parasite, we consider that these points may be taken as characteristic of the genus *Piroplasma*.

An interesting report on a new piroplasm affecting dogs is that written by Patton [5] on a disease affecting the hounds of the Madras Hunt. A large unexplained mortality led to investigations, and a new parasite was found which differed from *P. canis* in being much smaller and never occurring in the characteristic pairs of large pyriform bodies. The disease is inoculable from dog to dog, and a previous attack of *P. canis* affords no immunity to this malady.

Patton concludes that the hounds are infected from jackals, which he has shown to suffer from this disease.

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[1] Jowett, W. (March, 1911), "Some Observations on the Subject of Marginal Points." *Journal Comparative Pathology and Therapeutics.*

[2] Nuttall, G., and Graham-Smith, G. (September, 1909), "Notes on an Attempt to Infect the Fox and Jackal with *P. canis*." *Parasitology.*

[3] *Idem* (September, 1909), "Notes on Immunity in *P. canis*." *Ibid.*

[4] *Idem* (June, 1908), "The Mode of Multiplication of *P. bovis*, etc." *Ibid.*

[5] Patton, W. S. (April, 1910), "Preliminary Report on a New Piroplasm (*P. gibsoni*, sp. nov.) found in the Hounds of the Madras Hunt." *Bull. Soc. Path. Exot.*

Piroplasmosis—*continued*

The proposed name for the new parasite is *P. gibsoni*. It is remarked that trypanblau is far less effectual with this parasite than with *P. canis*. The characteristic symptoms are an insidious onset, a chronic course with anæmia, hypertrophy of the liver, and especially the spleen, fever and weakness. Hæmoglobinuria was not noticed.

The jackals harbour ticks, *Hæmaphysalis bispinosa* and *Rhipicephalus*, a new species, closely allied to *R. simus*.

Nuttall[1] has published a note on the degenerative appearances of *P. canis* following treatment by trypanblau, a note of especial interest when we consider that the drug is influencing the parasite while it is yet contained within the red blood cell.

The essential changes remarked were (*a*) the disappearance of the typical intra-corpuscular pyriforms, whilst (*b*) the surviving parasites appear rounded or irregular prior to the disappearance from the peripheral circulation. It was noticed, too, that masses of chromatin were often extended from the degenerating parasites.

The note is illustrated with diagrams.

Possibly the most striking work on the subject of treatment in canine piroplasmosis was the introduction of the dyes trypanblau and trypanrot as curative agents for this disease. Nuttall and Hadwen's[2] work has demonstrated the great utility of these drugs, and their results are discussed in some interesting papers.

They observed that the drugs appeared to affect the parasite even while in its intra-corpuscular stage, though of course the parasite is principally acted on when it is exposed free in the plasma in the extra-corpuscular stage. Concerning the experiments with trypanblau, the authors state that it appeared to exert a more marked effect upon the parasites than did trypanrot. They summarise their results as follows :—

(1) We have discovered that Trypanblau and Trypanrot are highly efficient remedies in the treatment of canine piroplasmosis, no drug or mode of treatment having hitherto been found to exert any effect upon this very fatal disease.

(2) The drugs exert a direct and observable effect upon the parasites (*a*) by causing the pyriform parasites to quickly disappear, and (*b*) in most cases, by causing the total disappearance of the parasites from microscopic observation in the peripheral blood.

(3) The disappearance of the parasites from the blood is usually temporary, the parasites reappearing in small numbers after an interval of 9 to 12 days, but the dogs, as a rule, show no symptoms and gradually progress toward recovery. In our experience there is but slight loss of weight in treated animals, this being in marked contrast to what is usually observed in dogs which recover naturally. In the two dogs which died of a relapse the parasites reappeared after an interval of 4 to 5 days.

(4) The experiments were conducted upon twenty-one dogs of all ages and of a variety of breeds. Many of the dogs were highly susceptible puppies. Twelve dogs were subjected to curative treatment, one dog received preventive treatment, and eight dogs served as controls.

(5) Twelve dogs received treatment as follows :—

(*a*) Two dogs were treated with Trypanrot and survived 111 days and 20 days respectively. In the latter case the dog was treated in an advanced stage of the disease, the parasites disappeared, and death appeared to be due to the after-effects of the malady.

Two control dogs died respectively on the 9th and 7th day after they were inoculated.

(*b*) Ten dogs were treated with Trypanblau and seven made a good recovery. Three of these dogs are still alive, having been respectively under observation for periods of 90, 83, and 65 days. Four of the recovered dogs died respectively of distemper on the 42nd and 43rd day, of severe mange on the 52nd day, and of distemper and mange on the 69th day. We failed to cure the disease in three out of ten cases treated; two small wormy ill-nourished puppies died from a relapse (on the 13th and 15th day) after they appeared to be on the road to recovery; one dog, treated only three hours prior to death, and when 50 per cent. of its corpuscles were infected, succumbed to the disease, but even in this case a visible effect was exerted upon the parasites by the drug.

Of the seven control dogs, six died of piroplasmosis within 7 to 13 days after inoculation with virulent blood, and the remaining dog died of piroplasmosis on the 36th day after inoculation.

(6) After the parasites disappear under the influence of the drug, the temperature usually falls to normal, but slight rises of temperature may at times occur, together with the subsequent reappearance of the parasites.

(7) When the parasites reappear after treatment they occur in small numbers, and can usually be detected only at the edge of the film. In such cases the parasites tend to occur in higher multiples (P P P P or more) within the individual corpuscles. The same appearance has been observed in one of the control dogs, which died of chronic piroplasmosis on the 36th day.

(8) In the two puppies ten and eleven, in which death followed upon a relapse, the parasites reappeared after a shorter interval (4 to 5 days) than in any of the other dogs. The blood counts made during the fatal

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[1] Nuttall, G. (July, 1910), "The Degenerative Appearances observed in Canine Piroplasmosis after Drug Treatment." *Parasitology*.

[2] Nuttall, G., and Hadwen, S. (June, 1909), "The Successful Drug Treatment of Canine Piroplasmosis." *Ibid.*

relapse are remarkable, as showing a high percentage of dividing forms; that rapid invasion of fresh corpuscles was proceeding is also shown by the high percentage of single pyriform parasites which occurred in the corpuscles. **Piroplasmosis—** *continued*

(9) One experiment is reported (dog 13) in which Trypanblau was injected twenty-four hours after the animal was inoculated, with the result that no parasites appeared in the dog's blood up to the 65th day, and the dog remained perfectly well. The control dog died of piroplasmosis on the 7th day. (This experiment has since been successfully repeated.)

Further experiments of this character will shortly be reported upon.

(10) Arsacetin and Soamin exert no curative effect upon canine piroplasmosis.

The most effective dose of trypanrot given was 6 c.c. of a 1 per cent. solution on the fifth, seventh, and ninth days after inoculation; and of trypanblau, 4·5 to 6 c.c. of a saturated solution on the sixth and seventh days after inoculation, the dose varying according to body weight.

At a later date[1] these same investigators published the results of using trypanblau as a preventive method of treatment. They found that (1) Trypanblau injected subcutaneously into dogs a day before or a day after they have been inoculated with blood containing *P. canis*, effectually prevents the development of piroplasmosis by destroying the parasites at the onset of infection; (2) Trypanblau given by the mouth is ineffective, since it exerts no apparent influence either upon the parasite or upon the course of the disease. Tryparosan they found to be ineffective.

In writing on the question of drug treatment, Nuttall[2] has catalogued a list of experiments which have been performed, and which concisely sums up most of the experimental work on this subject. These results may be of value to investigators who come across this disease in the Tropics.

(1) Drugs which have been found ineffective in the treatment of canine piroplasmosis are—

Arsacetin, tested on one dog by Nuttall and Hadwen (1909).

Soamin, tested on one dog by Nuttall and Hadwen (1909).

Sodium-methylarsenate, tested on two dogs by Nuttall and Graham-Smith (1908).

Tartar emetic, tested on two dogs by Nuttall and Graham-Smith (1908).

Sodium nucleinate, tested on two dogs by Levi della Vida (1907).

Beta-napthylamine, tested on two dogs by Nuttall and Graham-Smith (1908).

Brilliant green, tested on two dogs by Levi della Vida (1907).

Brilliant green, tested on one dog by Nuttall (1909).

Benzopurpurine, tested on one dog by Nuttall (1909).

Tryparosan, tested on two dogs by Nuttall and Hadwen (1909).

Methylene blue, tested on two dogs by Levi della Vida (1907).

Methylene blue, tested on two dogs by Nuttall and Graham-Smith (1908).

(2) Of doubtful value are—

Fowler's solution, tested on one dog by Levi della Vida (1907). The dog is stated to have had but a mild attack of piroplasmosis.

Atoxyl, tested on six dogs by Gonder (1907) with negative results, in that all the dogs died of piroplasmosis. Levi della Vida (1907, p. 360) states that he cured some dogs by atoxyl treatment, but does not state how many.

Quinine bihydrochloride, tested on one dog by Nuttall and Graham-Smith (1908) with negative result. Memmo, Martoglio, and Adani (1905) state that they cured two dogs by injections of quinine, but give no particulars of their experiments.

Oil of turpentine, tested on three dogs by Levi della Vida (1907) with negative results. Memmo, Martoglio, and Adani (1905), however, claim to have cured all of the twelve dogs they treated with turpentine.

(3) Apparently the following drugs may exert some effect :—

Dichlorobenzidine—two *molecules* of *amido-napthol-disulpho*, tested on twelve dogs, two of which recovered, Levi della Vida (1907).

Sodium cacodylate, tested on seven dogs, six of which are stated to have recovered, Levi della Vida (1907). (I am about to test this remedy afresh, since the Italian author gives very few particulars regarding his experiments.)

Congo red, tested on three dogs by Nuttall. All of the dogs died, but the drug exerted a decided effect upon the parasites.

(4) Definite curative or preventive effects are exerted by—

Trypanblau (C H N O S Na, the tetrazo compound of toluidine and amidonaptholsulphonate of sodium) cured seven out of nine dogs in the experiments by Nuttall and Hadwen (1909), and when given early prevented the appearance of the parasites in the dogs' blood. These results have been confirmed by Jowett (1909), who tested

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[1] Nuttall, G., and Hadwen, S. (September, 1909), "Further Experiments on the Drug Treatment of Canine Piroplasmosis." *Parasitology.*

[2] Nuttall, G. (December, 1909), "The Drug Treatment of Canine Piroplasmosis." *Ibid.*

Piroplasmosis—*continued*

the dye on fourteen dogs, two of which were moribund. The latter died, whilst twelve recovered. Six of Jowett's cases were due to experimental infection, and a number showed severe clinical symptoms. The drug is ineffective when given by the mouth. (Nuttall and Hadwen, 1909; confirmed by Jowett, 1909.)

Trypanred, tested on two dogs by Nuttall and Hadwen (1909), caused the parasites to degenerate and disappear. (Further experiments with this dye are in progress. The initial experiments indicated that trypanred is not as satisfactory as trypanblau for purposes of treatment, as it produces a more irritant effect.)

(5) In dogs which have recovered from piroplasmosis after treatment with Trypanblau and Trypanred the blood remains infective and virulent for six or seven months or more after treatment. Such dogs resist re-inoculation with virulent blood obtained from dogs suffering from acute piroplasmosis and, consequently, are to be regarded as "salted" animals. From a practical point of view the "salting" of dogs (and cattle) by the method of inoculation followed by the dye treatment appears to offer decided advantages. The method is at present on its trial in respect to cattle which are being "salted" in England prior to their exportation to Africa.

Levaditi and Nattan-Larrier[1] tested the effect of arsenobenzol ("606") in canine piroplasmosis, and obtained excellent results with it when given intravenously. The dose employed was 4 cg. for every kilogramme of the dog's weight. They carried out these tests on three dogs showing a heavy infection with *P. canis*. The parasites disappeared entirely from the blood (as early as four hours after the injection in one of the dogs), and all the dogs recovered from the disease.

Equine Piroplasmosis.—Schein,[2] in South Annam, found piroplasms present in a mare suffering from trypanosomiasis—*T. evansi*.

He describes the forms seen by him as rounded, oval and irregular, rarely pyriform. The disease appears to be rare, as this is the only case he saw.

Marzinowsky[3] has obtained cultures of *P. equi* by adding 10 c.c. of infected blood to sterilised tubes containing 1·5 to 2 c.c. of a solution of 10 per cent. sodium citrate; the salt must be chemically pure.

After incubating at a temperature of 87° C. for two or three days, star-shaped developmental forms are found, like those shown by Kleine in the cultivation of *P. canis*. From the third to the seventh day small forms with a big nucleus are apparent; it is not shown how these little forms are derived from the larger star-shaped forms; the author compares them to spores. The infectivity of these cultures was not demonstrated.

Theiler[4] has contributed a long paper on a series of experiments on protective inoculation against equine piroplasmosis. From observations made in his previous experiments he used the blood (*a*) from young immune weaned horse foals, and (*b*) from immune donkey foals still suckling.

The results of the experiments are given in full. In his conclusions he found that the reactions caused by the injection of horse foal blood were more severe than those resulting from the injection of donkey foal blood; in the latter case the mortality was nil, while in the former, in two series of experiments, the mortality was 3 per cent. and 4·5 per cent. respectively. He says "no cases of relapse after discharge have occurred, proving that the immunity given by the injection of donkey foal blood is as good as that afforded by horse foal blood."

The paper should be consulted in the original, as there are several points not suitable for abstraction.

According to Nuttall and Strickland,[5] there are two kinds of equine piroplasmosis, one the better known, which is produced by *P. equi*, Laveran, and the other which has been studied and described in Russia by Marzinowsky which Nuttall would call *P. caballi*. The authors have had an opportunity of observing the last named for themselves. A horse cured of this form of piroplasmosis has been shown to be susceptible to *P. equi*, or, according to the new classification, *Nuttallia equi*, and has succumbed.

Baldrey,[6] in writing of piroplasmosis in India, speaks of an obscure form of piroplasma

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[1] Levaditi, C., and Nattan-Larrier, L. (May 10, 1911), "Traitement de la piroplasmose canine par l'arsénobenzol." *Bull. Soc. Path. Exot.*

[2] Schein, H. (January, 1911), "Piroplasmose du cheval dans le Sud Annam." *Ibid.*

[3] Marzinowsky, E. (March, 1909), "Über die Züchtung von *Piroplasma equi*." *Zeit. f. Hyg. u. Infekt.*, Vol. LXII.

[4] Theiler, A. (June, 1908), "Continuation of Experiments on Protective Inoculation against Equine Piroplasmosis." *Journal Comparative Pathology and Therapeutics.*

[5] Nuttall, G., and Strickland, C. (December, 1910), "Die Parasiten der Pferdepiroplasmose resp. der Biliary Fever." *Cent. f. Bakt.*, I. Orig., Vol. LVI.

[6] Baldrey, A. (October, 1910), "Piroplasmosis in India." *Journal of Tropical Veterinary Science*, Vol. V., No. 4.

which occurred among cavalry and artillery horses in 1910, the outbreaks being somewhat numerous. **Piroplasmosis—** *continued*

He says that the symptoms were not quite typical of bilious fever, rather resembling acute or chronic influenza.

The parasites were found free and in intra-corpuscular forms, and in some cases the corpuscles showed bodies similar in form to *Anaplasma marginale*. The article is illustrated and contains numerous references.

Belizer and Marzinowsky,[1] working on equine piroplasmosis in Russia, have proved that all the infected horses were carriers of a species of tick—*Dermacentor reticulatus*.

Also, they have assured themselves that the locally-bred horses scarcely suffer at all from this disease and appear immune; on the other hand imported horses are very susceptible, and often die.

They found in the blood and intestines of the ticks different stages in the life history of the piroplasm such as have already been described by R. Koch and Christophers. They obtained by the injection of extracts of adult infected ticks typical attacks in horses—injections of extracts from larvæ were less successful.

Immunisation, according to these authors, can be obtained by injection of very small quantities of infected blood, which first brings on a benign form of the malady.

The above are the more important species, but one may note that Yakimoff[2] has found that hedgehogs suffer from a form of piroplasmosis. The parasites are small, and are classified in the group *Theileria;* he notes their occurrence in nucleated red cells as well as in normal red blood corpuscles, and even speaks of intranuclear parasites in the former.

The hedgehogs are infested with numerous nymphs of the tick *Dermacentor reticulatus*, and the inter-relationship of this disease and equine piroplasmosis is discussed. Transmission of the disease by infected blood to horses, dogs, etc., has proved negative, while infection is readily produced from hedgehog to hedgehog; the name *P. ninense* is proposed.

Piroplasmosis has also recently been found to exist in field-mice, reindeer, yaks, and bears, and doubtless is more widely distributed than was at one time supposed.

Plague. It is not an easy matter to arrange for reference the various papers dealing with the different aspects of this disease, but one trusts that they will be considered useful if grouped as follows—(1) Etiology, including bacteriology, and the question of transmission by animals, and their ectoparasites; (2) epidemiology; (3) clinical manifestations, including diagnosis; (4) prophylaxis; (5) treatment.

Belleli[3] has pointed out that in cases of plague in which buboes only are present, one can find large numbers of plague bacilli in the blood of the patient if large quantities of this fluid be centrifugalised. Sometimes the bacilli can apparently be found in the blood before the appearance of the buboes, and even before the fever commences.

Gibb,[4] in a recent article, gives the sugar cultural reactions of the *B. pestis* isolated during the Harbin epidemic.

Glucose, acid formation in less than 24 hours; maltose, acid formation in less than 24 hours; levulose, acid formation in less than 24 hours; dextrose (*sic*), acid formation in 24 hours; mannite, acid formation in 24 hours; galactose, acid formation in less than 48 hours; dextrin and salicin, acid formation in less than 48 hours. With lactose, saccharose, and inulin there was no acid formation. In no case was there production of gas. There was no change of colour in neutral red broth.

Mention may be made of a paper by Vay,[5] who, by employing special staining methods, was able to demonstrate the presence of granules in plague bacilli obtained from agar and broth cultures.

In a short paper, Nicolas[6] gives an account of a small epidemic of plague at Bondé.

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[1] Belizer, A., and Marzinowsky, E. (September, 1908), "Recherche sui la piroplasmose des chevaux en 1907, (en russe), 1908." Quoted in *Bull. de l'Inst. Past.*

[2] Yakimoff, W., "Die Zecken und Piroplasmen des Igels." *Cent. f. Bakt.*, I. Orig., Vol. LII., No. 4.

[3] Belleli, V. (November 6, 1909), "Plague." Epitome, *British Medical Journal.*

[4] Gibb, J. G. (April 29, 1911), "Culture Tests for the Plague Bacillus." *Lancet.*

[5] Vay, F. (December, 1909), "Über körnchenartige Bildungen in Pest-Bacterien." *Cent. f. Bakt.*, I. Orig., Vol. LII., No. 3.

[6] Nicolas, C. (January 11, 1911), "A propos d'une petite épidémie de peste." *Bull. Soc. Path. Exot.*

Plague—*continued*

In this paper he mentions that in New Caledonia plague is almost continually present, the bacillus apparently existing in a latent form. He is inclined to find the explanation of this in the light of Yersin's discovery in Hong-Kong, where this observer found, at the beginning of an epidemic, in the soil of houses infected by plague, a bacillus having identical morphological cultural and staining reactions with *B. pestis*, but devoid of virulence.

Gauducheau [1] describes a clinical case, which, if it had occurred in a plague-stricken country, would, in all probability, have been diagnosed as an infection with Yersin's bacillus, for the bacillus isolated from the bubo was morphologically somewhat like that of *B. pestis*, but differed in staining and cultural reactions. The bacillus, however, was proved to belong to the anthrax group of organisms.

Mention must be made of Verjbitski's [2] experiments which were carried out in 1902, dealing with the part played by insects in the epidemiology of plague. Owing to the fact that his original paper—a thesis written in the Russian language—was not published in any scientific journal, it was apparently overlooked. The English translation of it was published with the reports of the plague investigations in India. Verjbitski's researches covered much of the ground subsequently traversed by the Indian Plague Commission. His experiments were carried out with the bed-bug, *Cimex lectularius*, and three species of fleas, *Pulex irritans*, *Typhlopsylla felis*, the dog-flea, and *Ctenocephalus musculi*, the common rat-flea of Russia. *Pulex* (now *Loemopsylla*) *cheopis* was not used throughout his experiments. A summary of the results obtained by this observer is worth quoting :—

(1) All fleas and bugs which have sucked the blood of animals dying from plague contain plague microbes.

(2) Fleas and bugs which have sucked the blood of animals which are suffering from plague only contain plague microbes when the bites have been inflicted from 12 to 26 hours before the death of the animals—that is, during that period of their illness when their blood contains plague bacilli.

(3) The vitality and virulence of the plague microbes are preserved in these insects.

(4) Plague bacilli may be found in fleas from four to six days after they have sucked the blood of an animal dying with plague. In bugs, not previously starved, or starved only for a short time (one to seven days), the plague microbes disappear on the third day ; in those that have been starved for 4 to 4½ months, after 8 or 9 days.

(5) The numbers of plague microbes in the infected fleas and bugs increase during the first few days.

(6) The fæces of infected fleas and bugs contain virulent plague microbes as long as they persist in the alimentary canal of these insects.

(7) Animals could not be infected by the bites of fleas and bugs which had been infected by animals whose own infection had been occasioned by a culture of small virulence, notwithstanding the fact that the insects may be found to contain abundant plague microbes.

(8) Fleas and bugs that have fed upon animals which have been infected by cultures of high virulence convey infection by means of bites, and the more certainly so the more virulent the culture with which the first animal was inoculated.

(9) The local inflammatory reaction in animals which have died from plague occasioned by the bites of infected insects is either very slight or absent. In the latter case it is only by the situation of the primary bubo that one can approximately identify the area through which the plague infection entered the organism.

(10) Infected fleas communicate the disease to healthy animals for three days after infection. Infected bugs have the power of doing so for five days.

(11) It was not found possible for more than two animals to be infected by the bites of the same bugs.

(12) The crushing of infected bugs *in situ* during the process of biting occasioned in the majority of cases the infection of the healthy animals with plague.

(13) The injury to the skin, occasioned by the bite of bugs or fleas, offers a channel through which plague microbes can easily enter the body and occasion death from plague.

(14) Crushed infected bugs and fleas and their fæces, like other plague material, can infect through the small punctures of the skin caused by the bites of bugs and fleas, but only for a short time after the infliction of these bites.

(15) In the case of linen and other fabrics soiled by crushing infected fleas and bugs on them, or by the fæces of these insects, the plague microbes can under favourable conditions remain alive and virulent for more than five months.

(16) Chemical disinfectants do not in the ordinary course of application kill plague microbes in infected fleas and bugs.

(17) The rat flea, *Typhlopsylla musculi*, does not bite human beings.

(18) Human fleas do bite rats.

(19) Fleas found on dogs and cats bite both human beings and rats.

(20) Human fleas, and fleas found on cats and dogs, can live on rats as casual parasites, and therefore can, under certain conditions, play a part in the transmission of plague from rats to human beings, and *vice versâ*.

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[1] Gauducheau (February 8, 1911), "Bactérie anthracoïde se rapprochant du bacille de Yersin." *Bull. Soc. Path. Exot.*

[2] Verjbitski, I. D. T. (May, 1908), "The Part Played by Insects in the Epidemiology of Plague." *Journal of Hygiene.*

Plague—*continued*

The rôle played by bugs as vectors of plague bacilli and transmitters of the disease has been undoubtedly proved, and Verjbitski's experiments have been confirmed by Jordansky and Kladnitsky,[1] who found that bugs fed on the blood of plague-infected mice do not appear to suffer any harm, and may be kept alive as long as two and a half months after feeding. They found that

> the plague bacillus remains alive and virulent in the body of the bug; up to the third day it does not appear to multiply in the digestive tube of the insect, since blood withdrawn from the bug at this period is not more rich in plague bacilli than the blood of the mouse which was bitten. But from the third to the sixth days the cocco-bacilli become more numerous and the preparations resemble those taken from a freely-growing pure culture. Towards the eighth or the tenth day the bacilli show modifications, and involution forms appear; fine filaments are seen which no longer take a polar staining, and at the same time cocci make their appearance. Later on, it is impossible to demonstrate the presence of plague bacilli in the bug by means of smear preparations, though the persistence of the organism may be shown by resorting to culture. Emulsions made from the bodies of the bugs are found to be virulent, particularly those prepared from insects fed from six to eight days previously—that is, when the period has been reached for the maximum development of the bacteria within the digestive apparatus. The results of their experiments compel the authors to dissent from the statement, published by other observers, that plague bacilli perish rapidly in the body of the bug.

Walker [2] has an interesting paper dealing with the rôle played by the bed-bug in a plague epidemic in India where there was an absence of rats in the villages affected. He examined the alimentary canal of bed-bugs (*Cimex rotundatus*) collected from infected huts, and found 22 per cent. of them infected with *B. pestis*. In uninfected huts 4·14 per cent. were infected. He carried out some feeding experiments, and successfully transmitted plague from human cases to rats by means of the *Cimex rotundatus*.

Wherry,[3] in an interesting paper, considers the occurrence of plague among the ground squirrels in California. These rodents have been found naturally infected, and are infested with the fleas *Hoplopsyllus anomalus* and *Ceratophyllus acutus*, which have been proved by experiment to be capable of biting man.

The close relationship between rats and squirrels is pointed out, as they frequently live in association, and Wherry considers that the ground squirrel acts as a host for *B. pestis* in the interim between the more noticeable outbreaks of plague in rats and man.

M'Coy,[4] in a more recent paper, describes the pathological lesions present in squirrel plague. His conclusions are :—

> Plague in the ground squirrel is a disease that is readily recognised by the gross anatomical changes it produces.
>
> The commonest lesion, and often the only one, is a bubo.
>
> Many of the cases are probably examples of subacute or chronic plague.
>
> In many cases the bacilli found in squirrel plague are highly virulent for guinea-pigs and white rats; in other cases the virulence is somewhat reduced.
>
> Smear preparations are negative for pest-like bacilli in the majority of cases.
>
> It is unsafe to trust to the cutaneous method of inoculation alone, as it will sometimes fail when the subcutaneous method yields positive results.

M'Coy and Wherry [5] also describe a case of subacute plague in a boy where the infection was undoubtedly acquired from contact with ground squirrels. The lesions were similar to those of subacute plague in guinea-pigs, rats, and squirrels.

M'Coy [6] tested the susceptibility of gophers, field mice, and ground squirrels to plague infection, and found that gophers were highly resistant to plague when inoculated by the cutaneous method, but were apparently often susceptible when inoculated subcutaneously, and therefore were not sufficiently susceptible to *B. pestis* to be of any importance from an epidemiological point of view. Field mice were probably about as susceptible as rats, but as they rarely come in close contact with man it was hardly probable they would be a serious

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[1] Jordansky, V., and Kladnitsky, N. (May, 1908), "Conservation du bacille pesteux dans les corps des punaises." *Ann. de l'Inst. Past.*

[2] Walker, E. A. (March, 1910), "Transmission of Plague in the Absence of Rats and Rat-Fleas." *Indian Medical Gazette.*

[3] Wherry, W. B. (December 18, 1908), "Plague among the Ground Squirrels in California." *Journal Infectious Diseases.*

[4] M'Coy, G. W. (November 28, 1909), "Pathology and Bacteriology of Plague in Squirrels." *Ibid.*

[5] M'Coy, G. W., and Wherry, W. B. (November 25, 1909), "Subacute Plague in Man due to Ground Squirrel Infection." *Ibid.*

[6] M'Coy, G. W. (June 12, 1909), "The Susceptibility of Gophers, Field Mice and Ground Squirrels to Plague Infection." *Ibid.*

Plague—*continued*

factor in the spread of plague. Ground squirrels were found to be highly susceptible, no example of immunity having been encountered.

In another paper, M'Coy [1] describes a number of inoculation experiments carried out to test the immunity of San Francisco rats to plague. He found that there was a considerable immunity to plague infection among the wild rats in that city, particularly among the old rats, and considered that the immunity was probably natural in most cases and not acquired. His paper is concluded by a short comparative description of the distinguishing characters of *Mus norvegicus*, *Mus rattus*, and *Mus alexandrinus*.

In a more recent article entitled "Plague among Ground Squirrels in America," M'Coy [2] makes mention of a plague-like disease of squirrels which is characterised by a caseous bubo (sometimes hæmorrhagic) and necrotic foci in the spleen and liver. The lesions present simulate plague infection. Guinea-pigs inoculated from infected squirrels die between the fifth and eighth day with lesions resembling those of plague. The cause of the disease, however, is feebly pathogenic for rats, and negative results yielded by stained smear preparations and cultures readily differentiate it from plague. M'Coy states that no etiological agent has been discovered. Under the heading of parasites this observer asserts that *Ceratophyllus acutus*, Baker, is the commonest species of flea found on the ground squirrel, *Citellus beecheyi*. It has been shown capable of carrying plague among the squirrels. The other flea, *Hoptopsyllus anomalus*, Baker, is not so commonly present. Among other ecto-parasites of squirrels, lice, mites, and ticks were found, apparently only at certain seasons and in limited areas. The paper is concluded by an account of the methods used for exterminating the squirrels by means of strychnine and bisulphide of carbon.

De Souza, Arruda, and Pinto [3] carried out a series of experiments to discover whether the common domesticated animals of Terceira Island were susceptible to plague. The results of their experiments were as follows :—

(1) Although our experiments on calves may not be extensive, we think we may affirm that the bovine race, in spite of the large doses inoculated, did not contract the plague.

On Terceira Island we had no knowledge whatever of any case of illness in bovines which could be put down to plague.

(2) As for the pigs, we consider the series of animals on which we experimented fairly large. The doses of virus inoculated were really enormous, far larger than what they would naturally receive.

The experiments led us to conclude that pigs do not contract plague.

(3) The experiments made on dogs seem to show that only with very large doses of plague bacilli can infection of these animals be obtained, and it seems beyond doubt that in its normal condition the dog is an animal practically refractory to plague.

This conclusion proved very interesting to Terceira Island, where dogs have rendered and continue to render great service in rat-hunting.

(4) The experiments made on rabbits led us to conclude that this animal is, on Terceira Island, very susceptible to plague.

(5) Our experiments on ferrets were made because these animals are extensively employed in rat-hunting, above all in the country.

According to these experiments the ferret is an animal susceptible to plague, but only able to contract an acute form of this disease by inoculation of large doses. However, as the ferret sucks the blood of the rats, its use in hunting these animals is not recommended.

(6) Our experiments corroborate those of the Austrian Commission, that cats can be infected by plague *per os*, after which they show at the autopsy an appearance with buboes in the neck very similar to those of cats spontaneously infected by plague.

(7) The general conclusion which we draw from our experiments on four kinds of birds—namely, pigeons, ducks, turkeys, and chickens, especially in regard to the latter, is that these animals are insusceptible to plague.

An important paper by the late Major Lamb [4] was read before the last Bombay Medical Congress, and deals with the etiology and epidemiology of plague. As it recounts most of the work carried out by the Plague Commission, reference to which was made in the first Review, there is no necessity to consider it fully here.

Kitasato [5] has a paper on rat fleas, with special reference to the transmission

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[1] M'Coy, G. W. (June 12, 1909), "The Immunity of San Francisco Rats to Infection with *B. pestis*." *Journal Infectious Diseases.*

[2] *Idem* (December, 1910), "Plague among Ground Squirrels in America." *Journal of Hygiene.*

[3] De Souza, A., Arruda, A., and Pinto, M. (August, 1910), "Report on Experiments undertaken to Discover whether the Common Domesticated Animals of Terceira Island are affected by Plague." *Ibid.*

[4] Lamb, G. (1909), "The Etiology and Epidemiology of Plague." *Transactions Bombay Medical Congress.*

[5] Kitasato, S. (1909), "Rat Fleas, with Special Reference to their Transmission of Plague in Japan." *Ibid.*

of plague in Japan. He states "that there is scarcely any doubt as to the possibility of transmission being effected by rat-fleas, and it is a noteworthy fact that in Japan, as well as in India, *Pulex cheopis* plays an important rôle in the plague epidemic." Plague—*continued*

Gauthier and Raybaud [1] carried out some experiments with *Ceratophyllus fasciatus* and *Ctenopsylla musculi*. They found that *C. fasciatus* was able to live when fed entirely on human blood, similar results being obtained by M'Coy and Mitzmain in San Francisco. Continuing their experiments with *C. fasciatus*, they found that it could live without food for a period of sixty-three days, whereas *P. cheopis* could only live ten to eleven days. Further, an interesting fact was proved, for they noted that plague bacilli did not lose their virulence when ingested by *C. fasciatus*, when the latter was kept without food for more than a month at a temperature of 0·3° C. Gauthier and Raybaud consider that in the northern regions the ceratophyllus fleas of rats and other rodents are able to hibernate and retain the latent virus for a very long time.

The *Reports on Plague Investigation in India* issued by the advisory committee [2] contain interesting material. The conclusions which have been provisionally reached by the advisory committee as the result of plague investigations in India between 1905 and 1909 are summarised, and may be conveniently quoted here :—

(1) Considerable epidemics of human plague consist almost entirely of cases of bubonic plague, and are directly dependent on the occurrence of epidemic plague in rats. The development of the rat epidemic precedes the human epidemic by an interval of about a fortnight. There is no evidence that any animals except rats play an important part in plague epidemics.

(2) *Epidemic plague in rats.*

(*a*) Rat-fleas which have sucked the blood of a plague-infected rat can transmit the disease to healthy rats to which they are transferred. The plague bacilli multiply in the stomach of the flea, and the flea may be still capable of conveying infection three weeks after having imbibed plague-infected blood.

(*b*) If plague-infected rats are kept in close confinement along with healthy rats, no epidemic of the disease occurs in the absence of fleas. In the presence of rat fleas the disease spreads from the infected to the healthy animals, and the rapidity and severity of the epidemic so produced is in proportion to the abundance of fleas.

(*c*) Rats may be infected by feeding them upon the bodies of other rats dead of plague. The distribution of the lesions in the bodies of naturally infected rats corresponds with that in rats experimentally infected by means of fleas with that in rats infected by feeding.

The Committee, therefore, conclude that, *in nature, plague is spread among rats by the agency of rat fleas.*

(3) *Epidemic plague in man.*

(*a*) Bubonic plague is not directly infectious from man to man, as is shown by the experience of plague hospitals where there is no tendency for the disease to spread from the sick to the attendants.

(*b*) Material epidemics of plague in man are always associated with epidemic plague in rats. Epidemic plague among rats provides a large number of infected rat fleas, and, owing to the mortality among the rats, brings these fleas on to human beings.

(*c*) Rat fleas (*Pulex cheopis*) bite human beings, especially in the absence of their natural host.

(*d*) Rat-fleas containing plague bacilli and found capable of transmitting plague to animals may be caught in plague-infected houses.

(*e*) Animals susceptible to plague (guinea-pigs, monkeys) placed in plague-infected houses, if unprotected from fleas, may contract the disease; whereas such animals, under the same circumstances, remain free from plague, if protected from fleas.

(*f*) The Commission have also performed numerous experiments with a view of testing other possible modes of infection, and have found that—

i. In the absence of fleas no epidemic resulted when animals susceptible to plague (guinea-pigs) were kept in close contact with infected animals, although the animals took their food off floors grossly contaminated by the excreta of their infected companions.

ii. Susceptible animals (guinea-pigs) caused to live upon and feed off floors artificially saturated with plague cultures failed to contract the disease.

iii. The excreta of plague-infected patients may contain plague bacilli, but the bedding, etc. of plague patients soiled with excreta containing plague bacilli was not found to be infective to highly susceptible animals caused to live in and upon the bedding.

The Committee, therefore, consider that *in the great majority of cases during an epidemic of plague, man contracts the disease* from plague-infected rats through the agency of plague-infected rat-fleas.

(4) *The seasonal recurrence and spread of plague.*

(*a*) The Committee has obtained no evidence that under ordinary conditions the plague bacillus survives for more than a few days outside the bodies of men, animals or fleas.

(*b*) In large towns plague may persist throughout the year, since a few cases of acute plague in men and rats occur during the non-epidemic plague season.

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[1] Gauthier, J. C., and Raybaud, A. (May 17, 1910), "Les puces du rat (*Ceratophyllus fasciatus et Ctenopsylla musculi*) piquent l'homme." *C. R. Soc. Biol.*, Vol. LXVIII. Quoted in *Bull. de l'Inst. Past.*, December 30, 1910.

[2] (November, 1910), "Reports on Plague Investigations in India." *Journal of Hygiene.*

Plague—*continued*

(*c*) In villages there is no satisfactory evidence that such persistence is of other than exceptional occurrence, and it seems probable that the recurring annual epidemics in such places are due in most cases to fresh importation of the infection.

(*d*) There is no evidence that plague infection is carried for more than short distances by the spontaneous movement of rats. Plague appears to be commonly imported into a fresh locality about the persons of human beings, though the transference of infected rats and fleas in merchandise must be considered.

(*e*) In districts which suffer annual epidemics of plague, the rat epidemic, on which the human epidemic depends, occurs during some part of that season when the prevalence of fleas is greatest.

In the 1907 epidemic, in the neighbourhood of Constantine, Billet [1] found that *P. cheopis* and *C. musculi* were the two common species of fleas infesting the rats, and that *P. cheopis* was more commonly found on *Mus decumanus*, whereas *C. musculi* were almost entirely found on *Mus alexandrinus* and *Mus rattus* (black variety). Of the other ecto-parasites that were found on rats, the dog flea, *Ctenocephalus canis*, was not frequently present, while *Ceratophyllus fasciatus* was usually found in large numbers on *M. decumanus*.

In the Oran epidemic (1907) Niclot [2] noted that *P. cheopis* had a marked predilection for *Mus rattus* (black variety).

Mention may be made of an interesting paper by Shipley [3] entitled "Rats and their Animal Parasites." In the first part of this paper, a short account is given of the characters of the common rat; their ecto-parasites are then named, and the paper is concluded by a short account of their endo-parasites.

Reference may also be made to a paper by Lloyd,[4] entitled "The Races of Indian Rats." He draws a comparison between rats found in the ports of Bombay, Calcutta, Madras and Rangoon, and refers to the part played by *Mus decumanus* as a carrier of plague. It harbours twice as many fleas as *M. rattus*, and, notwithstanding many statements to the contrary, he mentions that *M. decumanus* only occurs in the seaports of India.

Gray [5] contributes a full and interesting report on the septicæmic and pneumonic plague outbreak in Manchuria and North China. After a careful review of the circumstances attending this outbreak he concludes that—

(1) The first outbreak in Manchuria was among men who handled the tarabagan—an animal susceptible to epizootic plague. (2) Beginning at a definite focus, plague was spread through the three provinces by these men returning home. (3) Infection was kept up mainly by these coolies travelling in parties and sleeping together in inns under circumstances of constant intimate contact with plague-stricken cases in their midst. (4) The extreme cold of Manchuria induced an indoor existence. Infection, by breath and personal contact of clothes and belongings, was thus made easy. (5) There is little evidence of infection having been contracted in the open air, otherwise than among groups of coolies. (6) The mortalities have been mainly among groups of south bound coolies. (7) The next classes affected were the adult males who stayed in infected inns travelling or mixing with the returning coolies. (8) When introduced into a house, infection often wiped out the whole family. (9) In towns which became thoroughly infected (as at Fuchiatien) by the passing crowds of coolies, the incidence of the disease persisted, and those residents who were affected were nearly all of the poorer classes. (10) That fairly close contact is necessary for conveyance of infection has been exemplified by the comparative immunity enjoyed by Russians living in the midst of the infected railway area at Harbin. The case of every Russian who died was traced to close contact with Chinese of the plague-affected class. (11) The rate of spread was parallel with the rate of travel, as shown by the early infection of places along the railway and those in close communication with it (*e.g.* Hu-lan-fu and Harbin), as compared with the later infection of such populous towns as Petuna and Kirin. (12) Towns that had adopted preventive measures before they became badly infected—such as Tientsin, Tongshan, and Peking—practically escaped. (13) Isolation of patients and their contacts, and disinfection, when efficiently carried out, have invariably been followed by diminution of the death-rate. (14) Among rats examined at Harbin by Dr. P. Haffkine, and in "20,000 "rats examined by the Japanese plague staff, no instance of plague infection was found.

Tuck,[6] in his inaugural address at the International Plague Conference, mentions some interesting points in connection with the recent epidemic of plague in Manchuria :—

Two factors seem to have contributed largely to the virulence of this epidemic. These were, first, the severe climatic conditions, the thermometer registering at times—30° C., which extreme cold prevented the people going outdoors; the second factor was the low, dark, dirty, and overcrowded houses which formed the majority of the dwellings. At the same time it is worthy of note that some of the double-storied houses with plenty of air-space and not overcrowded were also badly infected.

A point of interest cited by Tuck was the fact that in one large city (Shuang cheng Fu),

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[1] Billet, A. (August, 1908), "La peste dans le département de Constatine en 1907." *Ann. de l'Inst. Past.*

[2] Niclot (June 10, 1908), "La peste à Oran en 1907." *Bull. Soc. Path. Exot.*

[3] Shipley, A. E. (1908), "Rats and their Animal Parasites." *Journal of Economic Biology*, Vol. III.

[4] Lloyd, R. E. (1909), "The Races of Indian Rats." *Transactions Bombay Medical Congress.*

[5] Gray, G. D. (April 29, 1911), "A Report on the Septicæmic and Pneumonic Plague Outbreak in Manchuria and North China." *Lancet.*

[6] Tuck, G. L. (April 29, 1911), "Plague." *Ibid.*

which was well planned and peopled by wealthy landowners and Chinese merchants—clean in their habits and houses—there were 1,500 deaths in seven weeks. Tuck considers that there may be other reasons as well as dirt and poverty to account for the high mortality. Plague—*continued*

Gill [1] has a note on the epidemiology of pneumonic plague in India. He considers it is commoner in the comparatively cool climate of the Punjab than in the warmer and moister parts of India. Apparently it occurs in the months of January, February and March, when epidemic plague is on the increase, but before the latter has reached its maximum intensity. His conclusions are as follows :—

(1) Primary pneumonic plague in all its stages is intimately associated with the bubonic variety.

(2) When occurring as an original infection it is associated with a preceding rat epizootic in the same way as bubonic plague.

(3) It rapidly tends to die out as such with or without being succeeded by a bubonic outbreak.

(4) Its mode of spread is " direct " from man to man, but owing to the readiness with which rats become infected, it is liable to give rise to a rat epizootic, which in turn gives rise to a bubonic plague epidemic.

(5) It occurs usually and chiefly at the commencement of the epidemic season, being chiefly confined to the first three months.

(6) That as regards individual epidemics it is mostly present at the commencement of such outbreaks.

(7) That in estimating the effect of pneumonic plague on the general spread of the disease its power of producing bubonic outbreaks requires to be taken into consideration.

(8) That pneumonic plague plays a definite though variable part in the specific septicæmia, called plague, of which, perhaps, it forms the expression of an unusual or " exalted " degree of virulence.

Ponce de Leon,[2] writing in *La Semana Médica* on the serum treatment of plague, mentions two cases which lead him to think that a recrudescence of the disease in perhaps one of its rarer forms, such as the gastro-intestinal or the meningitic, may occasionally be met with some considerable time after the patient has regained his usual health, and therefore may entirely escape recognition as being in any way connected with the original attack. After convalescence, these cases in a little more than a month from the date of admission became ill again with signs of meningitis. Death eventually occurred, and the necropsies revealed gastritis, pulmonary œdema, hepatic congestion, myocarditis and suppurative meningo-encephalitis. The pus contained numbers of Yersin's cocco-bacilli, which when injected into guinea-pigs killed them, cocco-bacilli being found in the organs. Ponce de Leon suggests that some of the plague bacilli may remain for a time in a latent state, eventually becoming virulent when the effect of the serum has worn off. He recommends, therefore, that the injections of serum should not be entirely stopped as soon as the patient appears to be convalescent.

Hossack,[3] in a somewhat controversial paper, discusses the frequency of pneumonia in plague. His experience of plague in Calcutta led him to consider that plague pneumonia is not an aberrant and rare type of a disease which is local rather than generalised, with buboes marking the site of skin infection, but is a frequent and occasionally a predominant expression of a disease which is essentially a septicæmia. He concludes his paper with the following remarks, which indicate his views as regards the rat-flea theory of plague transmission :—

The sooner it is generally recognised that plague is not largely a local disease caused by the bites of the infected fleas, but a general septicæmic disease that is fostered by insanitation and is conveyed in many different ways and channels, the sooner we will reach sound and practical preventive measures. To accept the rat-flea theory in its entirety, it is necessary to premise that pneumonia and septicæmia are very rare in man. I maintain that there is a large body of reliable evidence against this presumption.

Browning Smith [4] has collected a great deal of information connected with the occurrence and recurrence of plague in villages in India. From the evidence gathered he comes to the following conclusions as regards recrudescence of plague in India :—

(*a*) Continuous signs of active infection remain in a few places in the Punjab throughout the period of abatement and definitely connect one epidemic with the following one.

(*b*) The hot weather interval is occasionally marked by sporadic signs of infection in rat and man.

(*c*) Such infections (*a* and *b*), however, only constitute a small part of the origin of the annual widespread visitation.

(*d*) Recrudescence of plague occurs in a very considerable number of cases, after an interval during which no signs of infection are apparent.

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[1] Gill, C. A. (April, 1909), " A Note on Epidemiology of Pneumonic Plague." *Indian Medical Gazette.*

[2] Ponce de Leon, J. (October 17, 1908), " Death after Apparent Recovery from Plague." Quoted in *Lancet.*

[3] Hossack, W. A. (August, 1909), " Plague Pneumonia: Its Bearing on Recent Controversies and Existing Preventive Measures; also a Personal Statement." *Indian Medical Gazette.*

[4] Browning Smith, S. (1909), " The Recrudescence of Plague." *Transactions Bombay Medical Congress.*

Plague— *continued*

(*e*) This interval between the epidemics of two successive plague seasons varies from quite a short one to one extending to many months, or even a year.

(*f*) Recrudescence may possibly occur after a still longer interval, including a complete plague season.

Although it must be admitted that the factors governing recrudescence are but imperfectly understood, it is possible to postulate from past experience certain general laws.

(*a*) Recrudescence tends to appear early the next season in those places which have suffered only incomplete epidemics in the previous one; that is to say, where the epizootic has been cut short by the hot weather before affecting the whole of the rat population.

(*b*) An incomplete epidemic is not a necessary precursor, for importation may be effected late in one plague season without any epidemic or even any signs of epizootic until, after an interval of apparent freedom, recrudescence occurs.

(*c*) Recrudescence following complete epidemics, where the rat population has been completely dealt with before the hot weather, more generally appears late in the following plague season, presumably because time for the recovery of the rat population is necessary.

(*d*) The severity of the epidemic accompanying the recrudescence will vary directly with the incompleteness of the previous one; the less the rat population has been affected during the first epidemic the more severe will be the following one.

(*e*) Generally, therefore, recrudescence occurs earlier, and is more severe after incomplete than after complete epidemics.

(*f*) The more insanitary a locality is the more liable it will be to recrudescence. The reappearance of infection usually occurs in the most insanitary part of a locality—in houses dark, damp, and ill-ventilated. Briefly, all conditions favouring rat and flea infestation are favourable for recrudescence.

Mention may be made of an interesting paper by Thornton,[1] in which he describes an outbreak of plague in Cape Colony, undoubtedly due to case-to-case infection.

An important monograph by Choksy,[2] consisting of an address on the general pathology and serum treatment of plague, is well worth perusal. The method of invasion and the development of the disease are first considered, and the various types, their prevalence, and fatality are discussed. The chief pathological lesions are also given. Reference to Choksy's remarks on treatment will be considered later on in this section.

Broquet [3] has a short and useful paper describing a method of preserving Yersin's bacillus in the buboes of plague, so that when these buboes are excised and sent any distance the material may be used for inoculation purposes into guinea-pigs or rats. The method consists of placing the glands in a solution of glycerine 1 part, and water 4 parts. When required for inoculation purposes the gland is triturated in normal salt solution, and injected into guinea-pigs or rats. By this method animals have been infected with plague, and Yersin's bacillus isolated six days after the glands had been excised. In a more recent paper,[4] however, he recommends the following procedure when suspected plague material requires to be sent for diagnostic purposes to a laboratory some distance away :—

A gland, or portion of a gland, is removed from the corpse as soon as possible after death, care being taken to prevent accidental contamination. It is then placed in a flask containing 125 to 175 cubic centimetres of the following solution—

Neutral glycerine (30° B.)	20 c.c.
Distilled water	80 c.c.
Carbonate of lime	2 grammes

The mouth of the flask is then flamed and sealed up with paraffin and sent to the laboratory as quickly as possible. On arrival at the laboratory a portion of the gland, ½ to 1 centimetre square, is removed with sterile instruments, wiped with sterilised paper to remove the glycerine, and pounded into an emulsion with 2½ cubic centimetres of normal saline solution. One cubic centimetre of the emulsion is then injected into a guinea-pig, and half a cubic centimetre into a rat. The advantages claimed for this method are that decomposition of the gland is prevented, and that a certain diagnosis can be given in three or four days, the material retaining its virulence as long as thirteen days.

This method commends itself for use in the Tropics, as plague material treated in this way can be sent by post to a laboratory some distance away.

The Local Government Board [5] issued a useful memorandum after the outbreak of plague

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[1] Thornton, E. N. (January, 1910), "An Extraordinary Series of Outbreaks of Plague in Cape Colony due to Case-to-Case Infection." *Indian Medical Gazette.*

[2] Choksy, N. H. (1908), *General Pathology and Serum Treatment of Plague.* Bombay.

[3] Broquet, Ch. (November 11, 1908), "Procédé de conservation des ganglions pesteux pour le diagnostic." *Bull. Soc. Path. Exot.*

[4] *Idem* (November 28, 1910), "Procédé de conservation des organes pesteux pour le diagnostic." *Ann. de l'Inst. Past.*

[5] Local Government Board (November 10, 1910), "Prevention of Epidemic Diseases." Quoted in *British Medical Journal,* November 19, 1910.

in Suffolk. It is headed "Prevention of Epidemic Diseases, Regulations as to Plague, Destruction of Rats." Plague—*continued*

Directions are given for obtaining and forwarding for bacteriological examination material from suspected plague cases. The directions are divided into four sub-headings as follows :—

From the Living Person.—(1) Clean with soap and water, and then with alcohol, the skin over the bubo. When dry, or after mopping with a clean cloth, pierce the bubo with the needle of a hypodermic syringe (previously cleaned with boiling water); empty the syringe into a small phial, previously cleaned with boiling water. Collect additional exuding fluid in capillary tubes. (2) When there is a discharging bubo, collect fluid therefrom in capillary tubes, as in the above case. When this discharge is not of a sufficiently fluid character for collection in this way, place some of it in a small glass-stoppered phial, previously well washed out with boiling water or with alcohol, care being taken that no alcohol remains in the phial. (3) If expectoration be obtainable, collect some in a phial in the manner prescribed in the previous sentence. (4) If the patient shows symptoms of lung disease, it should be considered whether fluid may not be obtained by aspiration under strict aseptic precautions from the lung over the affected part, and collected as above.

From the Dead Body.—(1) Cut out any inflamed lymph gland, together with some of the surrounding tissue, wrap the whole in fresh gutta-percha paper, and place it in a wide-mouthed glass-stoppered bottle, previously well washed out with alcohol, care being taken that no alcohol remains in the bottle The bottle should have the stopper well secured and sealed. (2) Obtain also a piece of the spleen, dealing with it in the same manner.

From Rats and other Rodents.—The suspected dead animal should be immersed in a solution of a strong disinfectant before being placed in the package. By this means fleas, if any, can be destroyed. The animal should then be packed in a tin box or a jar with a close-fitting cover, and this placed in a larger wooden box filled in with sawdust.

Directions for Forwarding Material.—(1) All suspected plague material should be very carefully packed so as to avoid risk of breakage and danger of infection during transmission. (2) The material may be sent by letter post, not parcel post, if the Post Office Regulations are complied with. The postage need not be prepaid. (3) The package should be addressed "The Medical Officer, Local Government Board, Whitehall, London." (4) A statement giving details as to the source of the material, and a preliminary account of the clinical character of the case, and other information respecting the patient, should always be sent under separate cover to the Medical Officer, Local Government Board, at the same time as the material is sent. (5) Where possible the Medical Officer, "Localise," London, should be advised by telegram that material has been despatched, specifying the route, and also, if possible, the time when the material may be expected to arrive.

Choksy [1] has a paper on the clinical features of septicæmic plague, and discusses the clinical significance of septicæmia in human plague. His conclusions are :—

(1) There exists no single clinical sign or symptom whereby the presence of a septicæmia can be recognised at the bedside.

(2) A strong presumption of septicæmia is raised by a thready, compressible, or imperceptible pulse, especially if accompanied with great nervous prostration, jaundice, and rapid wasting of the face.

(3) Although a patient with a septicæmia may recover, the probability of recovery is only 3 to 4 per cent.; no recovery with a grave septicæmia is possible; and, even with a moderate one, recovery would be greatly helped by the use of the anti-plague serum.

(4) Plague marasmus is an almost invariable concomitant in those cases that survive over a week. If acute, it is always fatal; if subacute, recovery may take place.

Amako [2] has tested the cutaneous and ophthalmo reactions in plague. In nine cases examined at the height of the disease, five gave a positive ophthalmo reaction, and four a positive cutaneous reaction. In ten convalescent cases, two gave a very marked ophthalmo and cutaneous reaction. In cases free from infection, some gave a slight conjunctival reaction, but the majority showed no reaction. This observer concludes that neither the cutaneous nor the ophthalmo reactions are of much use in the diagnosis of plague.

A good paper by Liston [3] deals with the question of plague prophylaxis in India. The measures considered refer chiefly to those relating to the prevention and suppression of plague in a country already infected.

He refers to the conditions which encourage the presence of rats, viz. abundant food, ample shelter, absence of enemies; and these are discussed seriatim. The centralisation or isolation of all the stocks of grain in a village, and the organisation of systems for the removal of refuse from towns and villages are strongly recommended. Defects in town and village planning, and defects in the enforcement of building regulations should be remedied, and the system of stabling of cattle and other animals in dwelling-houses abolished. The method of destroying rats is considered. A number of traps equivalent to at least 2 per cent. of the population must be used.

Great stress is laid on the disinfection of clothing and kit of travellers from infected places, and mention is made that this procedure is frequently neglected, and sums of money spent on other measures less efficacious. Liston calls attention to the fact that the prevention of the importation of infection can be carried out with the

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[1] Choksy, N. H. (1909), "On the Clinical Significance of Septicæmia in Human Plague." *Transactions Bombay Medical Congress.*

[2] Amako, T. (October 9, 1909), "Über die konjunktivale und kutane Reaction bei Pest im Vergleich mit Agglutination und Komplementierungsvermögen des kranken Serums." *Cent. f. Bakt.*, I. Orig., Vol. LI.

[3] Liston, G. W. (1909), "The Prophylaxis of Plague in India." *Transactions Bombay Medical Congress.*

Plague—*continued*

best hope of success at the close of the active plague period. It is, he says, "during this period that the disease can be most easily tackled; yet it is the period generally chosen for holidays, the period when efforts at stamping out the disease, as it has been called, are brought to a standstill. Fear has departed, and the stimulus for work has gone. No greater mistake could be made than to curtail operations and expenditure at this time. It is the period which offers the greatest hope of success." Inoculation he considers is the third and last line of defence.

The paper concludes by dividing anti-plague measures into two classes—(1) The essential and advantageous, including the removal of conditions which favour rat infestation, destruction of rats, and the prevention of the importation of infection from infected to healthy localities; (2) The non-essential and doubtfully efficacious. In this group are included isolation and treatment of the sick in hospitals, disinfection and evacuation.

Nesfield,[1] in a letter to the *Pioneer*, which is quoted in the *Journal of Tropical Medicine and Hygiene*, gives an explanation as to the diminishing virulence of plague in the early spring months in the central provinces of India. His suggestive explanation is quoted:—

The diminishing virulence of plague during the last spring months has proceeded hand in hand with the falling off of food supplies. In villages and country districts the virulence of plague has markedly decreased in the tracts affected by famine, which is only what is to be expected by working on the theory that the outbreak of plague in the winter months is due to the storing of a great part of the autumn harvest in the dwelling-houses, coupled with the scarcity of food for rats in the fields. The natural consequence resulting is a great exodus of rats from the fields into the villages. There are three conditions during this harvest to bring about the recrudescence of plague—(1) The manner of drying the grain. (2) The method of storing it. (3) The condition of the dwelling-houses, and the custom of sleeping indoors in the winter with every door closed. As to (1) the method of drying grain: During the day the grain is spread out in the sun on *charpoys*, or on prepared spaces on the ground. At night it is collected, placed in baskets or *ghurrahs*, and taken indoors for protection. This continues for two to six weeks or longer, till the grain is quite dry. It is then frequently stored for the use of the household in earthen vessels unprotected from the ravages of rats, though large unbaked mudden receptacles closed at the top, and with a hole at the bottom shut with a plug, are sometimes used. The daily dole is obtained by removing the plug, and permitting the grain to pour out like fluid from a barrel. (This is an excellent method.) During the drying, rats have free access to the grain and hence come in large numbers; later, when dry, and even if securely stored, they still pick up a living from scraps of food left over, etc. Natives' houses (except in certain districts, which also are plague free, *e.g.* Purneah) are built without windows or any vent for air or light, so much so that it is pitch dark inside when the door is closed.

Here, then, are the ideal conditions for the outbreak of a plague epidemic—people sleeping in a vitiated atmosphere, in closely sealed up houses infected with rats. The rats themselves, from overcrowding and close contiguity, become more liable to epidemic disease; and it is probable that the plague epidemic among rats is due to the disease which is present in some of them in a dormant and non-virulent form, acquiring vigour on account of the unhealthy state of the hosts. Famine has killed off many rats, and the scarcity of food in the villages has failed to attract the remnant. It is probably on this account that plague has been so mild this spring. It is very probable that, after a short time, rat-killing and disinfecting campaigns will be discontinued, as the resulting benefits are so temporary, and even inoculation will fall into disfavour. It may then be possible to divert some of the energies to teaching villagers the importance of not storing grain in their dwelling-houses, and the importance of making windows in the walls of their houses. I believe that these, and only these two things, will stamp plague out of India.

It is a significant fact that the houses in the Purneah district are made of bamboo, and each well ventilated, each with its own granary, and that, though plague is frequently imported, it never spreads, but always quickly dies out.

Reference may be made here to the measures adopted for quarantine and disposal of the dead in the recent plague epidemic at Harbin. Tuck and Gray (*loc. cit.*) describe these measures in papers recently published in the *Lancet*:—

Two items of interest which proved their utility during the Harbin outbreak, in such manner as to have an important bearing upon any future epidemic, may be alluded to. First, the use of railway wagons for quarantine work, and, secondly, the disposal of the dead bodies by burning. The ease with which a railway wagon, holding at the most not more than twenty persons, enables a segregation camp to be divided into small units, completely isolated from each other, also the simplicity of disinfection, the early detection of suspects, the satisfactory ventilation by small windows and sliding doors, and the heating by a central stove, suggest at once a most efficient form of quarantine which can be quickly established at any place in proximity to a railway. The second—viz., the burning of the dead—which though not unheard of in Chinese annals still conjures up in the native mind all that is repulsive and contrary to natural feelings, yet once decided upon by the Government was accepted by the people without complaint or hindrance. At a time when severe frost made burial almost impossible, burning, by its ease and simplicity, commended itself to all of us. A pit, 20 ft. square and 10 ft. deep, which had been blasted by dynamite, was capable of holding 500 bodies at a time. When bodies were in coffins the wood of the coffins was sufficient for complete burning, but bodies without coffins required at the rate of four pieces of wood, 2 ft. long by about 4 in. in diameter, for each body, and upon the whole mass, in the pit, kerosine oil was pumped from a fire-engine, at the rate of 10 gallons to every 100 bodies. This, when lighted, burned so rapidly and fiercely that little or nothing remained but ashes.

Blackmore,[2] in a paper read at the last Bombay Medical Congress, discusses the important question of the carriage of plague by sea, and points out that most of the countries in which

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[1] Nesfield, V. B. Quoted in *Journal Tropical Medicine and Hygiene*, September 15, 1908.

[2] Blackmore, G. J. (1909), "The Carriage of Plague by Sea." *Transactions Bombay Medical Congress.*

plague exists have become infected through their ports. He calls attention to the important fact of noting the temperature when making an inspection of passengers on boats, for many persons who have contracted plague have a marked rise of temperature even as long as two or three days before any other symptoms of plague have appeared. The paper contains an account of the method of disinfecting the clothing so as to rid it of fleas. Plague—*continued*

On the whole, the use of steam for most clothes, and of sulphur or formaldehyde for clothes which cannot be steamed, and for boots, would appear to be the best available method of ridding clothes of fleas. If clothes are dealt with, the boxes in which they are carried should also be treated. In Bombay these boxes are washed and scrubbed under a tap and are then swabbed with a disinfectant. It would probably be a quicker and more effectual method to insert the empty box over a steam jet for a moment or two, in the way employed to disinfect milk cans in England. If, however, the swabbing method is continued it would be better to employ kerosine oil emulsion than the disinfectants now in use. In the case of Bombay, where crew's clothing is practically always carried in boxes, I am inclined to think that the cleaning of boxes and swabbing them with kerosine oil emulsion might, without risk, be substituted for the disinfection of the clothes carried in the boxes.

The paper is concluded by a description of the various methods of destroying rats.

Reference may be made to a very good paper by King [1] entitled "Plague and the Destruction of Rats." The various methods of destroying these rodents are described, and a list of rat poisons is given. The paper concludes by mentioning a preparation consisting of sulphuric acid and *crude* gas tar, which King claims is of particular value in keeping houses rat-free, and preventing the return of these rodents for some considerable period. Referring to it, he says :—

Dr. Hubert Marshall, D.Ph., who was then in charge of a large plague hospital camp at Jollarpeth, Madras, where rats were intrusive and troublesome, kindly undertook carefully conducted experiments with the preparation. He effectually kept the whole camp free of rats by its use. It has since been used largely in the Madras Presidency, under my direction, as a routine plague measure after cleansing and disinfection of houses, with undoubted success. I found that, provided the mouths of *all* holes were treated with a sufficiency to ensure that should the rat attempt to exit, the feet must be smeared, rats could both be got rid of and prevented from returning for a period varying from a fortnight to six months. This is not only due to the irritating nature of the preparation to the skin, but also to the prolonged throwing off of gases, to which the rat objects. To escape from burrows so treated, rats will rapidly make new exits. Plastering holes here and there is, consequently, of little use; these must be diligently searched for, both in and outside dwellings, attached stores, stables, etc., etc. Care should be taken to see that the mixture of tar and commercial sulphuric acid is made only when about to be immediately used. Where particular goods are to be kept free from attacks of rats, it suffices to make a continuous circle of the fluid mixture on the floor around them. Following the same principle, during severe plague infection of rats, I have seen a large market made free of rats, and then *kept free* by this method. It is of particular value in keeping houses rat-free, when circumstances compel persons to live in dwellings within a badly-infected area. Further, by its aid a plague-infected area may be limited by protecting houses not yet invaded—a result worth aiming at.

The recent Committee [2] on Plague in India has published a report. The chief conclusions and recommendations are of sufficient importance to justify them being quoted here :—

(1) An active anti-plague policy on the part of the Government is necessary, and should be continued.

(2) The destruction of rats in Punjab villages by means of poison for the purpose of preventing plague epidemics is not attended with success, and should be abandoned on a large scale.

(3) Systematic trapping with traps in the ratio of two *per cent.* of population does not reduce the rat infestation of Punjab towns and villages sufficiently to prevent plague epidemics.

(4) To diminish adequately the rat infestation of Punjab towns and villages by means of systematic trapping present difficulties of such magnitude as to render it an impracticable policy on a large scale.

(5) The destruction of rats by means of poisoning and trapping on the present lines does not yield results commensurate with the expenditure incurred, and it should be discontinued.

(6) The greatest prospect of success in preventing the spread of plague by means of rat destruction consists in attacking the comparatively new localities where plague persists during the quiescent period.

(7) Anti-plague inoculation is essentially a personal prophylactic measure, and in recommending its adoption everything savouring of compulsion or pressure should be carefully avoided.

(8) During severe epidemics of plague, regimental medical officers might with advantage be temporarily employed as inoculating officers in the recruiting area of their regiments.

(9) For dealing with plague epidemics in villages, evacuation is a most important anti-plague measure, and means are suggested to facilitate its more widespread adoption.

(10) Measures directed towards improving village sanitation and domestic hygiene are of the utmost importance, and efforts should be made to give effect to such simple measures of this nature as public opinion may endorse.

(11) The erection of model houses at the headquarters of districts, the removal where possible of manure from close proximity to village sites, and an increased conservancy staff for villages, are desirable measures.

(12) The disinfection of infected houses during the course of an epidemic, or after its cessation, is not ordinarily necessary.

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[1] King, W. G. (December, 1910), "Plague and the Destruction of Rats." *Journal Royal Institute of Public Health.*

[2] *Punjab Plague Committee Report* (1910). Quoted in *Indian Medical Gazette,* December, 1910.

Plague—*continued*

(13) Disinfection as applied to the clothing and baggage of persons coming from infected areas is a valuable means of preventing the spread of plague into uninfected areas, and should be carried out wherever possible.

(14) The only measures of a compulsory nature which are permissible are those demanded by public opinion, and capable of being put into operation by the people themselves.

(15) The adoption of certain measures to facilitate quarantine, isolation, and refusal of access in the case of villages.

(16) The extension to the inhabitants of towns as well as villages of legal powers to prevent the access of persons coming from infected areas.

(17) The power possessed by commissioners of prohibiting fairs in infected localities should be more freely exercised.

(18) An efficient system of intelligence, whereby the presence of plague is rapidly reported, is of the utmost importance.

(19) Certain alterations are suggested with a view to accelerating the receipt of infection reports by civil surgeons.

(20) The present procedure in regard to the reporting of plague occurrences should be cancelled, and regulations practically identical with those already in force for dealing with cholera should be substituted.

(21) Substantial money rewards should be offered for information regarding plague occurrences during the hot weather.

(22) The organisation and training of a lay agency are most important measures, and honorary plague officers should be appointed in all districts subject to infection.

(23) The submission by commissioners, to the Inspector-General of Civil Hospitals, Punjab, of a quarterly return showing the grants-in-aid made to local bodies from provincial funds.

(24) Rat destruction operations on the limited scale recommended by the Committee should be a charge on provincial funds.

Buchanan [1] was practically the first to advocate the use of cats as plague preventers. Since his original article, published a few years ago, another [2] has appeared in which he is more convinced than ever of the useful rôle played by cats as plague preventers. He concludes his paper by saying :—

It is as clear as anything can be, that the question of plague or no plague in this country is a question of Nature's balance between cats and rats. We may assist the cat by using traps and poison, but we can never hope to compete with the cat, and a great point is the strong religious feeling in favour of keeping cats. The people in this district have seen for themselves that where there are cats it is the rare exception to find plague; and I feel that the weak point in this paper is my failure to convey an idea of the very strong opinion that cats are the best plague preventers, which is held by those who have seen for themselves the freedom from plague of those villages and mohullas where cats are numerous and of those houses in which cats were present. I fully admit that there will be a difficulty in the case of Jains and some Marwaris, and with some of the worshippers of Vishnu.

Of course it would take some time to get a sufficient number of cats, but in the meantime other measures should be pushed with vigour. What I should like to lay special stress on is the importance of recognising that the *ultimate* method of preventing plague will be by keeping cats. Cats breed twice a year in India, and have about three kittens each time. Many of the kittens now die from neglect, or are eaten by the males, and it is only when the value of the cat is recognised that sufficient protection will be given to the young cats.

In a paper read before the Bombay Medical Congress, Buchanan [3] brings forward and lays great stress upon the two measures, inoculation and the keeping of cats, discussing them from the point of view of (1) efficiency, (2) availability, (3) acceptability.

In a more recent article he [4] replies to the objections that have been made regarding the cat as a plague preventer, and quotes the views of Gimlette [5] and the late Professor Koch on the advantages of keeping cats in plague infested districts.

Nicol [6] has a short note referring to the use of cats as plague fighters in India, and mentions the work done by the Salvation Army in establishing two cat farms—stocked with British cats—in Bombay.

A short reference is given to a paper by Kitasato [7] on "Plague in Japan." In that country cats were being used, more especially when plague was not present. Kitasato regarded the use of cats rather as a prophylactic measure, and stated that one of the drawbacks in regard to the use of cats was the fact that they ceased to be good ratters when well fed.

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[1] Buchanan, A. (October, 1907), "Cats as Plague Preventers." *Indian Medical Gazette.*

[2] *Idem* (October 24, 1908), "Cats as Plague Preventers." *British Medical Journal.*

[3] *Idem* (1909), "Cats as Plague Preventers." *Transactions Bombay Medical Congress.*

[4] *Idem* (August 6, 1910), "Cats as Plague Preventers." *British Medical Journal.*

[5] Gimlette, J. D. (April, 1909), "Plague in Further India." *Journal of Hygiene.*

[6] Nicol, A. M. (October, 1908), "The Cat as a Plague Fighter in India." *The Journal of the Incorporated Society for the Destruction of Vermin.*

[7] Kitasato, J. (August 29, 1909), "Plague in Japan." *Sixteenth International Medical Congress, Budapest.* Quoted in *Lancet,* September 18, 1909.

Billet [1] describes a method of killing rats in sewers by what he terms "chlorination." A solution one-third chloride of lime is poured into the sewer, followed half-an-hour afterwards by one-third solution of hydrochloric acid; chlorine gas is thus liberated, which, owing to its weight permeates the rat runs, and either drives them from their retreat or kills them. As a rat poison he uses pulverised squill (3 ounces) with cooked meat (2·2 lb.) and essence of fennel (30 drops); the rats are attracted by the fennel. Small balls of this preparation, almost the size of a hazel nut, are scattered about the premises infected by rats. Plague—*continued*

A good deal of work has been carried out by members of the Plague Commission and others, to find out an efficient pulicidal substance which at the same time has a bactericidal property for the plague bacillus.

Up to the present time the best results have been obtained with a mixture of cyllin and petrol in equal parts, as recommended by Sommerville,[2] and confirmed later in experiments carried out by members of the Indian Plague Commission.

Mention may be made here of a recent paper by Zupitza,[3] who advocates the use of iodoform as a means of guarding against plague infection. This paper is considered under the section headed "Insects."

Cunningham [4] has carried out some interesting experiments in connection with the destruction of fleas by exposure to the sun. A note of these experiments is given in this Review under the section headed "Insects."

Reference may also be made to another paper by Manaud,[5] dealing with flea destruction in Siam. As this paper is also discussed under the section headed "Insects," no further mention of it need be made here.

Standage [6] records some striking results as regards the value of anti-plague inoculation in Bangalore. He considered that the method of "house-to-house" inoculation contributed largely to the success of his campaign.

Dunn,[7] with the view of estimating the period during which inoculation against plague causes immunity from the disease, investigated the results of inoculations carried out in villages in which over fifty inoculations had been done. He is of opinion that the immunising action of the prophylactic remains for a much longer period than is generally admitted, that this action is still strongly in force two years after the inoculation is carried out, and that if a population of a village gets inoculated once every second year no other prevention is necessary.

A short, practical and useful paper by Stanley [8] gives a description of the measures of plague prevention adopted in Shanghai. The following summary of them contains many practical points :—

(1) Plague survey by collection of rats, found dead throughout the settlement, for examination in the laboratory in order to locate plague among rats.

(2) Rat destruction in infected areas, beginning at the periphery and working towards the centre.

(3) Plague-proofing of houses—

(*a*) Temporary, by service of notice on occupiers asking for co-operation in cleansing, pulicidal disinfection, demurisation and rat-proofing by minor repairs, etc.

(*b*) Permanent, by service of notice on owners, requiring solid basements, removal of stair linings, hollow ceilings and hollow partitions, so as to deprive rats of accommodation.

(4) Preventive inoculation with plague vaccine, beginning with the sanitary staff.

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[1] Billet, A. (August, 1908), "La Peste dans le département de Constantine en 1907." *Ann. de l'Inst. Past.*

[2] Sommerville, D. (October, 1908), "The Transmission of Plague by Fleas." *Journal Royal Army Medical Corps.*

[3] Zupitza, M. (March, 1911), "Ein Mittel zur Abwehr von Pestflöhen." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XV., No. 6.

[4] Cunningham, J., "The Destruction of Fleas by Exposure to the Sun." *Scientific Memoirs of the Medical and Sanitary Departments of the Government of India*, No. 40.

[5] Manaud, A. (April 12, 1911), "Prophylaxie de la peste par la désinfection 'pulicide.'" *Bull. Soc. Path. Exot.*

[6] Standage, R. F. (1909), "Anti-plague Inoculation at Bangalore." *Transactions Bombay Medical Congress.*

[7] Dunn, C. L. (November, 1908), "The Duration of the Immunity conferred by Plague Inoculation." *Indian Medical Gazette.*

[8] Stanley, A. (September, 1910), "Plague Prevention in Shanghai." *Public Health.*

Plague—*continued*

INDIVIDUAL MEASURES

No rats, no plague.

A house that is rat-proof is plague-proof.

(1) Keep cats.

(2) Rid your house from rats also by trapping and poisoning.

(3) Make your house as rat-proof as possible.

(4) Provide no food for rats. Keep all food in places inaccessible to rats. Grain and such-like food for ponies, fowls, etc., should be kept in covered galvanised-iron receptacles. See that your servants keep their rice-bags where rats cannot get. Keep house refuse in properly covered galvanised-iron receptacles, and see that they are covered, especially at night. Keep the kitchen and its surroundings very clean: let no refuse lie about.

(5) See that the gratings into the space below the ground floor keep out rats, and that the brick-work of the basement is impervious to rats.

(6) See that all openings into covered drains are kept in good repair to prevent egress of sewer rats. Carefully inspect all corners of the house from top to bottom once weekly, moving furniture where necessary. Do the same in the stable, fowl-house, and other outhouses. Arrange for the plastering up of rat-holes or any place that may afford ingress to rats and mice.

(7) All rats trapped or poisoned should be burnt. Other rats found dead in or about the house should not be touched with the hands, but should be picked up with tongs, put into Jeyes' fluid and water (1 in 20), and sent to the health officer for examination of plague.

(8) Get vaccinated against plague in September in each year that plague threatens.

(9) If you have any difficulty in carrying out the above measures, communicate with the health officer in writing.

Choksy,[1] in a paper read before the Bombay Medical Congress, claims that the serum treatment of plague is the main line of defence in fighting this disease. The large experience that this observer has had in the serum treatment of this disease gives considerable weight to his convictions. Yersin's serum injected subcutaneously has been employed by him in 580 cases, and according to his figures there is a difference of 10·5 per cent. in favour of the serum treated cases, and a gain of 57 per cent. in the recovery rate. Choksy advocates early treatment, and considers that a combination of the intravenous with the subcutaneous method of treatment holds out the best prospects of success.

My conviction is that, however successful the combination of the two methods may eventually be proved to be, its adoption in hospital practice would not be feasible on an extended scale during an epidemic, on account of the time involved in carrying out the intravenous method with due aseptic and other necessary precautions and the extra skilled assistance that would be necessary.

In private practice it would be impracticable for the same reasons, in addition to the reluctance of patients to submit even to subcutaneous injection. The subcutaneous method must therefore hold the field as it hitherto has in the case of diphtheria. The method is easy of application, special skill is not required, and any intelligent practitioner can carry it out after studying the directions laid down. The best procedure is to inject 100 c.c., and to repeat the dose after 12 hours. Thereafter an interval of 24 hours is necessary, when another injection of 100 or 50 c.c. may be given, regard being had to the general condition of the patient, his temperature and pulse, the size and tenderness of the bubo, etc. In all ordinary non-septicæmic cases, if treated within 48 hours, 250 to 300 c.c. thus administered will suffice. If the treatment is begun late, or if septicæmia is present, or the temperature persists and no amelioration in the patient's condition is noticeable after the third injection, further injections will be necessary, and should be repeated every 24 hours, the dose being gradually reduced as improvement progresses. In such cases, abrupt stoppage of the injections is not desirable lest relapse should occur. No hard and fast rules for repeating the injections after the third injection can be laid down; every case must be judged on its own merits; but it is always safe to err on the right side, and to use a little more serum than less.

A short account of the after-effects of the serum treatment, "the serum disease," concludes this excellent paper. Choksy has noted that habitual meat eaters suffer more from the after-effects than vegetarians. The after-effects consist of rashes (circinate, scarlatiniform erythema), urticaria, local œdema, joint and muscle pains, and the only preventive treatment as recommended by Netter consists in the administration of 15 to 20 grains of calcium chloride or lactate twice or thrice daily as long as the serum is being administered, and for a week at least after the last injection.

Castel and Lafont[2] have a short paper describing the good results obtained by the intravenous injections of large doses of anti-plague serum supplied by the Pasteur Institute, Paris. Out of nine very severe cases treated by this serum seven recovered and two died. The number of injections and the amount of serum injected varied in different cases. One of the cases that recovered had as many as ten injections in eight days. The amount

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[1] Choksy, N. H. (1909), "The Serum Therapy of Plague in India." *Transactions Bombay Medical Congress.*

[2] Castel and Lafont (April 14, 1909), "Cas de peste traités par le sérum antipesteux en injections intraveineuses massives." *Bull. Soc. Path. Exot.*

Plague—*continued*

of serum injected was 1,140 c.c. The injections were employed in the early stages of the disease, at periods varying from twelve hours after the onset to the third day of the illness.

Sinclair [1] has reported the use of dried Yersin-Roux serum in three cases of plague; in one case it failed to effect a cure, in the second case one injection gave good results, and in the third two injections were necessary. Sinclair advocates the use of the dried serum in preference to the liquid form.

Conseil [2] in a short article dealing with an account of plague in Tunis for the year 1910, gives further evidence in support of the use of plague serum in the early stages of the disease.

For an excellent description of the symptomatic treatment of plague one could not do better than refer to a paper by Choksy.[3] It is full of practical points and is well worth a careful study, as it represents the line of treatment of an observer whose vast experience of plague treatment cannot be questioned.

Thornton [4] has a paper on the use of adrenalin chloride in the treatment of plague. Adrenalin, 1 to 1000, 30 min., with tinct. strophanthi 10 min., was given four-hourly by the mouth for the first three days, and three times a day for the next fourteen days. In bad cases, the drug was given hypodermically or intravenously in somewhat smaller doses. The death-rate by this treatment was only thirteen out of fifty cases, of which eight were practically moribund before admission.

Mention may be made of a note by Paton,[5] who has had success with carbolic acid in the treatment of bubonic plague :—

One grain of carbolic acid in pill or mixture is given every hour, and two to fifteen minims of the same drug is injected into the bubo, the amount varying according to the size of the bubo. The urine has to be carefully watched during this line of treatment.

Fornario [6] succeeded in conferring immunity by causing animals to swallow small doses of virulent plague bacilli at intervals of ten to fourteen days :—

Four out of nine rats, six out of seven rabbits, and three out of fourteen guinea-pigs tested by subcutaneous inoculation were found immune, but a rather large proportion of the animals died during the course of the treatment.

By giving a preliminary dose of culture heated for an hour to 53° C., followed by a dose of a virulent culture, thirteen out of twenty-eight proved immune, and two died during the treatment.

By the rectum, Fornario succeeded in immunising some guinea-pigs by feeding with bacilli heated for an hour and a half at 53° C.

The result of these feeding experiments caused a congestive condition of the intestinal tract in insufficiently vaccinated animals, and their dejections contained virulent bacilli, which Fornario considers negatives their employment in man or in animals sensitive to plague.

Further researches have been carried out by Klein [7] in connection with the possible therapeutic use of organ extracts of animals recovered from plague :—

After a large number of fruitless experiments Klein found that the filtrate of a watery emulsion of the tissues in doses of 100 milligrammes injected into rodents twenty-four hours after infection of these animals with virulent *B. pestis* had a marked therapeutic effect, and that this effect was more pronounced in the case of the rat than in that of the guinea-pig.

Klein holds that there is here a basis for securing a satisfactory therapeutic agent from cases of naturally acquired plague.

Pneumonia. Although this can hardly be considered a tropical disease, the fact that it frequently occurs in severe epidemic form in tropical countries justifies some reference being made to it.

Pope [8] refers to a specific skin eruption seen by him in a case of pneumonia. The eruption

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[1] Sinclair, A. N. (February 4, 1911), "Serum Treatment of Plague." *Journal American Medical Association.* Quoted in *The Prescriber*, April, 1911.

[2] Conseil, E. (1911), "La peste en Tunisie pendant l'année 1910." *Arch. de l'Inst. Past.*, Tunis, II.

[3] Choksy, N. H. (1909), "The Symptomatic Treatment of Plague." *Transactions Bombay Medical Congress.*

[4] Thornton, E. N. (April 9, 1910), "Notes on the Use of Adrenalin Chloride in the Treatment of Plague." *Lancet.*

[5] Paton, B. L. (August 29, 1908), "The Treatment of Bubonic Plague." *British Medical Journal.*

[6] Fornario, G. (April, 1908), "Sur la vaccination contre la peste par le tube digestif." *Ann. de l'Inst. Past.*

[7] Klein (1906–1907), "Report on Further Research in Connection with Plague." *Thirty-sixth Annual Report of the Local Government Board.* Quoted in *Journal Royal Institute of Public Health*, January, 1909.

[8] Pope, F. M. (November 21, 1908), "A Specific Skin Eruption in Pneumonia." *British Medical Journal.*

Pneumonia —*continued*

took the form of papules, which later became pustules, from which the pneumococcus was isolated. Pope mentions that the eruption simulated that of small-pox.

A number of papers have been published dealing with the treatment of pneumonia by means of vaccines.

Butler Harris [1] has an interesting paper on the therapeutic value of the pneumococcus vaccine in the treatment of pneumonia and some of its complications. Various clinical cases are described and the method of preparing autogenous vaccine. The dosage of vaccine employed varied in amount according to the clinical conditions presented by the patient. Harris advocates the use of a potent and reliable stock vaccine in the treatment of pneumonia, and concludes his paper by stating :—

(1) That successful inoculation for pneumonia is possible.

(2) That inoculation does no harm.

(3) That a vaccine from one or a number of virulent strains should be used.

(4) That it should be introduced as early as possible.

(5) That the estimation of the opsonic index is not necessary.

(6) That the observation of the temperature and physical signs is, in pneumonia, a sufficient guide in gauging the repetition of the dose.

Infections of the lung by the pneumococcus which fail to resolve after an acute pneumonia, as well as pneumococcic infections of other areas, ought certainly to be treated with a pneumococcic vaccine; and these cases appear to afford a reasonable prospect of success.

Wilson and Morgan [2] give the results of vaccine treatment in twenty-four cases of pneumonia. In addition to the two usual methods of obtaining pneumococci for the preparation of an autogenous vaccine, viz., from the sputum and from a blood culture, these observers advocate a third, viz., aspiration of the pleural cavity or superficial part of the lung, and state that this is the most rapid method of obtaining the organisms for an autogenous vaccine. As regards dosage they are guided by the clinical condition of the patient, and recommend 20 to 30 million for an initial dose. No bad effects appear to have followed an inoculation of 20 to 50 million for an adult. In cases where the ordinary stock vaccine gave no benefit an autogenous vaccine produced striking results. Large and frequent doses between the fifth and the seventh day when the crisis might be expected were contra-indicated, and these observers recommend that if vaccine treatment is employed it should be commenced as early as possible in the disease.

Landmann [3] claims to have found a very powerful anti-bacterial serum for the pneumococcus. He used horses, oxen, and sheep to gain his anti-bacterial serum, and employs these serums mixed. He obtained successful results in animal experiments.

Lees [4] has a very important and instructive paper on the treatment of pneumonia. He lays stress on the importance of the earliest possible discovery of the local lesion, and having located it to commence local treatment by means of ice-bags, so as to include between them the inflamed area of lung. This line of treatment is based on bacteriological experiments which have shown the inhibitory and destructive effect that a cold temperature has on the pneumococcus. The employment of ice-bags in the treatment of pneumonia calls for two precautions :—

In the first place, the size of the right auricle must be carefully ascertained by light percussion in the fourth right intercostal space. One finger-breadth of dullness is present in this situation in every normal heart; this is an elementary fact which has not yet found its way into the text-books, yet which can be verified by any one. In an early stage of a pneumonia an increased extent of this dullness soon becomes perceptible. If it amounts to more than a finger-breadth and a half, and if some dullness can be detected also in the third right space close to the sternum, it is generally wise to relieve the right heart by the employment of leeches (three or four for an adult, one or two for a child) before the ice-bags are applied. The neglect of this precaution may imperil the success of the treatment.

The second precaution necessary is to keep the legs and feet of the patient thoroughly warm by the employment of hot-water bottles and warm woollen stockings. A third precaution is useful, especially in the case of children; it is a frequent use of the clinical thermometer by a careful nurse.

If these precautions are adopted the treatment by ice-bags may be practised without fear. In the earliest stage it will sometimes abort the disease. When the pneumonia has advanced so far that this is no longer possible it will yet limit the spread of the inflammation, diminish the local pulmonary engorgement, and repress the

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[1] Butler Harris, A. (June 26, 1909), "The Therapeutic Value of the Pneumococcus Vaccine in the Treatment of Pneumonia." *British Medical Journal.*

[2] Wilson, W. H., and Morgan, W. (October 9, 1909), "The Treatment of Pneumonia by Inoculation." *Ibid.*

[3] Landmann, G. (February 27, 1909), "Anti-pneumococcic Serum." Epitome, *British Medical Journal.*

[4] Lees, D. B. (February 25, 1911), "The Treatment of Pneumonia." *Lancet.*

Pneumonia —*continued*

active increase of the pneumococci. Careful examination of a pneumonic pulmonary area, before and after the use of ice-bags, shows that the dullness is less absolute, and often also less extensive, and that the air entry is considerably greater.

In addition to this local treatment, the writer advocates the continuous inhalation of some volatile antiseptic, and as a third line of attack against the pneumococcus, vaccine treatment is considered, the patient being injected with a stock vaccine, to be followed as soon as possible by an autogenous one. For the dilatation of the right heart, leeches are strongly recommended in the slight cases, to be followed by venesection in the more severe ones, and Lees calls attention to an important fact that feebleness of the pulse in the later days of a pneumonia is not a contra-indication against blood-letting, but is a strong indication of its necessity. After blood-letting the pulse becomes stronger.

As regards cardiac stimulants, Lees considers that the most powerful cardiac stimulant is bleeding, and states that neither oxygen nor strychnine, nor both combined, are of any great service in pneumonia unless the intra-auricular tension is lowered by judicious blood-letting. The inhalation of oxygen bubbled through alcohol, as recommended by Willcox and Collingwood, is strongly recommended in cases of cardiac failure. As regards diet the addition of malted milk powder to milk greatly increases its nutritive value, and at the same time diminishes the amount of fluid in the diet. Half an ounce of malted milk powder dissolved in two ounces of milk may be given every hour while the patient is awake; for a child the amount may be two teaspoonfuls in one ounce of milk. After the right heart has been relieved by leeches, copious draughts of water are recommended to relieve thirst and aid the renal excretion. Half a pint of water may be given every three hours in the day following the use of leeches or venesection.

Lees considers that one is apt to overlook the great importance of securing sleep during the first two or three nights of a pneumonia, and recommends that an effective hypnotic may be given at this time. In the early stages morphine is safe; in the later, morphine is not safe, unless the right heart has been relieved.

McKechnie [1] has an interesting and instructive paper on pneumonia, in which he makes some suggestive observations on the mechanical conditions which may occur in the chest in adults suffering from an infection with Frænkel's pneumococcus. McKechnie's views on the treatment of the disease will not be accepted by all physicians. His suggestion that the alimentary canal should be kept empty, and that only water should be given, is one which will hardly assist elderly or weakly patients to combat the disease. Although certain cases might benefit by this line of treatment, no general rule should be made as to carrying it out. McKechnie considers that the chief danger in pneumonia is the formation of a thrombus which blocks the pulmonary artery, for which he suggests operative measures by trephining the sternum and exposing the pulmonary artery. He strongly advocates the use of morphine on the first and second day of the disease, as it induces sleep, prevents restlessness, and has a direct action whereby it tends to minimise those impediments to the discharge of carbon dioxide from the lungs. When the disease is well established it must be used with great caution, and the hypodermic injections are better replaced by Dover's powder. McKechnie's paper, apart from several questionable points in it, contains useful information and is well worth perusal.

Mention may be made of a paper by Crowly,[2] entitled "An Efficient Treatment for Pneumonia," in which the method recommended by Ewart,[3] was carried out in nine cases with success. After an initial dose of calomel the patient was given a mixture containing 4 grains of potassium iodide, 10 grains of citrate of potash, and a half drachm dose of ammonium citrate.

Weber [4] recommends the use of injections of camphor in oil made aseptically, the needle being thrust well down into the cellular tissue. This line of treatment was successful in a case of pneumococcal septicæmia. Truche and Gosset [5] have a short paper dealing with the polymorphology of the pneumococcus, and discuss chiefly the three types—(1) coccal, (2) elongated variety, which has occasionally been mistaken for the diphtheria bacillus, and (3) a bacillary form resulting when the surrounding medium is unfavourable to the growth of the pneumococcus.

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[1] McKechnie, W. E. (September 24, 1910), "Pneumonia." *Lancet.*

[2] Crowly, D. (January 16, 1909), "An Efficient Treatment for Pneumonia." *Ibid.*

[3] Ewart, W. (January 21, 1905), "The Principles of Treatment of Pneumonia." *Ibid.*

[4] Weber, L. (March 11, 1911), "Camphor in Large Doses in Pneumonia." Epitome, *British Medical Journal.*

[5] Truche, C., and Gosset, M. (January 28, 1911), "Sur la morphologie du pneumocoque." *C. R. Soc. Biol.*

Pneumonia —*continued*

Mention may be made of a paper by Strouse and Clough [1] entitled "Blood Cultures in Pneumonia." They experimented with various liquid media and found that the pneumococcus grew about equally well in all of them. They obtained the pneumococcus by blood culture in fourteen out of twenty-five cases.

Additional Note

Sill [2] has a paper dealing with the treatment of pneumonia in infants by means of a polyvalent pneumonia serum, and gives detailed histories of twelve cases. He states that—

> the best hope of a specific remedy for pneumonia is in the use of a polyvalent serum. It should be made in a concentrated form. Pneumonia is generally a mixed infection with the pneumococcus as the prevailing germ. The polyvalent composite serum is an advance in the right direction, and in a number of cases seemed to limit the disease. The serum should come from horses immunised to the pneumococcus and also to the other germs commonly found present. The child should be injected early in the disease with a good-sized dose of the serum.

Preservatives. There are few questions concerning Public Health which have been more fully discussed of late years than those dealing with preservatives in food. Medical, chemical, sanitary experts and others have given evidence for and against the use of preservatives in foods, and at the present time the question is still somewhat in an unsettled state. A good deal of interesting work in connection with this subject has been accomplished, as reference to some of the papers mentioned below will show.

The penetrative power of preservatives was tested by Richards,[3] who, in the report of the medical department of the Local Government Board, showed that boric acid, when in contact with hams for a period of three or four weeks or more, actually penetrated their substance. Quantities varying from two to fifteen grains per pound were found even in the most remote parts of the muscular substance of the hams. The muscular tissue appeared to be more liable to extensive penetration by boric acid than did the fatty tissues.

Considerable work has been done by the United States Bureau of Chemistry under the guidance of Wiley [4] and others in determining the effects of cold storage on the healthfulness of foods. Experiments were carried out on chickens and eggs, and

> the preliminary results showed that the fresh and cold storage chickens are easily distinguishable, the differences being progressive and dependent on the length of the storage period. A histological examination of the muscle of both fresh and stored chickens showed a progressive change in the structure of the fibres, which is deep-seated, and after long periods renders the tissue almost unrecognisable. A bacteriological investigation revealed the presence of an appreciable number of organisms in the edible portions of cold-stored chickens, but no organisms were observed in the same portions of fresh fowls. There is no perceptible change produced in a chicken by freezing it for a short time, possibly for six weeks or even longer. After three months the difference is very noticeable, the eyes and skin being shrivelled and the bird possessing a dilapidated appearance, the deterioration increasing with the length of the storage. The changed condition of the chicken is appreciable even after cooking, and there is no indication that cold storage improves the quality of the bird as regards odour or flavour. Hence the conclusion is drawn that in the case of chickens cold storage for a period of six months or longer is distinctly detrimental so far as palatability is concerned, apart from the question of the wholesomeness or otherwise of such food. In storing eggs the temperature must be kept above the freezing point of an egg, and during the process eggs undergo various chemical and histological changes. Certain constituents have a tendency to become crystalline, developing small rosette crystals in the yolks in the course of a few months. It is probable that the existence of such crystals may be regarded as a means of distinguishing eggs that have been kept in cold storage from fresh eggs. As the work progresses some of the inferences drawn from this preliminary work may have to be modified, but one fact has been established beyond doubt—that foods kept in cold storage tend to undergo certain changes which render them less palatable.

Wiley [5] has carried out a series of interesting tests to show the effect of formaldehyde on digestion and health. As in previous investigations with boric, salicylic, sulphurous and benzoic acids and their salts, twelve healthy men voluntarily took a prescribed diet for a given time, observations on their pulse, temperature, body weight and excretions being recorded. After a preliminary period of ten days a daily dose of formaldehyde, varying from 100 to 200 milligrammes, was given; the total amount of this preservative administered during these

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[1] Strouse, S., and Clough, P. W. (August, 1910), "Blood Cultures in Pneumonia." *Bulletin of the Johns Hopkins Hospital.*

[2] Sill, E. M. (April 22, 1911), "Serum Treatment of Pneumonia in Infants." *Medical Record.* Quoted in Epitome, *British Medical Journal,* June 10, 1911.

[3] Richards, P. A. E. (July 11, 1908), "Preservatives in Meat Foods." Quoted in *Lancet.*

[4] Wiley, H. W. (1908), "The Effects of Cold Storage on Chickens and Eggs." *Bulletin* No. 115. *Bureau of Chemistry, United States Department of Agriculture.*

[5] *Idem* (February 6, 1909), "The Effect of Formaldehyde upon Digestion and Health." Quoted in *Lancet.*

tests being 2·5 grammes per man. It was given in the form of an aqueous solution mixed with milk. The symptoms produced were headache, nausea, vomiting, and intestinal cramps. Preservatives—*continued*

From a general study of all the data, Dr. Wiley draws the conclusion that the admixture of formaldehyde with food is injurious to health, even in the case of healthy young men, and therefore that in the case of infants and children the deleterious effects would be more pronounced. The metabolic functions were disturbed in a notable way, both by the retardation of the nitrogen and sulphur metabolism and by the acceleration of the phosphorus metabolism as shown by an examination of the excreta. There seemed to be a tendency to an increased absorption from the alimentary canal, indicating that formaldehyde has a stimulating effect upon the intestinal digestive juices. The loss in body weight was found to be very slight, amounting to 0·2 kilogramme per day in the subjects taking freshly preserved milk, and 0·5 kilogramme in those taking milk that had been preserved two days. An increase was noted in the volume of the urine and in the moisture of the fæces. Dr. Wiley argues that a retarded katabolism cannot be beneficial to health, as old tissues cannot be expected to function as perfectly as newer tissues. There was a general tendency to produce a slight decrease in the temperature of the body which was probably associated with the retardation in the breaking down of tissues. There was also a slight tendency to produce albumin in the urine. Dr. Wiley finally concludes that the addition of formaldehyde to foods tends to derange metabolism, to disturb the normal functions, and to produce irritation and undue stimulation of the secretory activities. Its use, therefore, is never justifiable. Milk is the most prone of all ordinary foods to undergo deterioration, and requires the most careful treatment, so that the temptation to use such an efficient preservative as formaldehyde is great, especially in the summer. All the conditions which relate to its use deserve the greatest care and consideration, because it is effective in minute quantities, which are difficult to detect. Apart from the harmfulness or otherwise of formaldehyde, its use as a preservative of milk or cream is especially inadvisable, because in dilute solution it prevents the growth of acid-forming bacteria while it does not retard the growth of many harmful micro-organisms. In other words, the milk is prevented from becoming sour and thus indicating its age, and the danger signal is removed while the other organisms which are capable of producing disease continue to multiply.

Richardson and Sherubel [1] carried out some experiments to determine whether or not there was any progressive change in the chemical constituents of meat when stored, such as would lead to an increase of the soluble substances produced by autodigestion of the insoluble proteins, and also an increase in the ammoniacal nitrogen. Most of the experiments were carried out with that portion of the carcase known to butchers as the "knuckle," lean meat being chosen for preference. The fresh samples were stored at a temperature of 2° to 4° C., and varied in age from 0 to 7 days. The frozen samples were stored at a temperature of 9° to 12° C., and varied in age from 33 to 554 days. Differences in the flavour of the fresh and the frozen samples could not be detected, and in fact there was very little difference in the results obtained between the fresh and the frozen samples when the percentage of moisture, fat, ash, total nitrogen, total solids, etc., was estimated. It therefore would appear that cold storage at temperatures below 9° C. is a perfectly satisfactory method for preserving meat for 554 days, and probably much longer.

An article in the *Lancet* [2] comments on the small amount of strongly salted or smoked foods consumed by the public nowadays as compared with some years ago. The old-fashioned antiseptics, salt and smoke, not only preserved food, but acted also as condiments :—

Assuming that the mild-cured article, and as a particular example we may choose butter, because it is an indispensable article of the dietary, is free from objectionable antiseptics, it is still left more helpless against the attacks of micro-organisms than were the old-fashioned cured foodstuffs. Experiments have, in fact, shown that the addition of salt to butter is a factor of great importance from the point of view of germs. In unsalted butter the growth of micro-organisms is more vigorous and continues for a longer time than is the case with salted butter. Mycelial fungi, if present, disappear entirely after a while in salted butter, while in fresh and unsalted butter they multiply rapidly. The quality of butter appears to be improved by a small percentage of salt (say 2·5); it encourages the development of a flavour which makes butter an attractive article of food, and it acts as a safeguard. Altogether there would appear to be certain valid reasons for thinking that the public preference for the mild-cured article may be an error of judgment, and there certainly is much to be said in favour of the old policy of preserving foods by salt and by smoke.

At the Second International Food Congress, food in all its branches was defined, as also were alimentary substances, such as drugs and ice. Douglas [3] gives a brief summary of the most important things that were brought up for consideration :—

One of the most important discussions took place concerning dairy produce, and the use of preservatives in butter and other produce. It was decreed that "boron preservatives" were not only allowable, but were absolutely necessary in the manufacture of butter. It was held that the addition of such a preservative should not require to be declared in future, any more than the presence of salt would require to be declared, and thus the addition of preservative would be reduced to the regular operations recognised as being essential to the good conduct of the butter industry. It was also decreed that the standard water contents of butter should be raised from 16 to 18 per cent.

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[1] Richardson, W. D., and Sherubel, E. (January, 1909), "The Deterioration and Commercial Preservation of Flesh Foods. Experiments on Frozen Beef." *Journal American Chemical Society*, xxx. Quoted in *Journal Royal Institute of Public Health.*

[2] (July 17, 1909), "Salt and Smoke." *Lancet.*

[3] Douglas, L. M. (February, 1910), "The Second International Food Congress." *Journal Royal Institute of Public Health.*

Preservatives— *continued*

Emmett and Grindley [1] studied the effect of cold storage on beef and poultry. The conclusions arrived at by these observers were as follows :—

(2) In the case of the refrigerated beef which was stored for twenty-two days, the averaged data indicate :—

(*a*) That there was no loss of water.

(*b*) That the percentage of the water-soluble solids, the soluble, insoluble, and total protein, the non-coagulable protein, the nitrogenous and total organic extractives, the forms of ash, the total nitrogen and the total phosphorus, all remained practically unchanged.

(*c*) That the only consistent real changes were a distinct increase in the total soluble and the soluble inorganic phosphorus, being 8·0 and 17·9 per cent. respectively, and a decrease of 8·3 per cent. in the non-nitrogenous organic extractives.

(*d*) That the nutritive value of the meat was unaltered.

(3) In the case of the refrigerated beef, which was stored for forty-three days, the averaged data show :—

(*a*) That there was a loss of water amounting to 1·3 per cent.

(*b*) That this loss of water, causing a proportional increase in all the other constituents, produced differences in some instances which were sufficient to overbalance the amounts in the fresh samples.

(*c*) That the ratio of the non-protein to the protein nitrogen in the meats was lower.

(*d*) That when allowance was made for the loss of moisture, the additional changes which occurred in cold storage consisted in a definite increase in the soluble dry substance, the nitrogenous, non-nitrogenous, and total organic extractives, the total soluble nitrogen, the soluble inorganic phosphorus, and a slight increase in the soluble, coagulable, and total soluble protein nitrogen, and also in the insoluble and total nitrogen.

(*e*) That the chemical changes in the 43-day refrigerated meats were greater in number than in the 22-day samples, yet as far as nutritive value was concerned, the former showed an increase in the organic extractives and soluble protein, and but an insignificant decrease in the total protein.

(4) That analyses of the frozen drawn and undrawn chicken showed, when allowances were made for the variations in fat and moisture, that there was almost no difference between the two, one being equally as good as the other.

(5) The analyses of the fresh and the frozen drawn and undrawn fowl, obtained from the same lot, showed that the latter changed but slightly and to such an extent that there was practically no difference in the nutritive value of the three, after correcting for the differences in the fat and moisture content.

Continuing their researches, Emmett and Grindley [2] carried out several cooking experiments upon fresh and refrigerated uncooked samples to ascertain what influence, if any, the cooked meats might show over the uncooked as to the changes brought about during cold storage. Their conclusions may be stated generally as follows :—

That many of the differences between cooked meats from the samples which were held in cold storage for 6 and 43 days, corresponded to those which were found to exist for the uncooked refrigerated samples.

That the cooked meats from the 43-day storage sample lost less in cooking either by boiling or roasting than did those from the 6-day sample, the broths and the drippings in these cases being on the average lower in their percentage content of soluble, insoluble, and total dry substance, of organic extractives, of soluble protein, of soluble ash, and of fat.

That the cooked meats from the longer stored sample were higher in their percentage content of moisture and were therefore juicier, higher in soluble and insoluble dry substance, in nitrogenous, non-nitrogenous and total organic extractives, in fat, in total ash, and in soluble inorganic, total soluble and total phosphorus. Further, the percentages of total nitrogen, insoluble and total protein were practically the same as were those for the samples from the 6-day storage meat. Therefore the cooked meats from the 43-day samples, judging from the chemical composition, were at least as nutritious as were those from the samples stored for the shorter period of time.

A very valuable and instructive paper entitled "Cold Storages," has recently been published by Wemyss Anderson.[3] This observer deals with all the important details of cold storage, viz., sites, construction, machinery, method of cooling stores, and temperatures to be maintained. In connection with the question of temperature this varies with the class of produce stored.

Frozen meat, rabbits, poultry, etc., may be carried at 18° F. to 22° F., or even much lower ; chilled meat at 28° F. to 29° F. ; fruit (in general), vegetables and milk at 35° F. to 40° F., but for all classes of goods, having determined the temperature at which it is to be carried, every effort should be made to keep that temperature to a degree, because the amount of moisture the atmosphere is capable of holding in suspension depends on its temperature, and if there are variations of temperatures in a cold store it means that the goods stored will at times act as condensers and have deposited on them a film of "dew," this moisture then becoming a fruitful source of mildew and mould.

Fruit in particular suffers very much from variations. A range of 35° F. to 40° F. has been given as suitable temperatures ; this, however, by no means indicates that you can vary with impunity from 35° to 40° F. Nothing could be worse ; it means that any figure in that range having been selected, every precaution should be taken to

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[1] Emmett, A. D., and Grindley, H. S. (July, 1909), "Chemistry of Flesh : A Preliminary Study of the Effect of Cold Storage upon Beef and Poultry." *Journal of Industrial and Engineering Chemistry.*

[2] *Idem* (August, 1909), *Ibid.*

[3] Anderson, J. W. (April, 1911), "Cold Storages." *Journal Royal Institute of Public Health.*

keep that temperature without any variation whatever. This is hardly possible with the air circulation method alone, and so we find the most successful cold stores for fruit carry a combination of the air circulation method and brine-pipe system, the chambers being very heavily piped, the brine in them acting as a "thermostatic balance" and preventing undue change. Preservatives—*continued*

The subject of abattoirs and ice-making is considered, and the use of a chilling chamber attached to an abattoir is strongly advocated, for it enables newly killed meat to mature quickly for the market, and having matured it, the cold store will hold the meat for any reasonable time.

Sectional plans for the construction of cold storages are shown in this excellent paper, and the author concludes by urging that

every town should have its cold store, and that the abattoir with properly equipped chilling rooms and ice-making factory are equally important, and may be economically run from the same plant and largely by the same staff. Further, that electricity should be favourably considered as a suitable means of power for driving compression machinery, inasmuch as the power required for refrigeration is a maximum in summer, when the demand for electricity in most towns is small, while the refrigerating plant could certainly be shut down in the winter when the lighting peak had to be met, say between 4 and 6 o'clock in the evening. Where waste steam is available, or where steam could be generated by waste heat (say in a destructor), it should be known that the absorption refrigeration machine can be employed with advantage.

In a report recently presented to the sanitary committee of the London Corporation, Collingridge [1] refers to the serious question of the unrestricted employment of preservatives in food, and urges that some form of legislation should be adopted for the protection of the public. He refers to the long list of preservative powders sold for the preservation of various foods, and the variety of food thus treated is so wide that the consumer may be confronted with chemicals at every meal. "He may have borax for breakfast, benzoates for lunch and tea, and salicylic acid for dinner!" In the opinion of Collingridge, where preservatives are added to articles of food and drink, not only the nature of the drug used, but the amount should be notified to the purchaser, and the use of any preservative in milk he considered should be a penal offence.

Bernstein [2] has an important paper dealing with a new aspect of the effects of boric acid as a preservative. While carrying out some experiments with sausages adulterated with 20 grains of boric acid to the pound, he found that this amount of acid had a peculiar and unequal effect on the varying processes of putrefaction. The saprophytic organisms, including those producing the odours of putrefaction, were inhibited, while the coliform group of organisms, including Gærtner's bacillus, were affected to a much lesser degree.

Some further experiments were carried out to determine the effect of boric acid on various organisms, and the conclusions arrived at were as follows :—

Boric acid to the extent of 0·3 per cent. (20 grains to the pound) prevents objective decomposition, such as is detectable by smell. If objective putrefaction has commenced, it inhibits further changes of this kind, possibly leading to diminution in the smell. It has a marked selective activity on the various organisms, inhibiting the growth of yeasts and organisms of the *proteus* group, and possibly other harmless saprophytes, though not the organisms of the *coli* group. Hence it seems obvious that, with the aid of boric acid, stale meat can be used for the making of sausages, and even meat that has already started decomposing. If, then, to such meats Gærtner's bacillus has obtained access, it will have had several days at least in which to grow, and, what is important, unhindered by the prolific saprophytes.

Klein [3] carried out a similar series of experiments, as well as additional ones, to test the bactericidal properties of boracic acid in a strength of ·5 per cent., when added to pathogenic organisms. He was unable to confirm Bernstein's preliminary experiments with *B. coli*, for he found that boracic acid in ·5 per cent. had a powerful inhibitory action on the life of *B. coli*, but his results were less striking with regard to its action on *B. Gærtner*. Experiments carried out on *B. typhosus* showed that ·5 per cent. boracic acid, when added to broth containing *B. typhosus*, had a marked restraining and disinfecting action on this organism.

The recent report of Hehner,[4] the analyst for West Sussex, shows how desirable it is that legislation should be adopted for the canned goods trade :—

During last quarter seven samples of preserved (tinned) lobster and seven samples of preserved (tinned) salmon were analysed for the purpose of detecting the quantity of metal that had been dissolved off the surface of the canisters. The following was the result expressed in grains per pound: Lobster, 1·28, 0·27, 0·12, 4·47, 0·80, 0·51

[1] Collingridge, W. (September 17, 1910), "Food Preservatives." *Report of the Sanitary Committee, Corporation of London.* Quoted in *Lancet.*

[2] Bernstein, J. (April 16, 1910), "A Preliminary Note on a New Aspect of the Effects of Boric Acid as a Food Preservative." *British Medical Journal.*

[3] Klein, E. (September, 1910), "The Action of Boron Preservatives on *Bacillus coli* and Allied Microbes." *Public Health.*

[4] Hehner, O. (February 25, 1911), "Canned Goods and the Public Health." Quoted in *Lancet.*

Preservatives—*continued*

and 0·09; salmon, 0·46, 0·21, 0·77, 0·24, 0·51, 0·38 and 0·35. These figures show that preserved (tinned) salmon is preferable to lobster, but Mr. Hehner explains that the quantities of tin dissolved in the salmon are comparatively small, probably because the oil in which the salmon is packed to some extent protects the surface. The quantity of contamination increases with the age of the goods, because the acid juices continue to act upon the metal. In course of time, therefore, all such preserved goods as are capable of attacking tin will contain an important quantity of the metal. Such materials are all meats and fruits; not condensed milk or syrup. The fixation of an age limit seems advisable. The date of packing ought to be compulsorily stamped on each can. It would be easy to ascertain when the maximum tolerable quantity, suggested by the Local Government Board at 2 grains of tin per pound, has been reached, but it would vary with the acidity of the material. The suggestion that the date of packing the goods should be clearly indicated on each can is an excellent one, and one which could easily be introduced. Dr. G. S. Buchanan and Dr. S. B. Schryver, on behalf of the Local Government Board, a year or so ago, were not able to gain any decisive evidence that tinned foods caused bodily harm attributable to tin salts, but it seems a pity that the simple precaution of lining tins with an innocuous varnish is not very generally adopted.

Davies,[1] in a recent paper, discusses the vexed question of preservatives in foods. He states that in some cases preservatives of one kind or another are absolutely necessary. "Even in Nature," he says, "we find the same primitive use of preservatives," and refers to the presence of formic acid in honey and salicylic acid in many ripe fruits. His arguments brought forward in favour of a restricted use of preservatives are very convincing. He concludes his paper as follows:—

> The manufacturer cannot do without some preservative; the public will not tolerate salt, the authorities will not tolerate borax, so he is approached on all sides by people offering to supply him with preservatives which cannot be detected by the public analysts. Generally this claim is all rubbish, but not always, and I know that there are substances used which are not detected, and I have myself found, and strongly denounced, sodium peroxide in milk, fluorine compounds, and all sorts of crafty preparations, organic and inorganic, about whose physiological effects we are quite ignorant. I would warn medical officers that of my own knowledge this evil is rapidly increasing, and that here and abroad highly-skilled chemists are trying to perfect preservatives which will evade the skill of the public analyst. What I suggest should be done is that the matter should be taken out of its present unsatisfactory state, where each bench of magistrates is able to set up its own standards, or want of standards, and that the whole thing should be settled by legislation, which I should like to see on the following lines:—
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> I would absolutely forbid all preservatives in milk. I should allow borax preservatives in certain foods, such as bacon, ham, sausages, meat pies, etc., within certain strictly defined limits, fixing perhaps two limits, one for summer, one for winter; such, however, should be notified. For temperance wines, jams, and the like, a small limited amount of salicylic acid might be used. That no other preservatives should be used except by permission of the Board of Agriculture within limits to be fixed by them.

Protozoa. It is quite beyond the scope of this Review to refer to all the recent published papers connected with the subject of protozoa, but it is hoped that the few selected for consideration in this section will be useful. A good deal of work has been carried out on the flagellates, notably of the genera *Trypanosoma*, *Herpetomonas*, and *Crithidia*, chiefly on account of the connection of various members of these genera with certain diseases affecting man. No mention will be made of the *Trypanosoma*, as they are considered elsewhere.

A paper[2] on insect flagellates published in the *Annual Report of the King Institute of Preventive Medicine*, 1907, gives a list of the species of herpetomonads found in India, together with a short description of them, and recounts the finding of a new species in the alimentary tract of *Lygæus militaris*, or dura plant bug. The life-cycle of this herpetomonad in the Lygæid bug has been worked out by Patton,[3] and his observations have been more or less confirmed by the writer in the same species of bug met with in the Sudan (*vide* Fourth Report of these Laboratories, Volume A). Reference is also made in this Indian paper of the *Crithidia gerridis*, found by Patton in certain water bugs. A full account of this crithidia is published in a more recent paper.[4]

A note by Patton and Strickland[5] will be found useful, as the first part of it is a critical review of the relation of blood-sucking invertebrates to the life-cycles of trypanosomes of vertebrates. The vexed question of the three genera—*Trypanosoma*, *Crithidia*, and *Herpetomonas*—is discussed, and their morphological characters compared. The genus *Crithidia* is defined as follows:—

> Flagellates which in their adult stages have a fusiform body with a blepharoplast, usually a large rod-shaped structure, situated close to the nucleus either anterior or a little distance posterior; their anterior ends are attenuated and drawn out along the flagella to which they are attached by a narrow undulating membrane, which never has

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[1] Davies, H. E. (May, 1911), "Preservatives in Foods." *Journal Royal Institute of Public Health.*

[2] (1907), "Insect Flagellates." *Annual Report of the King Institute of Preventive Medicine*, Guindy, Madras.

[3] Patton, W. S. (1908), *Herpetomonas lygæi. Arch. f. Protist.*, XIII.

[4] *Idem* (1908), "The Life-cycle of a Species of Crithidia Parasitic in the Intestinal Tract of *Gerris fossarum*, Fabr." *Arch. f. Protist.*, XII.

[5] Patton, W. S., and Strickland, C. (December, 1908), "A Critical Review of the Relation of Blood-Sucking Invertebrates to the Life-cycles of the Trypanosomes of Vertebrates, with a Note on the Occurrence of a Species of Crithidia, *C. ctenopthalmi*, in the Alimentary Tract of *Ctenopthalmus agyrtes*, Heller." *Parasitology.*

the characteristic folded appearance seen in adult flagellates of the genus Trypanosoma. Their posterior ends may be blunt or pointed. They have three characteristic stages in their life cycles—pre-flagellate, round, or oval bodies—with a nucleus and blepharoplast which multiply by simple fission, flagellate stage, when they multiply by longitudinal division, which may be either equal or unequal. In this stage they often exhibit marked polymorphism, post-flagellate stage, when the flagellates shorten, divide and then encyst; some species (in ticks, leeches, and *Melophagus ovinus*) pass this stage in the eggs of their hosts.

In this paper there is also described a species of crithidia, *C. ctenopthalmi*, found in the alimentary tract of two fleas.

Patton,[1] while continuing his researches on crithidia, found in the intestinal tracts of *Tabanus hilarius*, and *Tabanus* sp. ? a species of this genus allied to, but distinct from, the species *minuta* and *subulata* of Léger.[2] A full description of the life-cycle of this crithidia, which he provisionally names *C. tabani*, is given. The conclusions he draws from his work on this crithidia are as follows :—

(1) This flagellate of Tabanids is a true parasite of the flies, exhibiting all the characteristics of a *crithidia;* though allied to the species *minuta* and *subulata*, as far as it is possible to say, it appears to be distinct, and I propose provisionally naming it *Crithidia tabani*.

(2) It is not related to any blood parasite, but passes its complete life cycle in the flies. It should be carefully avoided in feeding experiments in connection with *surra* and allied trypanosomiases suspected to be transmitted by horse-flies.

(3) It is transmitted from one fly to another by accidental contamination and is not inherited, so that flies reared in the laboratory are free of the infection. The exact method of infection of these species of *crithidia* and *herpetomonas* which encyst in their hosts can only be found out by looking for the early stages of the development of the parasites, and at the same time by making careful observations into the habits and life histories of their hosts.

(4) It is a close ally of one of the flagellates of the *Glossinæ*, which should be placed in the same genus. The theory that this flagellate of *G. palpalis*, *C. grayi*, in order to complete its life cycle, must pass through either a bird or a crocodile is, I believe, based on an incomplete study of its life history. Until the life cycles of the *crithidia* of tsetse flies are completely worked out, the exact methods by which man and the lower animals become infected with *Trypanosoma gambiense* and *Trypanosoma brucei* will not be finally settled; this is one of the most urgent problems awaiting solution.

(5) The fact that 80 to 90 per cent. of tsetse flies (*G. fusca*) bred in captivity by Stuhlmann developed a flagellate infection from two to four days after their first feed, strongly suggests that the flagellate of this fly is transmitted hereditarily. These observations are in exact accordance with mine on the *Crithidia* of *Clepsina;* about the same percentage of young leeches develop a rich infection a few days after their first feed, and the small forms observed by Stuhlmann are similarly found in the anterior diverticula of the leech.

(6) It will be seen that my results differ essentially from those of Minchin, in that he regards the flagellates of tsetse flies as true *trypanosomes*, while I consider they are insect parasites of the genus *Crithidia*, and are allied to such forms as occur in horse-flies, mosquitoes, bugs, ticks, and leeches.

(7) My researches on these flagellates of arthropods and leeches throw considerable doubt on the so-called developmental cycles of trypanosomes in certain invertebrate hosts.

Mention may be made of a paper by Porter[3] on the "Morphology and life history of *Crithidia gerridis*, as found in the British water bug, *Gerris paludum*." Porter has noted crithidia parasites pass from the unruptured gut to the adjacent ovaries, where they have been found in a large percentage of the adult female *Gerris* that were examined. Porter considers that there is little to debar the genus *Crithidia* from a position in the family *Trypanosomatidæ*. The possession of nucleus, blepharoplast and definite undulating membrane and flagellum places the crithidia very near the trypanosomes. Their habitat is, however, different, although Porter considers that this difference in habitat has been somewhat exaggerated, for the medium in which most of the crithidia live is of much the same density as blood, and quotes the fact that *Crithidia melophagia*[4] is commonly found mingled with either freshly-drawn or partially-digested blood of the sheep contained in the gut of *Melophagus ovinus*.

Porter[5] has also worked out the life-cycle of *Herpetomonas jaculum* (Léger), parasitic in the alimentary tract of *Nepa cinerea*. In this particular herpetomonad there was no evidence of hereditary infection, although flagellate forms were found in the ovaries.

Mention may also be made of an interesting discovery by Lafont[6] of a flagellate,

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[1] Patton, W. S. (1909), "The Life Cycle of a Species of Crithidia Parasitic in the Intestinal Tracts of *Tabanus hilarius and Tabanus* sp." *Arch. f. Protist.*, pp. 333–362.

[2] Léger. L. (1904), "Sur un nouveau flagellé parasite des Tabanides." *C. R. Soc. Biol.*, Vol. LVII.

[3] Porter, A. (December, 1909), "The Morphology and Life History of *Crithidia gerridis*, as found in the British Water Bug *Gerris paludum*." *Parasitology.*

[4] Flu, P. C. (1908), "Über die Flagellaten im Darm von *Melophagus ovinus*." *Arch. f. Protist.*, XII.

[5] Porter, A. (December, 1909), "The Life Cycle of *Herpetomonas jaculum* (Léger), Parasitic in the Alimentary tract of *Nepa cinerea*." *Parasitology.*

[6] Lafont, A. (June, 1909), "Sur la présence d'un parasite de la classe des Flagellés dans le latex de l'*Euphorbia pilulifera*." *C. R. Soc. Biol.*, Vol. LXVI.

Protozoa—*continued*

Herpetomonas davidi, parasitic in the latex of *Euphorbia pilulifera*, a shrub which is more or less ubiquitous in the Tropics.

Georgewitch [1] has noted all the stages of the development of *Crithidia simuliæ*, as well as the adult forms of this parasite in the stomach of *Simulium columbacensis*. The evolutive cycle of Georgewitch's species commences with ring forms which resemble piroplasms, passes on to round forms which correspond to *Leishmania*, and lead on to gregarine forms which are clearly polymorphous and which give birth to the various forms of the adult series.

Mention may be made of a good illustrated paper by Mackinnon [2] dealing with herpetomonads from the alimentary tract of dung flies, *Scatophagia lutaria* F., *Neuroctena anilis*, Fallen, and *Homalomyia*. These herpetomonads resembled *H. muscæ domesticæ*. Mackinnon notes that *Musca domestica* and other non-biting flies frequenting similar feeding grounds, are probably all liable to infection with a common flagellate which may vary in form in the larvæ when compared with those found in the adult. As regards the life-cycle of these herpetomonads they resemble those described by Patton.

Aders [3] found in the melon bug (*Aspongopus viduatus*) a flagellate of the herpetomonad type, *H. aspongopi*. This melon bug causes considerable damage to the melon crops around Khartoum. The percentage of bugs infected was small.

Patton,[4] by means of feeding experiments, has conclusively proved the following points in relation to the life-cycle of *H. muscæ domesticæ* :—

1. *Herpetomonas muscæ domesticæ* may be transmitted from one fly to another in three ways :—

(*a*) By a fly ingesting the long flagellates.

(*b*) By a fly ingesting the short encysting forms.

(*c*) By a fly ingesting the cysts.

2. If the food is suitable, the long flagellates multiply continuously for at least fourteen days, and then begin to encyst.

3. The short encysting forms, if ingested, pass down the alimentary tract of a fly, and become cysts either in its colon or rectum.

4. The cysts when ingested develop in a few hours into long flagellates, which multiply as described above.

5. The food of the house-fly plays an important part in the life history of *Herpetomonas muscæ domesticæ*.

6. This flagellate has three different stages—*pre-flagellate*, *flagellate*, and *post-flagellate*, and in none of these has it a double flagellum.

7. In the early stages of the infection the parasites are seen as typical herpetomonads with the blepharoplast lying close to the anterior end, they then have the appearance described by some authors as being characteristic of the genus *Herpetomonas* (Kent). In a later stage they are long slender bodies with well-developed single flagella, and would then belong to the genus *Leptomonas* of Chatton, and in a still later stage (*pro-encysting forms*) the blepharoplast moves close to the nucleus and even passes behind it.

Swingle [5] has a note on the life history of a flagellate (*Crithidia melophagi*, n. sp.) in the alimentary tract of the sheep tick, and the same observer has recently contributed an interesting illustrated paper containing a description of a herpetomonas [6] (*H. pattoni*) found in the rat-fleas, *Ceratophyllus*, sp., and *Pulex*, sp., and also a description of two new herpetomonads, *H. calliphoræ* and *H. lineata*, found in the flies *Calliphora coloradensis* (Hough), and *Sarcophaga sarraceniæ* (Riley). In his paper he points out the great similarity between some of the herpetomonas forms and the stage met with in the life-cycle of *T. lewisi*, and considers that there is ample evidence to show that trypanosomes change over into true crithidia-like forms when taken up by insects acting as hosts. This changing over of a blood trypanosome into a true *crithidia* when taken up by an insect host, signifies that the natural crithidia of insects are the more primitive, and that the trypanosomes are merely insect crithidia which have been successfully introduced into the blood stream of vertebrates. If this suggestion of Swingle's be a true one, animal inoculations with these insect flagellates would surely be followed by positive results, but so far the experimental work that has been carried out in this line has been attended by negative results (R. G. A.). The writer's transmission experiments with *H. lygæi* all gave

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[1] Georgewitch, J., "Sur le développement de *Crithidia simuliæ*, n. sp." *C. R. Soc. Biol.*, No. 32.

[2] Mackinnon, D. (September, 1910), "Herpetomonads from the Alimentary Tract of Certain Dung Flies." *Parasitology*.

[3] Aders, W. M. (September, 1909), "*Herpetomonas aspongopi*." *Ibid.*

[4] Patton, W. S. (April 13, 1910), "Experimental Infection of the Madras Bazaar Fly, *Musca nebulo*, Fabr., with *Herpetomonas muscæ domesticæ* (Burnett)." French résumé by F. Mesnil, *Bull. Soc. Path. Exot.*

[5] Swingle, L. D. (February 18, 1909), "A Study on the Life History of a Flagellate (*Crithidia melophagi*, n. sp.) in the Alimentary Tract of the Sheep Tick, *Melophagus ovinus*." *Journal Infectious Diseases.*

[6] *Idem* (March 6, 1911), "Transmission of *Trypanosoma lewisi* by Rat Fleas (*Ceratophyllus* Sp. and *Pulex* Sp.), with Short Descriptions of Three New Herpetomonads" *Ibid.*

Protozoa—*continued*

negative results, *vide* Fourth Report of these Laboratories, Volume A. The fact that these crithidia-like forms are natural flagellates of the insect, and not transitional forms of trypanosomes, is more probable, and is a view which should be held till the pathogenic properties of these crithidia-like forms can be proved. A most useful paper by Fantham consists of a review and a new classification of the schizogregarines. It is too long to be considered in detail. The value of the paper is enhanced by an appendix consisting of a glossary of terms relating to schizogregarines.

One must mention Patton's [1] discovery of a flagellate in the Malpighian tubes of *Lucilia serenissima*, Walk. Morphologically, it is allied to the crithidia, and more especially to the trypanosoma, in that the blepharoplast always lies posterior to the nucleus; it, however, differs from these forms, as the flagellum is entirely limited in the adult stage to a small part of the body of the parasite, and has no free portion. Patton created a new genus for this flagellate, viz., *Rhynchomonas* (rhynchus; a snout), but subsequently has changed its generic name to *Rhynchoidomonas luciliæ*.[2]

Darling [3] has a very interesting illustrated paper dealing with a fatal infectious disease of tropical America resembling kala-azar in India, and named by him *Histoplasmosis*.

It is characterised clinically by splenomegaly, emaciation, irregular pyrexia, leucopenia and anæmia. The pathological features are the invasion of endothelial cells in the smaller lymph and blood-vessels and capillaries by enormous numbers of a small encapsulated micro-organism (*Histoplasma capsulatum*) causing necrosis of the liver with cirrhosis, splenomegaly, pseudo-granulomata of the lungs, small and large intestines, with ulceration of the latter and necrosis of lymph nodes draining the infected viscera.

The disease is caused by a small round or oval micro-organism 1 to 4 μ in diameter possessing a polymorphous, chromatin nucleus, basophilic cytoplasm and achromatic spaces all enclosed within an achromatic refractile capsule.

The micro-organism differs from the Leishman-Donovan body of kala-azar in the form and arrangement of its chromatin nucleus, and in not possessing a chromatin rod.

The distribution of the parasite in the body is by the invasion of contiguous endothelial cells of the smaller blood and lymph vessels and capillaries, and the infection of distant regions by the dislodgment of infected endothelial cells and their transportation thither by the blood or lymph stream. Thus, the skin, intestinal and pulmonary nodules may be due to secondary distribution of the parasite.

The micro-organism apparently lives for a considerable period of time in the tissues, because in the older areas of necrosis there are myriads of parasites all staining like recent organisms.

The mode of infection and the portal of entry are unknown; these, together with the zoological status of the micro-organism, may yet be ascertained by physicians living in less salubrious regions of tropical America than Panama, and in those not yet disturbed by the sanitarian.

This same observer gives a description of a case of Sarcosporidiosis [4] occurring in a Barbadian negro, who had passed through an attack of typhoid fever, complicated with necrosis and myositis of some of the striated muscles. Portions of muscle (biceps) removed showed the presence of sporozoa. About three weeks later the sporozoa had disappeared, the parasite apparently being abortive. The infection in all probability was a chance one by sarcosporidia, whose customary habitat was some one of the domestic animals. In a more recent paper Darling,[5] has shown that guinea-pigs can be infected with sarcosporidiosis by feeding them with rat's muscle naturally infected by *Sarcocystis muris*, and by ripe mobile sporozoites from the same source. The guinea-pigs showed the infection after an incubation period varying from 152 to 164 days. Morphologically, the guinea-pig sarcosporidia derived from *Sarcocystis muris* were identical with those found in the human case previously described by this observer.

Reference may be made to Montgomery's [6] interesting discovery of coccidiosis in East African cattle. This paper has been reviewed in another section (Veterinary Diseases), so no further mention of it need be made. In the Sudan, Stevenson (*vide* Fourth Report, Vol. A) has found coccidiosis in goats, and Balfour [7] has referred to the possibility of this disease affecting the cattle in the upper Nile and Bahr-el-Ghazal districts.

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[1] Patton, W. S. (May 11, 1910), "*Rhynchomonas luciliæ*, nov. gen., nov. spec. A New Flagellate Parasitic in the Malpighian Tubes of *Lucilia serenissima*, Walk." *Bull. Soc. Path. Exot.*

[2] *Idem* (July 13, 1910). *Ibid.*

[3] Darling, S. T. (July 17, 1909), "The Morphology of the Parasite (*Histoplasma capsulatum*) and the lesions of Histoplasmosis, a Fatal Disease of Tropical America." *Journal of Experimental Medicine*, Vol. XI.

[4] *Idem* (April, 1909), "Sarcosporidiosis." *Archives of Internal Medicine.*

[5] *Idem* (1910), "Experimental Sarcosporidiosis in the Guinea-Pig, and its Relation to a Case of Sarcosporidiosis in Man." *Journal of Experimental Medicine*, Vol. XII., No. 1.

[6] Montgomery, E. (May 11, 1910), "Coccidiosis of Cattle in East Africa." *Bull. Soc. Path. Exot.*

[7] Balfour, A. (July 13, 1910), "Coccidiosis of African Cattle." *Ibid.*

Protozoa— *continued*

Ingram [1] reports the finding of cysts of *Rhinosporidium kinealyi* in two rather unusual situations, viz., one in a conjunctival polypus and the other in a papilloma of the penis. The usual sites for these cysts are either in the nose or naso-pharynx. A feature of these cysts is the presence of a pore in the cyst wall. The largest and most mature pansporoblasts were situated in the vicinity of this pore.

Darling[2] reports a case of infection by *Lamblia intestinalis* in an American child. The source of infection in this case was the contamination of the child's food by the fæces of infected rats. Darling notes that *Lamblia intestinalis* as usually seen in stools is encysted and non-motile.

Castellani and Chalmers [3] have observed in the stools of patients in Ceylon, suffering from agchylostomiasis a flagellated organism, pear-shaped or rounded, measuring 8 to 20 μ in diameter, capable of amœboid movements, and possessing two flagella and an undulating membrane. It is easily cultivated together with other bacteria on several media, the best of which are apparently nutrose agar and nutrose broth. The flagellate is named by these observers *Bodo asiaticus*.

Wenyon [4] gives a description of a new flagellate (*Macrostoma mesnili*) from the human intestine. In the character of its movements there was little to distinguish it from trichomonas. It lacked, however, an undulating membrane. The body is pear-shaped, and there are three long flagella directed forwards from its blunt end. A characteristic feature of this flagellate is the presence of a very large cytostome extending from the base of the three flagella towards the posterior end of the body for about a half to two-thirds of its own length. The presence of this flagellate in the intestine was productive of no ill-effects.

Attention has been drawn by some observers to the *Chlamydozoa*. These are micro-organisms whose attacks on the host cell result in formations of peculiar reaction products. By means of nuclear staining their existence is generally proved. Mention may be made of a paper by Flemming [5] on the *Chlamydozoa* from the standpoint of medicine. They appear to be causal factors in vaccinia, hydrophobia, variola, scarlatina, etc., and in a recent paper Sieber [6] records his belief from morphological experiments that *Anaplasma* (Theiler) should be classed among the *Chlamydozoa*.

A paper by Martini [7] gives a description of an intestinal flagellate (*Prowazekia cruzi*).

Refuse Disposal. Maxwell,[8] in a concise article, describes the chief methods for the disposal of town refuse. They may be summarised as follows :—

(1) Depositing upon waste or low-lying land, filling of pits, excavations or raising the level of marsh land, such sites being temporarily described as "tips" or "shoots."

(2) Mixing household ashes, dust, etc., with pail excreta for the purposes of their common disposal by sale or otherwise to farmers for agricultural purposes.

(3) Selling or giving away to brickmakers.

(4) Mixing with sewage sludge and ploughing or digging into the soil of sewage farms.

(5) Mixing with precipitated liquid sewage sludge, or with pressed sewage sludge-cake, and cremating in destructor furnaces.

(6) Crushing or pulverising the refuse by machinery, and employing the resulting product as a manure or in the manufacture of fuel with an admixture of tar.

(7) Riddling, burning cinders, and vegetable refuse to generate steam, and using the fine dust in connection with a manure manufactory, the old iron being sold, and the pots, etc. used for the foundations of roads.

(8) Selling by tender yearly.

(9) Barging away down canals to country districts.

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[1] Ingram, A. C. (September 3, 1910), "*Rhinosporidium kinealyi* in Unusual Situations." *Lancet.*

[2] Darling, S. T. (1909), "An Infection by *Lamblia intestinalis* in an American Child." *Proceedings Canal Zone Medical Association.*

[3] Castellani, A., and Chalmers, A. J. (July, 1910), "Note on an Intestinal Flagellate in Man." *Philippine Journal of Science*, B.

[4] Wenyon, C. M. (1910), "A New Flagellate (*Macrostoma mesnili*, n. sp.) from the Human Intestine, with some Remarks on the Supposed Cysts of *Trichomonas*." *Parasitology*, Vol. III.

[5] Flemming (October 4, 1910), "Über Chlamydozoen vom Standpunkte des Mediziners." *Cent. f. Bakt. Ref. Beilage zu Abt. I.*, Vol. XLVII.

[6] Sieber, H. (1909–1910), "*Anaplasma marginale* (Theiler)." *Union of South Africa, Department of Agriculture, Report of the Government Veterinary Bacteriologist.*

[7] Martini (December 7, 1910), "Über *Prowazekia cruzi* und ihre Beziehungen zur Ätiologie von ansteckenden Darmkrankheiten zu Tsingtau." *Zeit. f. Hygiene.*

[8] Maxwell, W. H. (1909), "Town Refuse Disposal." *Transactions Bombay Medical Congress.*

Refuse Disposal—*continued*

(10) Taking out to sea in hopper barges and sinking refuse in deep water, as done at Liverpool.

(11) Utilising by "sorting" by hand or by machinery, and selling the ingredients for use in such trades or manufactures as can employ them, as done at dust contractors' yards.

(12) Destroying the crude refuse by fire in destructor furnaces, and utilising the residual clinker and surplus steam for various purposes.

Maxwell then mentions the improvements that have been made in connection with the destructor system, which may be shortly stated, thus :—

(1) The maintenance of high temperatures within the cells, combustion chambers, etc., ranging between 2000° to 3000° Fahr., and the reduction of air leakage into the cells.

(2) Improvements in the durability of the furnaces under high temperature, and the avoidance of defects caused by contraction and expansion owing to frequent variations of temperature.

(3) The use of forced draught and hot-blast and the reduction of power consumed in its working.

(4) The extraction of the full calorific value from the refuse, and the interception and utilisation by means of boilers, economisers, or feed-water heaters, superheaters, regenerators, hot-blast draught, etc. of all heat given off by its combustion, and the fullest possible application of the same to the performance of profit-yielding work.

(5) Improvements in the generation of high-pressure steam and the maintenance of steady steam pressures, but with means of affording a certain amount of elasticity of output, as by thermal storage, or storage of refuse fuel.

(6) The reduction of labour costs involved in the handling of the raw refuse, in the stoking and charging of the furnaces, and in the removal and disposal of clinker, fine ash, etc.

(7) The introduction of all possible means of full utilisation of residuals created at the works, such as clinker, fine ash, solder, or other marketable material from the refuse.

(8) The perfecting of various necessary plant employed in the utilisation of residual clinker, etc., as in the manufacture of paving slabs, carriage-way pitching blocks, building bricks and tiles, mortar, and graduated clinker for sale.

(9) Sanitary improvements in connection with the handling and storage of the refuse, and the prevention of dust or smells from the tipping platform, chimney shaft, or elsewhere.

(10) The reduction in capital cost in the erection of destructor works.

Maxwell concludes his paper by calling attention to the utility of modern destructors as power producers in addition to being mere destructors of refuse.

Beevor[1] deals with the problem of the disposal of refuse in hill stations. He unhesitatingly condemns the trenching system for hill stations, for the

soil is mostly sandy, the crust very thin, with underlying rock, and vegetation so abundant that the digging of proper trenches is an impossibility; the removal of sewage from bungalows and barracks, situated on steep inclines, is extremely disagreeable, and very dangerous, for sweepers cannot be expected to carry out the necessary precautions during the rains. Shallow trenches cannot be constructed, for they are rapidly filled with water and washed away; the hill-sides are slippery. pathways rugged, and sweepers constantly fall when conveying "bhaltis" on their heads; and lastly, the nitrifying organisms are very scanty in forest soil.

At Dalhousie, little change was found to have taken place after the trenches had been filled in for over a year.

Beevor advocates the bactericidal destruction of refuse by fire to ensure complete incineration. The question of dealing with native sewage is a difficult one, and the types of incinerator recommended by him are the gridiron pattern or the English Army Field pattern.

Reference may be made to a paper by Thomas,[2] in which is given a technical description of a modern refuse destructor plant. It is a useful paper, and may be consulted with advantage by the medical officer whose duty it is to report to his authority on the advisability of erecting a refuse destructor in his district, but it hardly comes within the scope of the medical officer in the Tropics. Still it contains many practical points.

Melvin[3] has a paper dealing with the "Bulk feeding of refuse destructors." The most ideal system employed, and one which appears to give excellent results, is one known as the "Tub Feed." A full description of this is given in Melvin's paper, and a table giving the cost of a year's working is appended, showing that the method is a cheap one; the cost of refuse destruction working out at one penny three farthings per ton.

To those who are interested in the subject of refuse disposal, a book entitled *Refuse Disposal and Power Production*, by W. F. Goodrich, can be strongly recommended. The illustrations are good, and the whole subject of refuse disposal both in England and in other countries is admirably treated.

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[1] Beevor, W. (1909), "The Disposal of Refuse in Hill Stations." *Transactions Bombay Medical Congress.*

[2] Thomas, A. E. (June, 1909), "Refuse Destructors and the Public Health." *Public Health.*

[3] Melvin, G. W. (July, 1910), "The Bulk Feeding of Refuse Destructors." *Journal Royal Institute of Public Health.*

Schistosomiasis. *Schistosomum hæmatobium.*—Letulle [1] made very complete post mortem examinations of two cases, one intestinal, the other urinary. He insists on the necessity for microscopical examination in order to determine if an organ is or is not infected, and he mentions the pelvic cavity as the seat of selection for bilharziasis. He also adduces arguments to prove that what may be called "embolic" spread by the blood or lymphatics is a more likely means of distribution than direct infection of tissues by contiguity.

May [2] has recorded a case of bilharzial infection of the gastric mucous membrane in the case of a Chinese coolie in the Transvaal. The eggs had terminal spines.

Elgood [3] conducted an interesting research into the prevalence of bilharziasis among women and girls in Egypt. Her conclusions may be quoted :—

(1) Bilharzia is common in young girls, even in those who do not bathe, and who use filtered water only; town children are frequently affected. (2) Bilharzia is rare in adult women, who may, however, have suffered from it in youth. (3) European women and girls are not known to be sufferers from bilharzia, though in the towns they drink and wash in water from the same source as natives use. Water, however, is not stored in European households. (4) The infection by bilharzia is probably not mainly due to bathing, as has been suggested. It is possibly due to faulty storage of drinking water, or to the eating of raw vegetables and fruit washed in dirty canals or rivers.

It may be noted that Mrs. Elgood examined the water in zeers and other utensils at one of the girls' schools in which her investigations were conducted, but failed to find bilharzia miracidia.

In a discussion upon the paper, Ruffer expressed a belief that infection might take place *per anum* owing to the habit of ablutions practised in Egypt. Sandwith stated that the paper threw doubt on Looss's theory of skin infection, and Manson followed suit, pointing out that apes which harbour schistosomes do not practise ablutions. To all this, Looss [4] replied in no uncertain fashion. While admitting the value of Elgood's researches, he takes exception to her final conclusions as regards the method of infection. He points out that the early years of life are those suitable for acquiring the disease, and that it is at this stage that poor native children paddle about in street puddles. He points out how easily these may become infected, and that when in contact with water the miracidia leave their egg shells without delay, so that moist places become infective immediately after contamination and then also have their greatest infective power. He summarises a very able paper as follows :—

(1) Any theory about the mode of infection with bilharziasis, in order to be at all acceptable, must (*a*) account for the passages of the miracidium both from man to water and from water back to man; it must (*b*) duly consider both the habits of the host and the biological peculiarities of the parasite.

(2) The theory of the infection taking place by the mouth (along with food and drink) must be refuted, because it is irreconcilable (*a*) with certain biological peculiarities of the miracidium, (*b*) with the general distribution of the disease among the population of Egypt.

(3) The theory of infection by the miracidium entering the urethra or the anus is (*a*) utterly improbable for general parasitological reasons; (*b*) in contradiction with a number of biological and anatomo-pathological facts (for example, the incapability on the part of the miracidium to resist the action of acids, even if very diluted; the part played in the infection by the liver, etc.).

(4) The theory of infection by the skin is in accordance with all the facts thus far known (*a*) of the biology of the parasite, (*b*) of the distribution of the disease among the population (native and foreign, town and rural) of Egypt. It shows (*c*) how the chief sufferers—the children in town, the adult males in the country—live under conditions which, from the epidemiological point of view, are essentially the same, and give the miracidia (*d*) the opportunity of passing, within the short time of their life, from man to water and from water to man.

Looss's view has recently received strong support from Captain Douglas Thomson's observations in the Sennar Province of the Sudan.

Turner [5] has dealt with bilharziasis in South Africa. He believes in the "skin-infection" theory, most cases apparently contracting the disease from bathing or wading. He points out that while monkeys do not bathe, they probably immerse their feet while drinking. He quotes Abercrombie, who puts the incubation period at about six weeks. Both terminal-spined and lateral-spined ova are found, derived, he thinks, possibly from two separate trematodes, and he enters into a description of the types observed, and notes that in the urinary form calculus does not appear to be a concomitant. He mentions three native remedies, but

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[1] Letulle, M. (May 13, 1908), "Bilharziose urinaire chez un nègre du Congo. Modes de dissémination des lésions parasitaires." *Bull. Soc. Path. Exot.*

[2] May, A. W. (August 29, 1908), "Bilharziosis of the Gastric Mucous Membrane." *British Medical Journal.*

[3] Elgood, B. S. (October 31, 1908), "Bilharziosis among Women and Girls in Egypt." *Ibid.*

[4] Looss, A. (March 27, 1909), "Bilharziosis of Women and Girls in Egypt in the Light of the 'Skin-Infection Theory.'" *Ibid.*

[5] Turner, G. A. (October, 1908), "Bilharziosis in South Africa." *Parasitology.*

personally employs urotropine with adrenalin if the hæmorrhage is severe. The same author has a paper [1] on the pulmonary form of the disease in South Africa. He found it comparatively frequent, and describes three naked-eye appearances apparently produced by the presence of the ova. Schistosomiasis—*continued*

Those who wish to follow the discussion between Sambon and Looss on the question of *Schistosoma mansoni* to which reference was made in our last Review, may consult Sambon's reply [2] to Looss's criticisms. It is too lengthy, and deals with too many points for quotation here. Leiper,[3] however, has studied the subject on material from the Transvaal, and has satisfied himself as regards the following facts :—

(*a*) Both terminal and lateral-spined bilharzia eggs occur together and separately in natives working in the mines in the Transvaal.

(*b*) The lateral-spined ova occur only in the rectal tissue, and occur there in very great numbers, thus precluding, to my mind, the idea that the ovum with a lateral spine is, as has been suggested, the product of a too early impregnated female.

(*c*) The lateral spine is exceedingly uniform in shape and character, and seems to be of a distinct type from the somewhat displaced terminal spines occasionally seen in cases in which the terminal-spined ova abound.

(*d*) The actual shape of the eggs is different.

(*e*) While it is true that the females containing lateral-spined eggs contain only one ovum at a time as a rule (so far as I have seen), the ootype is much larger than the contained débris. Now it is an essential point in Looss's explanation of the orientating of the egg as it passes into the ootype that it cannot do so easily, but meets with resistance from the amount of the abortive ova and yolk cells that block the cavity of the ootype, and that this causes it to be shelled asymmetrically.

(*f*) In the males of bilharzia specimens collected from the portal vein in cases of mixed infections, as ascertained by microscopical examination of bladder and rectal walls, I have been able to separate into two groups males having four somewhat angular large testes from others having seven to nine small spherical testes. In other cases all the males obtained belong to one type. The difference in character, and especially in number of testes, would be considered by helminthological authorities, if occurring in other groups, and if constant, as it seems to be here, as a specific character of some reliability.

(*g*) In order that this character can be utilised in support of the view that the two forms of bilharziasis, rectal and urinary, are caused by parasites specially distinct, it remains to be shown that males having one particular type of testes are usually or always in sexual conjunction with females producing one type of eggs.

(*h*) The probabilities are, granting for the moment that these types of testes and of egg be found constantly to occur, that the male with four testes is the mate of the female giving rise to the terminal-spined egg. For this is the normal arrangement of testes that has up to the present been figured and noted, and is that given by Looss, while the terminal-spined ovum is the one recognised by him as being the normal product of the mate of this form.

(*i*) In support of this view I am able at present to offer only one actual observation, in itself a striking one owing to the lack of females in copulation with the males in any material. In the one specimen of a pair in this position the number of the testes can easily be made out to be seven, at any rate in the male. The female lies in the gynæcophoric canal, but its posterior half has broken off. Lying also in the canal, however, is a small clot containing several lateral-spined ova. We have then evidence of the association of the multi-testicular male with the female having lateral-spined eggs.

" These observations " he says, " by no means finally settle the question at issue or completely dispose of the theories based on an assumption that the atypical egg is a pathological product, but they certainly render a reconsideration of the detailed anatomy of the *Schistosomum hæmatobium* highly desirable."

Blanchard,[4] considering the case of an infected scholar, recommends as preventive measures the voiding of the urine into a special receptacle containing sulphuric acid or formalin, and the inspection and, if necessary, disinfection of the stools. These are questions to which, perhaps, more attention should be directed in schools in the Sudan and elsewhere.

Allen [5] believes that, so far as cases in Natal are concerned, infection almost invariably takes place *per urethram* while bathing. As an argument in favour of this hypothesis, he cites the fact that the membranous portion of the urethra is the first, and sometimes the only point, to be infected. He thinks that circumcision would act as a preventive by doing away with water collections under the prepuce. The paper is interesting, but in the light of Looss's views and other recent work the theory is scarcely tenable.

De Silva [6] gives an account of the disease in Bahia, Brazil, and seems to think that there

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[1] Turner, G. A. (December, 1908), " Pulmonary Bilharziosis in South Africa." *Transvaal Medical Journal.*

[2] Sambon, L. (January 1, 1909), " What is '*Schistosoma mansoni?*' " Sambon, 1907. *Journal Tropical Medicine and Hygiene.*

[3] Leiper, R. L. (1909), *In Report Advisory Committee for the Tropical Diseases Research Fund.*

[4] Blanchard, R. (October 10, 1908), " Le Renvoi d'un Collégien atteint de bilharziose est-il légitime ? " *Arch. de Parasit.*

[5] Allen, J. T. (May 8, 1909), " Bilharzia Hæmatobia and Circumcision." *Lancet.*

[6] De Silva, P. (June 1, 1909), " Contribution to the Study of Schistosomiasis in Bahia, Brazil." *Journal Tropical Medicine and Hygiene.*

Schistosomiasis—*continued*

it may be caused, at least in its intestinal form, by a new species of Schistosome. The paper must be studied for details.

It is interesting to note that Ruffer [1] has found undoubted evidence of bilharziasis in Egyptian mummies of the twentieth dynasty.

Noc [2] has apparently found that the intestinal form of the disease, characterised by lateral-spined eggs, alone exists in Martinique, thus, according to Brumpt, confirming the view of Sambon that there is a distinct and separate *S. mansoni*. The same author also records [3] a rectal case associated with malignant ankylostomiasis.

Madden,[4] whose monograph on the subject is well known, describes, along with Owen Richards, the symptoms and treatment of cases of localised bilharziasis of the large intestine. In Egypt, especially in a fellah, Madden regards any hard abdominal tumour as presumably bilharzial until the contrary is proved, and testifies to the excellent and remarkable results which may be obtained by merely cutting down on the mass, performing enterotomy, and closing the abdominal wound.

Richards, in the second part of the paper, so far as fellaheen are concerned, considers that resection should be limited to cases where there is sharp and narrow localisation combined with great local severity.

Pfister [5] reviews the whole question of the treatment of the disease, dealing even with radium-therapy and the use of Röntgen rays. It is evident that little is to be hoped from the internal administration of drugs.

As Looss [6] says in a recent lecture, even supposing a certain drug could kill the worms in the veins without otherwise injuring the patient, its administration in nine cases out of ten would come too late. The worms only live a few years (3 to 5 probably, though this is only a surmise), while the eggs remain and are the real cause of the disease. The only way to cure the latter would be to dissolve the thin shells, and at present we know of no substance which can do so without at the same time injuring the patient. This lecture by Looss gives a very succinct account of the life history of the worm, as does one by Ferguson in the same journal of the disease it produces.

Amongst other points Looss notes that in the course of a year perhaps 100,000 to 200,000 eggs are produced by a single female worm. Every new infection, however, must happily come from outside the body, so that unless repeated re-infection occurs cases may remain slight and become eventually cured. He returns to the question of skin infection, and cites the successful cutaneous transmission experiments of Fujinami and Nakamura on domestic animals with *S. japonicum* as confirmatory of his view. The danger of infected puddles is again insisted upon. If any small collection of water has been exposed to contamination, it should not be used for bathing, washing, or working in for about two days. In large bodies of standing or flowing water, as for example the Nile, any embryos present are soon so much dispersed that they are not very likely to be a source of infection.

In the light of what Looss says, a paper by Kay [7] on prognosis is of interest. In South Africa he has never found the lateral-spined eggs in Europeans, and he presents statistics from Sir Alfred Keogh, derived from R.A.M.C. records, which go far to prove that insurance companies need not fight shy of bilharzia cases, and that in the absence of opportunities for re-infection the disease is usually benign.

Conor [8] describes cases in association with hot springs in Tunisia under conditions which suggest skin infection, and Brumpt, discussing this paper, mentioned that Cobbold had apparently succeeded in infecting the monkey, *Cercopithecus fuliginosus*, with *S. hæmatobium*, so that it might be possible now to prove Looss's view experimentally. He also mentioned the recent researches of Katsurada and Hashegawa with *S. japonicum* in Japan, which confirmed

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[1] Ruffer, M. A. (January 1, 1910), "Note on the Presence of 'Bilharzia Hæmatobia' in Egyptian Mummies of the Twentieth Dynasty (1250–1000 B.C.)." *British Medical Journal.*

[2] Noc, F. (January 12, 1910), "La bilharziose à la Martinique." *Bull. Soc. Path. Exot.*

[3] *Idem*, "Un cas d'ankylostomiase maligne compliqué de bilharziose rectale." *Ibid.*

[4] Madden, F. C., and Richards, O. (March 15, 1910), "Two Papers on Localised Bilharziosis of the Large Intestine." *Journal Tropical Medicine and Hygiene.*

[5] Pfister, E. (1910), "Ein Rückblick auf die bisherige Therapie der Bilharzia—und einige Ausblicke." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIV., No. 3.

[6] Looss, A. (June, 1910), "The Life History of the Bilharzia Worm." *Cairo Scientific Journal.*

[7] Kay, J. A. (April, 1910), "The Prognosis of *Bilharzia hæmatobia*." *Transvaal Medical Journal.*

[8] Conor, A. (July 13, 1910), "Sources thermales et bilharziose en Tunisie." *Bull. Soc. Path. Exot.*

previous work as regards skin infection with that worm, and cited the fact that Matsuura had accidentally infected himself by letting his skin come in contact with contaminated water. Schistosomiasis—*continued*

Turner [1] has described infection of the vermiform appendix, and finds the changes thereby produced resemble macro- and microscopically the vesical lesions much more closely than those found in the rest of the alimentary tract. He thinks it may only be common on the East Coast of Africa and in Central Africa.

Conor [2] has made some interesting observations on the miracidia. He finds moist heat (30–40° C.) necessary for the escape of the embryo from the egg and for its vitality. He finds it can live in water for 48 hours, but that drying proves rapidly fatal. Waters comparatively rich in sodium chloride and sulphate of magnesia do not kill the embryos, but soapy waters destroy them at once, one part of Marseilles soap in 1000 of water causing immediate death. This fact suggests an easy method of rendering infected urines harmless. The same author [3] at a later date treated cases with " 606," but, as might have been expected, without benefit resulting.

Tweifel [4] has recently carried out researches on the blood of bilharzia cases, and has compared his findings with those obtained in ankylostomiasis. Like other workers he found a considerable eosinophilia. His paper may be consulted for details. We would only note here that he finds the hæmoglobin content lower than in normal cases and in those suffering from ankylostomiasis. Goebel,[5] who gives a summary of the pathological changes, states that the eggs get into the tissues by rupture of the capillaries.

Schistosomum japonicum.—Reference has been made to some experimental work with this schistosome, and these notes need not be repeated.

Tsuchiya [6] describes the symptoms produced by this fluke as hepatic and splenic enlargement with diarrhœa, anæmia, and ascites. Dogs and cats are infected in endemic regions. The eggs are spineless. The worm inhabits the portal vein and its branches, but lays its eggs only in the intestinal wall. Some are carried by the blood-stream to the liver and produce cirrhosis. The onset is insidious, and patients are usually first seen when the disease is well advanced. It occurs in Japan, China, and the Philippines, and is treated by mild purgatives and change of locality.

Daniels [7] states that the eggs of *S. japonicum* may be found in the lymphatic glands in large numbers, causing hypertrophy and fibrotic changes, but no obstructive symptoms.

Phalen and Nichols [8] describe the hepatic changes as met with in cases in the Philippines. The cirrhosis is marked, and it is difficult to account for the destruction of whole lobules when only a few ova are present. Embolic plugging is put out of account owing to the very free anastomoses of the vessels. Possibly a toxin may play a part. They consider the marked differences in the pathology of bilharziasis and schistosomiasis may possibly depend on the locations of the parasites, the one being on the venous, the other on the arterial side of the portal circulation, and also on the morphological difference in the ova. Manson [9] has described a case in a European who had been resident in North China. Peake [10] gives a good account of the disease, and his summary of symptoms may be quoted with advantage.

(1) History of " malaria " and subsequent attacks of "fever."

(2) History of dysenteric attack, with pain, straining, mucus, and blood.

(3) Abatement of dysenteric symptoms, but in their place an irregular chronic diarrhœa, with a little blood-stained mucus, but no pain or straining.

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[1] Turner, G. A. (July, 1910), " Bilharziosis of the Appendix." *Transvaal Medical Journal.*

[2] Conor, A. (October 12, 1910), " Quelques particularités biologiques du *miracidium* de *Schistosomum hæmatobium.*" *Bull. Soc. Path. Exot.*

[3] *Idem* (January 11, 1911), " Bilharziose et '606.'" *Ibid.*

[4] Tweifel, E. (1911), " Blutuntersuchungen bei Bilharzia hæmatobia." *Arch. f. Schiffs-u. Tropen-Hyg*

[5] Goebel, K. (July 5, 1909), " Die pathologische Anatomie der Bilharzkrankeit." *Berl. Klin. Woch.*

[6] Tsuchiya, I. (1908), " Über eine neue parasitäre Krankheit (' *Schistosomiasis japonica* ')," etc. *Virchow's Arch. f. Path. Anat.*

[7] Daniels, C. W. (October 31, 1908), " Discussion on Lymphatic Conditions in the Tropics." *British Medical Journal.*

[8] Phalen, J. M., and Nichols, H. J. (July, 1908), " Notes on the Condition of the Liver in Schistosomiasis." *Philippine Journal of Science.*

[9] Manson, P. (November 16, 1908), " *Schistosoma japonicum* in a European." *Journal Tropical Medicine and Hygiene.*

[10] Peake, E. C. (March 1, 1909), " Three Cases of Infection by *Schistosomum japonicum.*" *Ibid.*

Schistosomiasis—*continued*

(4) Macroscopic similarity in the nature of the stools, due to large amount of undigested food passed.

(5) Microscopic evidence of infection by *S. japonicum* from the finding of ova in the fæces.

(6) Dyspeptic symptoms.

(7) Ascites.

(8) Enlargement of liver and spleen.

(9) Tenderness of liver and spleen.

(10) Listless, wearied expression of countenance.

(11) Extreme weakness, lassitude, and disinclination (even inability) for physical or mental effort; breathlessness on least exertion; sluggishness of the patellar reflex.

(12) Evident malnutrition and history of losing flesh.

(13) Sleep much disturbed by nightly-recurring fever and restlessness.

(14) Temperature usually sub-normal, but rising to 101° F. or more during night fever attacks.

(15) Marked eosinophilia.

He believes in infection through the skin, and cites the liver, spleen, mesentery and intestine as the organs for which the eggs have a special predilection. For those familiar with German the recent experimental work of Katsurada and Hashegawa [1] may be consulted. These authors have shown the susceptibility of the miracidia to acid salts, and have proved the "skin infection" theory correct.

Houghton [2] has some interesting notes on the disease. He states that greatly exaggerated knee jerks occur in practically every case, and thus, as will be seen, differs from Peake. He also mentions the lack of anæmia and of leucocytosis. Like Logan he thinks the ova of *S. japonicum* are more likely to be mistaken for those of *A. lumbricoides* than for ankylostoma eggs. The eggs of the schistosome are, however, very refractile, and they are sticky and gather debris. In the blood, leucocytes may adhere to them.

Additional Notes

Leiper [3] recently found a nipple-like knob or spine to be a constant characteristic of eggs of *S. japonicum*. This has led him to make a further study [4] of the spines in the ova of *S. hæmatobium*. The types encountered are illustrated, and his researches tend to support the view enunciated by Ward that there may be a separate species with normal lateral-spined egg, whilst an abnormal lateral-spined egg may be produced occasionally by *S. hæmatobium*. A good clinical paper on *S. japonicum* infection is the work of Skinner,[5] who describes two interesting cases, and gives the following list of conclusions :—

(1) From a consideration of cases of this disease met with in Hankow, in Chinese, and also of the two cases reported herewith, the writer inclines to the belief that in early or mild infections there are no certain symptoms or signs by which we can definitely diagnose the disease. It is probable that not merely may the eggs in the fæces be scanty and infrequent, but that in mild cases they may be absent for long intervals. (*See* Tsuchiya's paper for an account of the manner in which the eggs are deposited and the primary situations involved.)

(2) Gross lesions (nodular liver, enlarged spleen, ascites, and long-continued passage of foul, slimy, undigested stools) are to be expected in advanced cases, in heavy infections, in poorly-fed and hardworked natives. But we must be chary of looking for such symptoms in better-class patients and in foreigners.

Moreover, we must keep in mind that most cases of the disease that come to mission hospitals in China have, or have had, also other intestinal and blood parasites (helminth and protozoal). Further, ordinary hepatic cirrhosis is far from uncommon, at any rate in the district around Hankow. (In an autopsy on such a case I have failed to find evidence of any parasites or ova whatsoever after sectioning and examining microscopically liver, spleen, omentum, mesenteric glands, and portions of small and large intestine.)

(3) In this disease there seems to be no one type of clinical picture. Of many symptoms one or more may be in evidence, but varying from time to time—nausea, flatulence, pain after food, "painful hunger," sleeplessness, weakness, languor, anæmia, colic, epistaxis, recurrent dysentery, etc. Jacksonian epilepsy has been reported, but I have not seen it. Nor have I noted diminished reflexes. To what extent pyrexia and erythema or urticaria form part of the symptomatology is uncertain. True icterus is uncommon. It should be noted that ascites may result not merely from fibrosis in and about the liver, but also from endophlebitis and thrombosis in the portal veins.

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[1] Katsurada, F., and Hashegawa, T. (February 12, 1910), "Bemerkungen zur Lebengeschichte des *Schistosomum japonicum* Katsurada." *Cent. f. Bakt.*, Or., Vol. LIII., No. 5.

[2] Houghton, H. S. (June 15, 1910), "Notes on Infections with *Schistosomum japonicum*." *Journal Tropical Medicine and Hygiene.*

[3] Leiper, R. T. (March 1, 1911), "Note on the Presence of a Lateral Spine in Eggs of *Schistosoma japonicum*." *Ibid.*

[4] *Idem* (April 15, 1911), "Some Variations in the Character and Position of the Spine in Eggs of *Schistosomum hæmatobium*." *Ibid.*

[5] Skinner, A. H. (May 1, 1911), "Infection by *Schistosomum japonicum*." *Ibid.*

Schistosomiasis—*continued*

(4) The disease is widely different clinically from the Egyptian Schistosomiasis, and deserves a fuller description than that commonly given in text-books. The eggs may involve any part of the digestive tract below the diaphragm, including apparently invariably the liver. The worms have never been proved to exist outside the veins, and usually are confined to portal veins. Cases where adult worms have been found in the iliac and pulmonic veins are recorded.

(5) Prophylaxis as regards native labourers seems to be out of the question in a province like Hupeh, where the land is so widely inundated annually.

(6) Animals known to be infected should be destroyed wherever possible.

(7) As Logan points out, foreigners in the Yangtse valley should be warned to be most careful as to where they bathe, since the balance of evidence at present points to the cutaneous mode of infection.

It seems likely that over the vast area of Central China there are relatively few districts where the water is infected, but the disease has been reported from several provinces of China, so that it may prove to be much more prevalent than is now suspected in the East.

(8) With the increasing trade and traffic facilities in the Yangtse valley the endemic areas may increase, and more cases may be found every year.

(9) While the disease, as Tsuchiya points out, is not necessarily immediately or even remotely fatal, it is a very disabling disorder, and patients of the most infected class are only too liable to be re-infected.

Doctors attending patients from the Far East must bear this disease in mind, and, if examination of the fæces be negative in any obscure abdominal condition, the presence of eosinophilia should suggest repeated search for the ova.

Brayton [1] has signalised the presence of *S. hæmatobium* on the Isthmus of Panama, and, in a discussion on the paper, Darling speaks of the necessity of searching the lower part of the rectum for the adult worms.

Scorpion Sting. The introduction of an anti-serum for scorpion venom is one of the advances that has been made in this subject since the publication of the last Review.

An article detailing the collection of the toxin, the preparation of the antitoxin, and testing of the serum, and containing besides many useful and interesting points, is one by Todd.[2]

His conclusions are as follows :—

(1) The immunisation of suitable animals with scorpion venom gives rise to the production of an anti-venom.

(2) This anti-venom is capable of neutralising the venom when mixed with it *in vitro*, and also acts both prophylactically and curatively in animals.

(3) The venom is not fixed by the central nervous system as in the case with tetanus toxin.

(4) Calmette's anti-venine could not be shown to have any neutralising effect on the venom used.

(5) Employed curatively in man, the serum appears to have a very marked effect on the intense pain following the sting.

One of the sub-headings of his paper, "Use of the serum in man," is also of interest.

During the past summer a certain quantity of anti-scorpion serum has been issued to the government medical officers in Cairo, and to the hospitals of Upper Egypt for the treatment of cases of scorpion sting, and a number of reports on the subject have been received. The number of cases, however, concerning which full details are available is not yet sufficient to allow of any conclusions as to effect on the mortality, particularly, as it is very difficult to obtain any reliable statistics as to the percentages of deaths in untreated cases.

Out of twenty-three cases in the town of Cairo which were treated with serum, only one death occurred. This was in a child two years old, who was not seen until two hours after having been stung, The child then received 5 c.c. of serum, but unfortunately the only serum at the moment was a somewhat weak one, over a year old.

The general impression gained by those who have used the serum is very favourable, and almost all the reports note a very striking effect on the severe pain of the sting.

A quantity of this serum has very kindly been sent for use in the Sudan, where scorpion sting is not uncommon, but it is too early yet to come to any conclusions as to its effect on mortality here.

The occurrence of gangrene following scorpion sting is not unknown. Thorn [3] describes a case of very extensive gangrene of the foot and lower half of the leg in a native. The patient certainly did not seek medical aid until the gangrene was in a very advanced state. The condition was local, and not accompanied by general health disturbances, and there was no pain. An interesting feature of the case was that the initial wound was caused by a dead scorpion which had been dried up by the sun, but the sting of which accidentally entered the foot. The gangrenous condition is attributed to the venom causing local thrombosis. Todd states, however, that the venom does not appear to have any coagulative action on the blood.

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[1] Brayton, N. D. (1909), "Bilharziasis in the New World." *Proceedings Canal Zone Medical Association.*

[2] Todd, C. (April, 1909), "An Anti-serum for Scorpion Venom." *Journal of Hygiene*, Vol. IX.

[3] Thorn, G. (October 20, 1910), "Two Cases of Gangrene following Scorpion Stings." *British Medical Journal.*

Scorpion Sting—*continued*

As a rule scorpion sting in an adult is followed merely by brawny swelling and more or less collapse, though the latter condition is not usually seen in native patients, owing probably to some immunity. This immunity is in some cases developed to a very marked degree, being brought about by repeated scorpion stings. In children, especially under the age of 12, scorpion sting produces a condition not unlike tetanus. Chloroform narcosis has been used with good effect in some of these cases.

A stone which is supposed to act in a similar way to the absorbent snake stone of India, is sometimes used by the natives in Egypt. Usually, however, they make multiple small incisions and apply a ligature above the sting. For those who have no access to anti-venom, incision with a tourniquet above the sting, followed by lead and opium lotion, will generally be sufficient when treating adults.

For a work on Sudanese scorpions the reader is referred to a detailed illustrated paper by Werner in the Fourth Report of these Laboratories, Volume B.

Additional Note

Dr. Charles Todd, of the Public Health Department Laboratories, Cairo, has very kindly permitted the publication of the following interesting statistics of the results obtained by the use of his new serum for scorpion sting. This is the first record of the kind published.

STATISTICS OF CASES TREATED WITH ANTI-SCORPION SERUM

From 1906 to August 20, 1911

Age	Number of cases	Lived	Died	Death-rate %
From 0–5	44	41	3	6·82
„ 6–10	32	32	0	...
„ 11–15	15	14	1	6·66
„ 16–20	9	9	0	...
Over 20	58	58	0	...
	158	154	4	

The details of the four fatal cases are as follows :—

(1) Child aged 2 years . . . stung at noon. 5 c.c. serum 2 p.m.; died next morning } serum used more than a year old

(2) Infant aged 6 months . . . 5 c.c. serum 1 hour after sting; died half-an-hour later.

(3) Boy aged 11 years . . . 10 c.c. serum 8 hours after sting.

(4) Child aged 1 year and 8 months . serum 1 hour after sting; death 5 hours later.

N.B.—This case was in the oasis of Dakhla, and it is possible that the sting was either not that of a scorpion, or was of a scorpion of a different species to those usually met with in the Nile valley.

Scurvy. Mention may be made of a paper by Macrae,[1] entitled "Notes on Scurvy in South Africa." A few points in this paper are of interest, for he calls attention to the fact that pyrexia was very commonly present among the 200 cases occurring in natives that came under observation, and notes that this sign is not particularly emphasised in medical literature dealing with the subject of scurvy.

In the post mortem examinations the constant presence of ante-mortem thrombi in the heart and blood-vessels was striking, and appeared difficult of explanation, in the light of the fact that the alkalinity of the blood of these cases during life was diminished. Macrae does not commit himself to a definite opinion as regards the cause of this outbreak of scurvy, but

[1] Macrae, D. M. (June 27, 1908), "Notes on Scurvy in South Africa." *Lancet*

considers that the evidence connecting the incidence of the disease with a deficiency of fresh vegetables is more or less direct, while that associating it with defective meat is less direct than inferential. Scurvy—*continued*

Giorgi [1] has had an opportunity of studying a small epidemic of scurvy occurring in a children's hospital. The signs and symptoms which were in evidence would have been readily accepted as instances of Barlow's disease. Giorgi, however, is of opinion that, given the necessary conditions, scurvy (the same as occurs in adults) is not so very uncommon in children, and is not a specific kind of scurvy or rickets *per se*. In his cases the relation between improper feeding, either by absence of the anti-scorbutic elements or by insanitary surroundings, was marked.

The question of the relationship of beri-beri to scurvy has been mentioned by a few observers. Monteith [2] has a note on an epidemic of beri-beri with which he had to deal, and in which the symptoms pointed very strongly to a scorbutic origin. The epidemic occurred among the crews of pearling vessels after they had been several months at sea. A change of diet ameliorated the symptoms. An account of the post mortem changes is given, and he concludes by recording his opinion that beri-beri has many points in common with scorbutus and post-anæsthetic poisoning or fatty acid intoxication, arising from faulty glycogenesis and disordered tissue metabolism.

In Christiania [3] the relationship between scurvy, ship beri-beri and true beri-beri, has been the subject of much discussion. Holst holds that ship beri-beri is the result of living on foods deprived of their anti-scorbutic properties by boiling, drying, etc. Experiments on animals, clinical observations, and the study of the records of many writers and observers, would seem to confirm Holst in his opinions. He further supports his theory by showing that the comparative immunity enjoyed by Italian sailing vessels from beri-beri is due to the nature of their food, which contains wine and onions. In the direction of clinical evidence there appears to be little or nothing to help differentiation, but much to strengthen the similarity and uniformity between scurvy and ship beri-beri.

Knowles [4] has an interesting paper dealing with the treatment of a case of acute scurvy. The patient failed to respond to the ordinary lines of treatment that were available, and was transfused intravenously with an alkaline solution consisting of sodium chloride 1 ounce, calcium chloride 3 grains, sodium bicarbonate 1½ ounces, and water 1 ounce. One ounce of this solution was added to a pint of water at 105° F. Three and a half pints of this solution were slowly given, nearly an hour being occupied in the administration, during which time the patient's condition rapidly improved. Copious diarrhœa with slime and blood in the stools then came on. Every morning a soap and water enema was given, followed by the administration of two pints of the alkaline solution per rectum, which was usually retained. This rectal injection was carried on for a period of three weeks, the scorbutic condition readily improving, and the patient finally becoming convalescent. The results obtained in this case certainly indicate that this line of treatment should be carried out in cases of acute scurvy.

Additional Note

Mathis and Leger [5] have carried out a study of the hæmatology of beri-beri and scurvy. In the latter disease they found that (1) the polymorphonuclear leucocytes were about normal or subnormal in number, viz. 55 per cent. (2) There was an increase of lymphocytes almost as high as in beri-beri, the average being 34·6 per cent. (3) The large mononuclears did not deviate much in numbers from the normal. (4) The eosinophiles showed either a slight increase or averaged about the normal, viz. 6·8 per cent.

Sewage. One may say at the outset that only special papers are considered which are of interest to those working in the Tropics. The whole question of sewage is too comprehensive to be dealt with in this Review, but for the benefit of those who are further interested a short list of recent text-books dealing with the subject is given at the end of this short section.

Harvey [6] has an illustrated paper on a new cremator latrine system adaptable to

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[1] Giorgi (February 26, 1910), "Epidemic Scurvy and Barlow's Disease." Epitome, *British Medical Journal.*

[2] Monteith, J. (October 3, 1908), "The Relationship of Beri-Beri to Scurvy." *Lancet.*

[3] (May 2, 1910), "Scurvy, Ship Beri-Beri and True Beri-Beri." *Journal Tropical Medicine and Hygiene.*

[4] Knowles, R. (February, 1910), "A Case of Acute Scurvy." *Indian Medical Gazette.*

[5] Mathis, C., and Leger, M. (May, 1911), "Contribution à l'hématologie du béri-béri et du scorbut." *Bull. Soc. Path. Exot.*

[6] Harvey, F. (November, 1909), "A New Cremator Latrine System." *Journal Royal Army Medical Corps.*

Sewage—*continued*

places where no water carriage system exists. Briefly it consists of specially manufactured rectangular boxes or tarred calico bags which are placed on a slide or suspended under each latrine seat. Sawdust, wood shavings or chips, dried leaves, etc., are placed in each rectangular box or calico bag in small quantities, and again sprinkled on when the boxes are full and a small amount of crude oil of the paraffin series may also be added. The whole box or bag is then removed from under the latrine seat and placed inside an incinerator which must be of a special type. An estimate is given of the cost of such a system, which undoubtedly appears to be an efficient method for fixed or semi-permanent camping grounds, and for civil and military communities under colonial or tropical conditions.

Morris [1] has a practical paper dealing with the treatment of excreta in India by perchloride of mercury and incineration. The type of incinerator recommended is a cheap destructor of bricks, mud, and some improvised iron work. The urine is boiled in a boiler enclosed in the incinerator. Kerosene oil is recommended for the floors and woodwork of the latrines as a preventive against flies.

In an illustrated paper Skinner [2] gives a description of the type of incinerator used at Sialkot designed with a view to the complete combustion of human excreta, fæces and urine. Its cost is small. Illustrations and descriptions are also given in this paper of the type of incinerators for use with troops in the field.

Tate [3] gives an account, with illustrations, of a new type of incinerator devised by Beevor, in which dry and wet refuse are reduced to a dry ash on a portable iron framework. Its main advantage appears to be its portability, and it appears to have been an efficient incinerator in the station in which it was employed, but it is not stated how the system is worked when dealing with excreta.

Safford [4] has a paper on the incineration of fæces in India. The incinerator used is a rectangular brick type, cheap in construction, producing little smoke and inoffensive in operation. Fuel, however, is the difficulty, and dead leaves or other inflammable materials are used in the pans instead of dry earth.

Skinner,[5] in a more recent paper, has come to the conclusion that the "Sialkot" type of incinerator is the one which has afforded the cheapest and most satisfactory solution to the problem of incineration in India. In discussing the prevention of flies getting access to the latrines he recommends the use of kerosene oil in the latrine pans and the prompt removal of the excreta into a receptacle or fire where flies cannot approach it. He gives an illustration of a device to prevent flies breeding in the litter supplied for incineration. It consists of a cage placed seven-eighths round the circumference of a mud incinerator, the gap being left for access to the fire by the sweeper. The bottom of the cage is 1 foot from the ground. The fly larvæ present in the litter and manure drop through the cage to the ground, and they are swept up and burnt.

Reynolds [6] describes the type of incinerator used in Sanawar. It has given satisfactory results. The cost of construction is about 50 rupees, and the fuel is supplied by litter rubbish and pine needles. Layers of night soil alternating with layers of rubbish are incinerated together. The urine is disposed of in a shallow trench, 3 feet deep, covered with a corrugated iron sheeting containing a trap door, through which the urine is poured. Earth is heaped over the edge of the corrugated sheeting, and stamped down. According to Reynolds this plan works well, as there is no smell, and flies are not attracted.

A paper on cantonment sanitation is contributed to *Indian Public Health* by Morris,[7] who deals with the question of conservancy in Indian cantonments. He compares the working and results obtained by (*a*) the dry earth system, (*b*) the wet system, (*c*) incineration, and refers to the danger arising from the dry earth system, and to the difficulty and frequent impossibility of carrying out incineration during the rainy season. Figures are given in this paper showing the incidence and mortality from enteric fever during the periods when the dry earth, the wet perchloride, and incineration methods were employed, and they certainly

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[1] Morris, W. A. (April, 1909), "The Treatment of Excreta in India by Perchloride of Mercury and Incineration." *Journal Royal Army Medical Corps.*

[2] Skinner, B. (April, 1909), "The Sialkot Incinerator and Incineration in the Field." *Ibid.*

[3] Tate, R. G. F. (May, 1909), "A New Type of Incinerator." *Ibid.*

[4] Safford, A. H. (July, 1909), "A Note on the Incineration of Fæces in India." *Ibid.*

[5] Skinner, B. (January, 1911), "Incineration of Human Excreta: Further Observations." *Ibid.*

[6] Reynolds, L. (December, 1910), "Sanitation in the Hills." *Indian Medical Gazette.*

[7] Morris, W. A. (November, 1910), "Cantonment Sanitation." Quoted in *Journal Royal Army Medical Corps.*

Sewage—*continued*

show an enormous reduetion in the incidenee and mortality from enteric fever during the perchloride regime. In order to test the baeterieidal power of this perehloride, Campbell carried out some experiments with non-acidulated watery solutions of perehloride of mereury in varying dilutions mixed with a fæcal emulsion. The results of these are tabulated, and Morris eoncludes from them that—

(1) A solution of perchloride of mercury 1/500 is an absolutely safe bactericide with emulsified excreta from which urine has been decanted.

(2) A solution of perchloride of mercury 1/1000 inhibits bactericidal growth in emulsified excreta from which the urine has been dccanted, and is, with rapid removal and auxiliary incincration, an effective disinfectant.

(3) A solution of perchloride of mercury 1/1000 has neither bactericidal nor inhibitory action on bacillary growth, but prevents smell and infection by imprisoning and encasing bacilli in an albuminate of mercury casing. This action is purely mechanical, and with rapid removal and auxiliary incineration has a distinctly protective influence.

Some experiments were also carried out to test the bactericidal effect of cresol. In the dilutions employed it proved to be of no praetieal value as a disinfectant for excreta.

The question of the type of latrine suitable for the Tropics is an important one, and the reader is referred to a recent paper by King,[1] in which sectional diagrams of the latrine reeommended are shown. He advoeates the use of reinforeed cement conerete as a suitable material for the latrine platform. Part of his paper is quoted in full :—

Granted it be dctermined to use reinforced concrete, it is evident that the type of platform can be varied to meet individual ideas of sanitary requirements *ad libitum*. In the pattern shown in the accompanying figure there is presented a platform in a single solid slab, provided in its front aspect with a rapid slope which permits of the passage of urine to a drain, whilst behind there is the usual hole for fæcal matter. It is evidcnt that a platform of this nature may be supported at any height desired, by old iron rails vertically and horizontally, or, if these be not obtainable, by the less desirable substitute of wooden beams rendered as impervious as feasible by tar. The superstructure may follow the ordinary typcs of pent roofs with bamboo matting walls or corrugated iron ; or, if funds be not limited, reinforced concrete may be used throughout—lined in the interior with white tiles or white glazed bricks. Separate compartments, furnished with doors or half doors, may be multiplied, so as to make the total length of the latrine furnish the full accommodation required. If funds demand this economy, the upper and exposed surface may be finished off with a layer of polished cement, but, preferably, it should be lined in its exposed surface with white glazed tiles, and the pathway be similarly treated. Whatever modc be pursued, however, in thus securing a surface more fit than plain cement to withstand the accidental contact of urine, *on parts designed to receive or guide the urine*, it should be arranged to employ glazed earthenware, so fitted as not to prcsent exposed junctions. In the diagram there is exhibited a single slab of this material forming the front lining of the platform, together with foot-rests so approximated to the slab as not to expose the junction to urine contact. This slab and foot-rest arrangement has been made for me by Messrs. Burns & Co., Calcutta, at a cost of Rs. 5, and, presumably quantities could be delivered at less cost. The urine slab allows of a junction with an ordinary open glazed drain made by the same firm, at a cost of 4 annas per lineal foot. The collar shown forms a desirable lining of the defæcation hole ; it may be either of iron or glazed earthenware. A satisfactory result of thc design is the clear space below thc platform, permitting of free perflation and facility for cleansing ; owing to the thinncss of the slab at once constituting the pathway and platform, and the tcnuity of the nccessary supports.

As regards measurements adopted, thcy represent the minima desirable, and have been secured from actual practice. The object of the scanty room allowed per head is to ensure that squatting shall not occur on thc pathway or direct on the platform, but shall be precisely in the position that shall secure that fæces and urine, respectively, shall proceed solely in the desired direction. This result is brought about in part by the scanty area at disposal, but chiefly by the use of a slope from before backwards of the footrests, of a grade ascertained by measurements in practice not to induce a want of stability of the squatter or his discomfort.

The simple latrinc described may be used according to the usual method by placing a bucket below it, or a pan of the design shown in the diagram may be inserted so as to fit on the rim of the platform. In the latter case, it is possible to use the platform in hospitals for ward latrines, and in private houses for ı se by Asiatics at floor level.

An instruetive paper is one[2] dealing with the danger of untreated exereta in a eommunity where it is not known whieh persons are earriers of typhoid, amœba, hook-worms, asearis, etc. Experiments that have been carried out show that night soil containing live fly larvæ and hook-worm larvæ (*Necator americanus*), when buried 6½ inches under sterilised sand is not rendered innocuous, for these parasites make their way to the surface through the sand. A pail system for the use of a mixture of water and kerosene is strongly advocated, for it has been shown that several inehes of water with a film of kcrosene on the top is inhibitory to the development of the eggs of *Ascaris lumbricoides* and *N. americanus*. The odour is also reduced to a negligible quantity, the full effect being obtained by placing the mixture in the pail before use.

An interesting paper is that by Menzies,[3] entitled the "Sewage Disposal Problem," which may be read with advantage by all interested in this subject. Sections arc

[1] King, W. G. (July, 1910), "A Latrine for the Tropics." *Journal Royal Institute of Public Health.*

[2] (August 19, 1910), "Disposal of Excreta." *The United States Public Health and Marine Hospital Reports.*

[3] Menzies, F. N. K. (October, 1909), "The Sewage Disposal Problem." *Science Progress.*

Sewage—*continued*

devoted to the composition and the various methods of disposal of sewage, the latter being treated somewhat fully. The conclusions of the Royal Commission in regard to filter beds are stated, and may with advantage be quoted :—

Within ordinary limits the depth of a contact-bed makes practically no difference to its efficiency per cube yard, and it is generally inadvisable to construct contact-beds of greater depth than 6 feet, or less than 2 ft. 6 in.

For practical purposes, and assuming good distribution, the same purification will be obtained from a given quantity of coarse material, whether it is arranged in the form of a deep or a shallow percolating filter, if the volume of sewage liquor treated per cubc yard be the same in each case.

In the case of percolating filters of fine material, if the liquid to be purified were free from suspended and colloidal solids, and if thorough æration could be maintained, the same statement made in regard to coarse filters might also hold good of fine bacterial filters. But in practice these conditions can scarcely be maintained with large rates of flow, and therefore probably the greatest efficiency can be got out of a given quantity of fine material when arranged as a *shallow* filter.

Taking into account the gradual loss of capacity of contact-beds, a cubic yard of material arranged in the form of a percolating filter will generally treat about twice as much tank liquor as a cubic yard of material in a contact-bed.

Lucas [1] gives a very interesting description of the biological treatment of sewage in Egypt. The purification process employed consists of (1) passing the sewage into closed septic tanks. At four different works the sewage is treated by four different preliminary methods before reaching the septic tanks. (2) Passing the effluent from the septic tanks on to contact beds and percolating filters composed of clinker and basalt. Tables are given showing the chemical composition of the sewage before and after treatment.

The nett result expressed in figures is that a decrease (or purification) of from 94 to 100 per cent. is effected in the amount of suspended organic matter, of from 90 to 98 per cent. in the suspended inorganic matter, of from 7 to 41 per cent. in the dissolved organic matter, of from 6 to 53 per cent. in the free and saline ammonia, of from 67 to 93 per cent. in the "albuminoid" ammonia, and of from 58 to 85 per cent. in the "oxygen absorbed," together with generally an increase (purification) in the amount of dissolved inorganic matter and usually a formation of nitrites and nitrates (purification).

From the results obtained Lucas is of opinion that sewage purification, so far as the liquid passing through the treatment area is concerned, is principally the result of physical operations resulting in a mechanical separation of suspended and colloidal matter, first in the septic tank and secondly in the filters. Biological and chemical changes do take place, but principally in connection with the separated solids. Thus, hydrolysis and gasification occur in the scum and sludge in the septic tank, and oxidation and other changes in the solid matter separated in the filter.

A comparison is forthcoming of the results obtained at the different works, and an account of some few experiments is given in which 10 c.c. of various sterilising agents and electrolytes were added to the different effluents, and the sterility of the latter tested. This excellent paper is concluded by some tests to show whether the opalescence of sewage is due to finely divided sulphur held in suspension. Various samples of sewage were extracted with carbon bisulphide, and in every case some free sulphur was found to be present, but the opalescence did not appear to be due to this, and did not appreciably diminish on removing the sulphur.

A paper by Clemesha [2] deals with the "purification of native sewage under defined conditions." The experiments were carried out in small model septic tanks and model contact beds, and the sewage used was a concentrated one, composed of fæces and urine mixed with 50 gallons of water. The sewage was allowed to remain in four different septic tanks for definite periods of 24 hours, 36 hours, 48 hours, and 72 hours. Both the primary and the secondary contact-beds were filled with the same material. From the analyses and tests that were carried out the following conclusions were arrived at :—

(1) That of the four tank effluents, that derived from tank 1, which has a period of rest in the tank of three days, is in every respect superior to any of the others. Further, that the quality of the effluents from the four tanks varies with the length of rest of the sewage in the tank, so that not only is the effluent of tank 1 the best, but that of tank 4 the worst.

(2) That the action of these contact-beds, both in nitrifying the ammonia and in the removal of other materials from the sewage, renders the effluent thoroughly satisfactory for passing into any river or stream.

(3) That with comparatively simple arrangements a very great amount of purification can be obtained even in a very concentrated sewage. The effluent from contact-bed 2 is eminently satisfactory from a chemical point of view, in spite of the fact that the original sewage was much stronger than what is usually met with.

Various papers dealing with sewage disposal are discussed in the *Transactions of the Bombay Medical Congress*, 1909. Some of these have a direct bearing on the question of

[1] Lucas, A. (October, 1910), "Some Small Sewage Disposal Works in Egypt." *The Cairo Scientific Journal.*

[2] Clemesha, W. W. (May, 1910), "Note on the Purification of Native Sewage under defined conditions." *Indian Medical Gazette.*

sewage disposal in the Tropics. Fowler [1] has a useful paper on the "Treatment of Sewage under Tropical Conditions." He discusses first of all the effect of temperature in the Tropics as affecting the treatment of sewage, and considers that if the proper conditions of the treatment are maintained the effect of the higher temperature in the Tropics will be to facilitate purification as it is favourable to the decomposition and final nitrification of nitrogenous organic matter. An interesting contrast is shown by the analysis of European and Native sewage, the differences depending on the different habits of the natives, and their almost exclusive vegetarian diet. The paper is too lengthy to be discussed in detail, but the general conclusions with regard to the treatment of sewage may be quoted :— Sewage—*continued*

General Method.—In general the most suitable treatment will be preliminary fermentation in anærobic tanks, followed by final oxidation in percolating filters of fine material.

Design and Management of Tanks.—Special care is needed in the design and management of such tanks. In particular the capacity must be carefully considered in relation to the number of users rather than the volume of the sewage. It is desirable, where possible, to "inoculate" a new tank with deposit from a tank already in satisfactory operation.

Utilisation of Gas.—The gases evolved from such tanks are mainly derived from the decomposition of cellulose, and by taking certain precautions it is possible economically to utilise such gases for lighting and power purposes.

Rate of Filtration.—The effluent from tanks in satisfactory operation can be purified on percolating filters at ordinary European rates, and therefore the area of filters necessary need not be excessive

Aerobic Methods.—It has been shown that satisfactory purification can be obtained if the conditions remain essentially aerobic throughout. Such a method of treatment would appear to find its application chiefly in installations of a temporary character, or as a standby to deal with sudden increases of flow.

Final Treatment of Effluents.—Where there is danger of bacterial pollution at the outfall, it is advisable where possible to utilise the effluent for flushing latrines. Where this procedure is impossible sterilisation by hypochlorites can be readily accomplished, and if certain precautions are taken no difficulties need arise at the outfall on this account.

Dibdin [2] has a short and interesting paper dealing with the "action of a slate bed." Tables of experiments are given illustrating the rate of destruction on the slate beds of various solid matters (chiefly articles of diet), together with the microscopic findings which show what a varied fauna is present, from the lowest type of bacteria up to the highly organised worms and larvæ, etc.

A short paper by Fowler [3] considers the somewhat difficult problem of purifying sewage in order to prevent the growth of sewage fungus, which in itself may enter into decomposition with the production of nuisance.

Various instances are quoted, such as the production of sulphuretted hydrogen, the development of crenothrix, of gnat larvæ, worms, and various crustacea, and the measures that have been adopted to cope with them.

The following books recently published dealing with the subject of sewage disposal will be useful to those interested in the subject: *Sewage Disposal in the Tropics*, by W. W. Clemesha; *Drainage Problems of the East*, 2 vols., by C. C. James; *Modern Methods of Sewage Purification*, by Kershaw; *The Practical Management of Sewage Disposal Works*, by W. C. Easdale.

Additional Notes

Lumsden [4] has recently published a preliminary note on a simple and inexpensive apparatus for use in safe disposal of night soil.

The apparatus consists of the following parts :—

(1) A water-tight barrel to be used as a liquefier.

(2) A covered water-tight barrel, can, or other container to receive the effluent.

(3) A connecting pipe about 2½ in. in diameter, about 12 in. long, and provided with an open "T" at one end, both openings of the "T" being covered by wire screens.

(4) A tight box, preferably zinc-lined, which fits tightly on the top of the liquefying barrel; it is provided with an opening on top for the seat, which has an automatically closing lid.

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[1] Fowler, G. J. (1909), "The Treatment of Sewage under Tropical Conditions." *Transactions Bombay Medical Congress.*

[2] Dibdin, W. J. (1909), "The Action of a Slate Bed." *Ibid.*

[3] Fowler, G. J. (June, 1910), "Sewage Purification in relation to the Growth of Sewage Fungus." *Journal Royal Institute of Public Health.*

[4] Lumsden, L. L., "A simple and inexpensive Privy." *United States Public Health Reports*, Vol. XXV., No. 45. Quoted in *Journal Tropical Medicine and Hygiene*, May 15, 1911.

Sewage—*continued*

An anti-splashing device, consisting of a small board placed horizontally under the seat and 1 in. below the level of the transverse connecting pipe ; it is held in place by a rod, which passes through eyes or rings fastened in the box, and by which the board is raised and lowered. The liquefying tank is filled with water up to the point when it begins to trickle into the effluent tank.

As an insect repellant a thin film of some form of petroleum may be poured on the surface of the liquid in each barrel.

When the privy is to be used, the rod is pulled up so that the anti-splashing board rises up to within 1 in. below the surface of the water. The fæcal matter falls into the water, but this board prevents splashing, and thus meets one of the greatest objections thus far raised to the wet system. Fly-breeding and feeding are prevented by the lid, the water, and the film of oil. This oil also prevents mosquitoes breeding. The fæcal matter becomes fermented in the water and gradually liquefies ; the addition of excreta naturally raises the level of the liquid, and the excess flows into the effluent tank, where it is protected from insects by the cover and the film of oil. This device solves the fly and mosquito problem so far as the privy is concerned. It liquefies fæcal matter and reduces its volume so that it may be safely disposed of more easily and cheaply than night soil. It reduces the odour, and reduces the labour of cleaning the privy. It is simple and of inexpensive construction.

The effluent can be disposed of by boiling, or burial, or by chemical disinfection previous to burial, when necessary. Toilet paper seems to be digested by the process. It is estimated that the amount of sludge from the dejecta of a family of five people would not be sufficient to require the cleaning of the liquefying tank oftener than once in six months to a year.

Lelean,[1] in continuation of his remarks on incineration in the field, refers to the essentials for a field service incinerator :—

(1) It must be of a closed type, ensuring rapid, economical combustion ; (2) strength to survive an average Indian campaign of three months ; (3) lightness for convenient human and animal transport ; (4) cheapness that permits of " scrapping " without economic scruples when its work is done.

He then describes two types of incinerators, with illustrations, and recommends that a chimney with a cowl be attached so as to prevent heavy rain interfering with the incineration process.

Type (*a*) forms a 2-ft. cube on four short legs. The sides are of sheet-iron, the base a grid ; the cover is of sheet-iron, with a swivel-lidded feed-hole and a hole for a 2-ft. high chimney.

Type (*b*) consists of grid and cover. The grid is laid in a trench which is covered by two-sheet iron shells, placed end-to-end to form a roof and shallow sides. Each roof section has a swivel-lidded feed-hole, and one has also a hole for a 2-ft. high chimney.

Under favourable conditions two such incinerators can dispose of the fæces and urine passed during defæcation by 900 men. Both of these were reduced to ash in four hours with a daily expenditure of the litter of 236 animals plus line sweepings and the contents of kitchen grease-traps.

Lelean discusses the details of the working of these incinerators, their cost and their applicability to active service conditions. Illustrations are given in this paper, and to those interested in field incineration it is one well worth perusal.

Skin Diseases. Under this heading only those cutaneous affections are considered that are met with in tropical or sub-tropical countries.

A paper dealing with the " Prevention of Prickly-heat Miliaria " [2] appears in the *Journal of Tropical Medicine and Hygiene.* As this is a common and frequently distressing skin condition affecting Europeans in the Tropics, the suggestions given in this paper, which are quoted in full, may be studied with advantage.

A frequent cause of prickly heat is drinking fluids to excess during hot weather. Aerated waters especially are provocative ; iced drinks add to the tendency, but plain water will bring out the skin eruption readily when taken in quantity. Coarse flannel undergarments also, in even temperate climates during hot weather, tend to set up prickly heat, and everything points to the ailment being provoked by the quality or nature of the underclothing.

In temperate climates, then, light woollen (or so-called woollen) garments next the skin should be worn during very hot weather. In tropical regions a light, open-textured vest of silk or cotton or linen, and a light flannel shirt is the proper equipment to wear at all times. In sub-tropical countries the same clothing is required during the hot weather as in tropical climates, but when the cold season comes round the underclothing and shirt must be adapted to the climatic necessity, and should approach as nearly as possible to the apparel in use in Britain in summer.

The covering for the loins and lower limbs remains a vexed question. Even in temperate climates drawers during cold weather are not worn by a few of the less rational young men who are " hardening " themselves, as they style it. This only leads to trouble, such as albumin in the urine from kidney congestion, to hepatic congestion, digestive upset, and occasionally jaundice. The commonest cause of albumin in the urine found in young men in Britain who come up for insurance examination or for inspection previous to being sent abroad is want of sufficient clothing. A young man presenting himself for examination who wears neither undervest nor

[1] Lelean, P. S. (June, 1911), " Incineration in the Field." *Journal Royal Army Medical Corps.*

[2] (June 15, 1910), " The Prevention of Prickly-heat Miliaria." *Journal Tropical Medicine and Hygiene.*

Skin Diseases—*continued*

drawers will in 80 per cent. of cases be found in a condition in which it is impossible for the doctor to pass him. His temperature will be found to be increased, amounting to one, two, or even three degrees almost constantly, a rapid and sometimes an irregular action of the heart, frequently albumin in the urine, a pallid aspect, and lined or drawn features.

In tropical and sub-tropical countries it is wise also to wear at least short drawers, although few do so. The texture should be of the same open texture as that recommended for the vest. If no drawers are worn, at least a loin-cloth should be worn so as to keep the scrotum from touching the inner aspects of the thighs, and thus prevent the tendency to eczema intertrigo. It is well also to keep the inner aspects of the hips apart, as post-anal eczematous cracks and fissure are apt to occur, the discharge from which reaching the anus is in danger of generating that most difficult of diseases to cure, pruritus ani. In fact, for this troublesome complaint it is imperative to prevent opposite surfaces touching each other, for without this precaution powders and ointments are useless.

No medicinal remedies are suggested, but one notes that Castellani [1] recommends the free use several times daily of a salicylic-alcoholic lotion (ac. salicylic, ʒi.; spir. rect., ʒviii.), followed by the general application of a salicylic or boracic powder, such as ac. salicyl., grs. x.; talci, ʒi.; ac. borici, ʒi.; talc. veni, ʒi. Greasy preparations should be avoided. After the eruption is cured the patient should be directed to use some Condy's fluid, cyllin, or other disinfectant in the bath, and afterwards to apply one of the powders mentioned.

Howard [2] has a paper on "Some Types of Tropical Ulcers as seen in Nyasaland." This paper deals chiefly with the non-infective types, and gives an account of the clinical signs of these ulcers and the treatment usually employed.

Under the title of "Tropical Dermatomycoses" Castellani [3] has an excellent and illustrated paper in which the skin diseases due to the fungi of the genus *Tricophyton* are described. It is not necessary, however, to quote from this paper, as the tropical dermatomycoses are more fully considered and illustrated in the text-book by this observer and Chalmers.

Two recent papers by Castellani [4 & 5] describe the method of cultivating the fungus of *Tinea imbricata* (*Endodermophyton concentricum*), and the appearances of the growth in the different media employed. During his earlier investigations this observer was of the opinion that there was a plurality of species of fungi which produced the disease. His subsequent researches have proved this, for in Ceylon two different species can be differentiated, *Endodermophyton concentricum*, and *Endodermophyton indicum*. It may be noted here that the genus *Endodermophyton* was established by Castellani to denote the hyphomycetes of *Tinea imbricata* and *Tinea intersecta* which are characterised by their growing between the superficial and deep strata of the epidermis forming an interlacing felt of mycelium which detaches the horny and granular layers from the rete Malpighi.

The microscopical and cultural characters of *E. concentricum* and *E. indicum* are described in full.

E. concentricum.

Preparations in liq. potass. from scales show a felt of interlacing mycelial tubes, the segments are rather regular in shape, somewhat square-shaped, and usually straight. If the liq. potass. be left to act some time, the mycelial articles, which are of very variable length, and $2\frac{1}{2}$ to $3\frac{1}{2}$ μ in breadth, will be seen to have a double contour.

Aspergillus-like fructifications are always absent. Fresh preparations from young cultures show abundant septate mycelium, with rather long, straight articles; in old cultures the shape of the mycelial tubes may be irregular. In hanging-drop cultures (Sabouraud's broth), long mycelial septate threads are seen, no free spores. Reproduction apparently is by sprouts from the mycelium, branching taking place.

The cultural characters on solid media, when the growth is fifteen to twenty-one days old, are as follows:—

Glucose-agar (4 per cent.).—Growth abundant, surface cerebriform or crinkled. The growth and the medium show a slight amber colour which later on may become of much deeper hue. No duvet.

Sabouraud-agar.—Growth comparatively scanty, whitish-grey, mostly submerged. The colonies have generally a small central knob, and never show any duvet. The submerged portion is very firmly imbedded, and presents projections deepening in the medium; colour of the medium unchanged.

Mannite-agar (4 per cent.).—Appearance somewhat similar to glucose, but growth less abundant. The medium may take a slight amber colour. No duvet.

Saccharose-agar (4 per cent.).—Growth rather scanty, similar to Sabouraud. Duvet absent.

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[1] Castellani, A., and Chalmers, A. J. (1910). *Manual of Tropical Medicine.*

[2] Howard, R. (August 15, 1908), "Some Types of Tropical Ulcers as seen in Nyasaland." *Journal Tropical Medicine and Hygiene.*

[3] Castellani, A. (September 1, 1908), "Tropical Dermatomycoses." *Ibid.*

[4] *Idem* (December 15, 1910), "The growth of the fungus of *Tinea imbricata* (*Endodermophyton concentricum*) on Artificial Media." *Ibid.*

[5] *Idem* (March 15, 1911), "Further Researches on the Hyphomycetes of *Tinea imbricata.*" *Ibid.*

Skin Diseases—*continued*

Glycerine-agar (4 per cent.).—Similar to Sabouraud; when the colonies coalesce, the growth shows a knobby surface. No duvet.

Nutrose-agar (4 per cent.).—Slow growth, separate young colonies have a central knob; when they coalesce, a knobby mass is formed.

Agar.—Scanty growth, somewhat similar to Sabouraud. No duvet.

Maltose-agar (acid).—Similar to Sabouraud.

Maltose-agar (alkaline).—Similar to Sabouraud.

Adonite-agar.—Not very abundant, cerebriform. Duvet absent.

Galactose-agar.—Knobby or cerebriform.

Levulose-agar.—Knobby.

Raffinose-agar.—Cerebriform.

Inuline-agar.—Cerebriform.

Saccharine-agar. (4 per cent.).—Somewhat knobby surface. Duvet absent.

Lactose-agar.—Similar to Sabouraud; but surface growth more abundant.

Gelatine.—Very slow liquefaction of the medium.

Milk.—Very scanty growth, after a time the medium becomes separated.

Sugar Broths.—(Maltose, lactose, etc.), slight growth at the bottom of the tube, no production of acid or gas.

E. indicum.

The microscopical appearance of this fungus is to all purposes identical to that of *Endodermophyton concentricum.* The cultural characters on solid media, when the growth is between fifteen and twenty-one days old, are as follows:—

Glucose-agar (4 per cent.).—Growth fairly abundant, with surface somewhat convoluted or furrowed—portion of the growth, often the central, is of a deep orange or pinkish-orange, or reddish-orange colour. The surface of the rest of the growth appears white and powdery, being covered by a very short delicate duvet.

Sabouraud-agar.—Slow growth, white powdered surface either with central knob or furrowed. The growth does not deepen in the medium so much as *Endodermophyton concentricum.*

Mannite-agar.—Growth knobby or convoluted, covered by white short duvet.

Saccharose-agar.—Cerebriform, covered by white duvet.

Saccharine.—Crinkled surface, delicate white duvet present.

Maltose-agar (acid).—Somewhat similar to Sabouraud, but the surface-growth is more abundant.

Maltose-agar (alkaline).—Similar to acid maltose, but the white duvet is more abundant.

Lactose-agar.—Knobby surface covered by snow-white duvet.

Glycerine-agar.—Growth abundant, yellowish or amber colour, delicate white; short duvet present on some portions of the growth.

Nutrose-agar.—Yellowish surface, crinkled; short white duvet present.

Agar.—Growth fairly abundant, knobby surface covered by snow-white, very short delicate duvet.

Levulose-agar.—Scanty growth, yellow or orange, scarce, very short white duvet present.

Raffinose-agar.—Same appearance as galactose.

Inuline-agar.—Same appearance as in galactose and raffinose agars.

Adonite-agar.—Cerebriform, surface covered with snow-white duvet.

Gelatine.—Very slow liquefaction.

Litmus Milk.—Very scanty growth (after a time the medium may become separated).

Various Sugar Broths (Maltose, lactose, etc.).—Slight growth at the bottom of the tube. No production of acid and gas.

Comparison between the Cultural Characters of Endodermophyton concentricum and of Endodermophyton indicum.

The annexed Table shows at a glance the different cultural characteristics of the two fungi in the principal media.

Media	E. concentricum	E. indicum
Glucose-agar	Amber colour, duvet absent.	Deep orange, with occasionally pinkish hue, white, very short delicate duvet present.
Sabouraud-agar ...	Growth scanty, mostly submerged, grey-whitish, duvet absent.	Surface growth more abundant, powdery white.
Agar	Scanty, mostly submerged, similar to Sabouraud-agar, no duvet.	Fairly abundant, knobby, well-marked snow-white duvet.
Glycerine-agar	Growth mostly submerged, surface growth very scanty, similar to Sabouraud-agar, no duvet.	Surface growth very abundant, crinkled appearance, white short duvet present.

Skin Diseases—*continued*

Castellani was successful in producing the disease in human beings by inoculating cultures either of *E. concentricum* or of *E. indicum*.

Mention may be made of a new epidermophyton isolated by Castellani from two cases of the so-called eczematoid type of *Tinea cruris*. This observer has given the name *E. rubrum* to it. It is characterised principally by the deep red pigmentation of its growth in glucose, Sabouraud and mannite agars, while in ordinary agar the growth is white. The pigmentation is remarkably persistent. Its microscopical characters are very similar to those seen in *E. cruris* and *E. perneti*.

Roberts [1] has a very interesting paper on the diseases of the domesticated animals communicable to man. He classifies them as being due to four types of organisms: (1) Bacteria, (2) mould fungi, (3) parasites belonging to the insect family, (4) parasites belonging to the spider family, and he has stated that—

"In connection with skin diseases of bacterial origin nearly the whole work of investigation still remains to be carried out. To this class belongs the so-called horse pox, which is readily transmissible from horse to man, and in all probability is of the nature of an impetigo. The mould fungi could be conveniently termed the 'keratomycetes,' as this included all the fungi which in varying degrees had the power of vegetating in the horny epidermis. Morphologically, its members presented a series of gradations in organisation from the microsporon at the one extreme to favus at the other. The microspora had been observed in man and in many of the higher vertebrates. The microsporon of the dog and the cat could pass indiscriminately from the one to the other, and to man, and vice versa. Tricophyton of the scalp, the author had seen acquired from a parrot, and tricophyton of the beard was nearly always contracted from the horse or cow. Ringworm might be acquired by the skinning of a dead animal. Many epidemics of keratomycetic disease among human beings yet of animal origin were on record. Roberts described the differences in the ringworms of different animals, and gave illustrations of their transmissibility to man, but the symptoms in animals were simpler and more uniform than in man. In animals, achorion produced symptoms similar to those in man, but transmission from animals to man was somewhat rare. The sarcoptes of animals were transmissible from one to another as well as to man, while the human sarcoptes was transmissible to horses. It was from the horse more frequently than from any other animal, excepting their fellow-men, that human beings acquired scabies."

Schomberg [2] draws attention to a condition of the hands and sometimes of the feet which is of importance to practitioners in the Tropics.

When sweating is pronounced, it is not uncommon to find pinpoint-sized, whitish scaling, which, as a result of peripheral extension, produces an annular exfoliation of the superficial horny layers of the skin of the hands. Several of these rings may be present, which may coalesce and produce large serpiginous patches. The condition is usually limited to the palmar and lateral surfaces of the hands and fingers, although a similar condition may occasionally be met with in the feet. The recognition of such a condition from simple sweating is important, as one is prone to consider lesions of the kind due to parasitic infection, and to take extreme steps to cure the ailment, or to insist upon isolation, in case others should acquire the disease. The condition is allied to sudamina, the appearance in the hands being merely due to the thickness and dryness of the epidermis of the hand.

Hale [3] has a useful paper on the treatment of Bromidrosis in the army. He recommends the following:—

Patient detained for the day, but first sent back to barracks for all his socks, boots, and shoes. All socks to be soaked for one hour in 1 in 2000 perchloride solution, and then well rinsed three times in hot water, and finally well washed. The inside of soles, vamps, quarters, and counters of boots to be painted with the following solution by a camel-hair brush.

Acid salicylic	1 ounce
Methylated spirits	4 ounces.

The shoes to be similarly painted. The feet to be well washed, and then thoroughly dried and painted with the above solution over the whole of the red area of soles, heels, and sides of the feet, not omitting any red patches which may be found between the toes and under them. The feet, after being thus painted, look thoroughly "snowed" from deposit of salicylic acid when the spirit has evaporated. A dried, clean, or new pair of socks can then be put on, and next morning the feet are repainted in the same way. When the feet are inspected, the great change from the former raw, grazed, sweaty surface is evident. The medical officer, at his inspection of the feet should thoroughly satisfy himself that there are no red areas between the toes that have not been treated, and if any are found, they should be at once well painted over.

Jones [4] has a short illustrated paper on the skin lesions caused by the hydroids of the hydrocoralline millepores.

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[1] Roberts, L. (October 24, 1908), "Diseases of the Domesticated Animals Communicable to Man." *British Medical Journal.*

[2] Schomberg, J. F. (October 17, 1908), "Sweat Desquamation." *Journal American Medical Association.*

[3] Hale, C. H. (June, 1910), "Bromidrosis of the Feet." *Journal Royal Army Medical Corps.*

[4] Jones, F. W. (March 13, 1909), "The Skin Lesions caused by the Milleporæ." *British Medical Journal.*

Skin Diseases—*continued*

The stony colonies of these hydrocorallines are generally called "corals" by the dwellers on coral reefs, and the Malays have given them the name of "Karang gatal," or itchy corals. In most of their obvious characters these colonies closely resemble the harmless madropore corals, which possess no power of causing skin lesions. In the case of the millepores, the injury is inflicted by numerous thread cells, whose spent threads may be seen waving over the surface of colonies kept under observation, and the injury that they cause may be very severe.

The immediate signs of contact with a colony are acute erythema and severe pain. In cases in which the contact area is large, papules rapidly form and become pustular, and a very extensive desquamation follows.

In the case figured, the flexor surfaces of both forearms were extensively affected. The patient was a Chinaman, who, in his efforts to avoid being knocked down by a wave, had grasped a colony of the millepore. Large pustules formed later on the sites of the stings, and the desquamation was extensive. One curious feature of the lesion is its lasting nature, for the site of a sting will remain red, and will sweat profusely, for more than a fortnight after contact with the colony. It is of interest that the different species of the species millepora possess different powers of stinging, and the sting of the species *Alcicornis* is more severe than that of *Complanata* or *Verrucosa*.

In the *Polyclinic*, Hutchinson [1] discusses the subject of leucoderma, and is inclined to consider that the white patches are aggressive in the majority of cases. Its etiology is still unknown, and it is probably of the nature of a trophoneurosis. Renshaw [2] is of opinion that leucoderma can be explained by palæogenesis, and considers that the clinical association of leucoderma with alopecia areata and dermatitis atrophicans is rather in support of the palæogenetic theory. Castellani [3] has noted the appearance of leucodermic patches following a burn and the application of a caustic, and they may also develop in chronic epiphytic skin diseases. In the Sudan a few cases have been observed among syphilitic patients. As regards the treatment, Castellani recommends arsenious acid in a pill ($\frac{1}{50}$ gr.), three to six times a day, or injections of atoxyl. The white colour of the patches may be partially hidden by the application of a lotion of silver nitrate or potassium permanganate, or by tattooing.

Cleland,[4] in collaboration with Hickinbotham, has an illustrated paper on ulcerative granuloma of the pudenda as it occurs in the aboriginal natives of Western Australia. Males are also affected, the disease commencing as small round nodules on the glans penis, varying in number from one or two to a condition in which the glans is thickly studded with them, presenting a tessellated cauliflower appearance. The nodules are prone to ulceration. The skin of the penis, scrotum, and adjacent parts of the thighs may become affected, accompanied by suppuration of the adjacent lymphatic glands, leading to a granulomatous type of ulceration, which spreads peripherally. The initial lesions in women consist of one or more condylomatous plaques which may occur on any part of the vulva. Cases occur presenting every degree of severity between an ordinary condyloma of the anal margin or of a labium majus, and a large granulomatous ulcer involving the whole of the vulva and adjoining skin, and by the destruction of the perineum and the intervening septa uniting the bladder, vagina, and rectum into one large cloaca. In these cases three processes go on side by side, viz., granulomatous growth, ulceration, and cicatrisation. Cleland describes the pathological changes present, and the finding of spirochætes in some of the material sent for examination. These spirochætes he assumed played a part in the etiology of the disease, and considered that there was no question of doubt as to the usual means of transmission being venereal. Carter,[5] however, in a more recent and illustrated paper, states that ulcerating granuloma of the pudenda is not a venereal disease. He employed the following staining method for sections removed from the growths, and as a result of his findings concluded that the disease was due to a protozoal infection :—

Thin sections fixed to a slide are stained in a solution of Giemsa diluted 12 drops to 10 c.c. of distilled water. After this stain has acted for 20 minutes each section is washed in tap water for about 30 seconds, then dipped in eosin solution, 1 in 50,000 for 45 seconds, dehydrated, and brought up through xylol into Canada balsam. The second method is to stain a fixed section with a saturated solution of eosin in alcohol (95 per cent.) for five minutes; the solution must be three months old. The stained section is then washed in distilled water, and counterstained with watery methylene blue, 1 in 1000, until the nuclei are stained deep blue. The slide is then washed in absolute alcohol for a few seconds, and taken up through xylol into Canada balsam.

The first thing that strikes the eye will be that in certain areas lie masses of very large mononuclear cells, their cytoplasm distended with from 15 to 50 bean-shaped bodies resembling the gregariniform stage of a herpetomonas or crithidium. On using the higher powers of the microscope these bean-shaped parasites are seen to contain the usual cytological elements. The parasite, though slightly smaller than that seen in sections of Oriental sore, is very similar, and in the light of the recent work on Oriental sore, showing the crithidial monadine forms, etc.

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[1] Hutchinson, J. (September, 1910), "Leucoderma in Dark Races." *Polyclinic.*

[2] Renshaw, G. (January 21, 1911), "Leucoderma and Palæogenesis." *British Medical Journal.*

[3] Castellani, A., and Chalmers, A. J. (1910). *Manual of Tropical Medicine.*

[4] Cleland, J. B., and Hickinbotham, J. R. (May 15, 1909), "On the Etiology of Ulcerative Granuloma of the Pudenda." *Journal Tropical Medicine and Hygiene.*

[5] Carter, R. M. (October 15, 1910), "Ulcerating Granuloma of the Pudenda a Protozoal Disease." *British Medical Journal.*

Skin Diseases—*continued*

assumed by this protozoon, I consider that the parasite of ulcerating granuloma is of the same class, and will be found similarly to develop monadine and gregariniform phases in suitable culture media. For the present I propose, therefore, to consider ulcerating granuloma of the pudenda as due to a localised protozoal infection of man with either a herpetomonas or crithidium.

The parasites are found in large swollen cells, in which the nucleus is pushed to one side of the cell. The cytoplasm of the infected cells contains from 15 to 50 protozoal parasites arranged roughly in groups of 15 to 20, round a central homogeneous mass simulating the zooglea mass of Leishmania in cultivation. No flagella have been noted, but the fact that a deep staining dot lies external to and in close relationship with what seems to be the more mature form of the parasite is highly suggestive. The nuclei of the parasites stain a deep reddish violet, the dot almost black violet, and the cytoplasm of the parasite pale blue. The rest of the tissues in the neighbourhood of the infected area stain light blue. Lastly, it is interesting to note that each parasite seems surrounded by a faint unstained area suggestive of the similar appearance seen in staining for Negri bodies.

Bruce [1] has recently given a short description of the Zambesi ulcer which is met with among the natives working in the Zambesi delta. It chiefly attacks field workers, and is rarely to be found elsewhere than in the foot or lower two-thirds of the leg. In its typical form it is a single shallow, punched out, round or oval ulcer about the size of a florin, with a slightly undermined edge, a soft base, and a flat purple coloured floor. A few show a fungating mass, others vary in size, and may extend more than half-way round the leg. Apparently it commences as a tender œdematous local swelling, which in about twenty-four hours time has a slough in its centre. The cavity of the ulcer is frequently filled with a purple gelatinous material resembling blood-stained mucus. No constitutional disturbance results, nor is there any concomitant enlargement of the lymphatic glands. The ulcer usually lasts for a week or more, and then heals by granulation. Bruce has found large numbers of spirilla associated with large fusiform bacilli, almost to the exclusion of any other organisms, in the lesions.

Kennan [2] has a paper on acute craw-craw as seen on the west coast of Africa. In certain cases the papulo-vesicular eruption spreads with great rapidity, and, being associated with fever and malaise, the condition simulates either variola or varicella. His description of acute craw-craw is as follows :—

The rash may be practically universal, and is vesicular in the very early stage. The vesicles have very little, if any, papular foundation, and always lack the well-defined base of a typical variola spot, and, moreover, the spot is vesicular at the earliest period. Pricking the vesicle in the early stage allows exit of a sticky, pellucid fluid, and the vesicle can be entirely emptied by slight pressure without further rupture of its walls, leaving the latter collapsed. In the early stage of the case the great majority of the spots show an almost equal degree of development, but careful search will usually reveal some dried up, scaly spots. The centre of each of these old spots is generally of a lighter colour, and round the centre iris-like rings of epidermic scales, attached by their outer borders are seen. These represent a late stage of the vesicular condition, and may, I believe, be the source from which auto-infection may become general.

A day or so after the first outbreak of vesicles, fresh vesicles are formed between the older ones, and fresh spots continue to appear for a week or so.

A few of the spots suppurate slightly, but definite adherent scabs are rare. A vesicle may show umbilication when a fine hair emerges from its centre.

The temperature is raised early and before any suppuration has appeared, and there is no "secondary" fever.

Constitutional symptoms are definite but slight, and no more than would be expected to accompany the moderate degree of fever usually present (100° to 102° F.), and which lasts for a few days only. Itching is not generally a marked symptom, and is usually not present till the later stage; it is rarely intense, and it usually ceases before the rash has entirely disappeared.

The face may be attacked, but usually less so than other parts; the palms of the hands and soles of the feet usually escape, the fingers show few if any spots. Disappearance of the rash with desquamation of the epidermis of the affected parts is slow and protracted, and even with frequent bathing and friction the skin may still show signs of the rash for a month or six weeks, or even longer. No pitting or discoloration is found afterwards. The mucous membranes are not usually affected, though I have seen spots on the prepuce and glans penis. The progress of vaccination is not influenced by the disease.

Lebœuf [3] gives a clinical description of the phagedænic ulcer met with in the French Congo. Spirochætes and the *B. fusiformis* were present in the purulent discharge exuding from the ulcers. Patterson [4] describes an epidemic of phagedænic ulcers in Assam, and the treatment employed, which gave the best results, was as follows :—

After douching the ulcer with hot water to clear off all exudation and debris, the grey base was thoroughly swabbed with pure carbolic acid and the air occluded with a dressing of carbolised vaseline or oil. As a rule, several applications of carbolic acid were necessary before the false membrane was completely destroyed. The oily dressings were continued until the granulations were flush with the surrounding skin. At this stage a thin

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[1] Bruce, W. J. (January 2, 1911), "Zambesi Ulcer." *Journal Tropical Medicine and Hygiene.*

[2] Kennan, R. H. (March, 1910), "Acute Craw-Craw." *Annals Tropical Medicine and Parasitology.*

[3] Lebœuf, A. (June 10, 1908), "Ulcère phagédénique au Congo français." *Bull. Soc. Path. Exot.*

[4] Patterson, R. L. (November, 1908), "Notes on the recent Epidemic of Phagedænic Ulcers in Assam, with remarks on a Bacillus present in the Sores." *Indian Medical Gazette.*

Skin Diseases—*continued*

sheet of lead, well oiled, was bandaged over the affected area, flattening all exuberant granulations and preventing the skin edges from becoming raised and indurated. Final healing was undoubtedly quicker and sounder under this lead plate than under any other dressing. The ordinary lead lining of tea boxes was used, and proved entirely satisfactory. To discard perchloride lotion and other tried antiseptics for the old-fashioned carbolic oil savours of heresy, but I am convinced that an oily dressing is best suited for this kind of ulcer. Vaseline with the addition of eucalyptus oil and iodoform was used in some of the hospitals, and gave satisfaction. If the specific bacillus is ærobic, possibly the occlusion of air may be unfavourable to its growth.

Occasionally in some of the larger ulcers healing was greatly delayed by the granulations degenerating into an unhealthy gelatinous surface unfavourable to skin growth, the surrounding skin edge forming a raised, almost cartilaginous ring. In these cases curettage and trimming, under an anæsthetic, followed by application of the lead plate, gave good results.

In this epidemic Patterson observed that the ulcers were not necessarily associated with debilitated or cachectic conditions of the patients. He concludes his paper by a description of a Gram-positive bacillus which he found constantly present in the phagedænic sores. Morphologically, it resembled *B. mallei*.

Stevenel,[1] as the result of his investigations on craw-craw in Zinder, has arrived at important conclusions, for he has proved that the phagedænic ulcer of tropical countries, craw-craw and oriental sore are identical conditions resulting from an infection with Leishmania.

Keyssellitz and Mayer,[2] in an illustrated paper, give a good description of the phagedænic ulcer of tropical countries and the relationship between the spirochætes and the *B. fusiformis*, which are constantly present in the lesions. According to these observers the spirochæte (*S. schaudinni*) commences the process of ulceration, which is eventually prolonged and continued by the *B. fusiformis*. The fungi, also frequently present, are described and figured. They consider that there is no relationship between this type of ulcer and hospital gangrene.

Heard [3] has a note on the treatment of tropical ulcer by means of potassium permanganate.

To treat the ulcer, persistent use of permanganate of potash is usually successful to a large degree. The best way, it is believed, is thorough application of saturated solution of permanganate every waking hour. In this case the patient will hardly have time for anything else. The solution should be poured into the ulcer and thoroughly swabbed. Do not dip the swab each time by soaking in water. Dusting on powdered permanganate or filling up the wound with it is another way, and the application need be made only about three times a day. A considerable exudation of blood or serum into the powdered permanganate causes it to become heated like quicklime and water. No dressing, or, at any rate, the lightest possible, to keep out dust and flies. The saturated solution causes no pain.

The ulcer begins to show improvement within four days, and steady healing may be noted day by day, but an ulcer as big as the brim of one's hat will possibly be months getting well. Whether ulcers healed in this way are likely to break down in the manner of those healing without treatment is not known.

Mention may be made of an illustrated paper on cutaneous blastomycosis in the Philippine Islands by Phalen and Nichols.[4] Clinically, the disease appears in three distinct forms, with intermediate types from the mildest to the most severe. The mild cases resemble the commonly observed skin infections with ordinary fungi. Their tendency to appear in unusual locations and with a symmetrical distribution are the features which clinically distinguish them from ringworm. The second type of the disease is most frequently met with. The lesions are large, circumscribed with a ridged border beset with miliary abscesses covered with crusts. The third or severe types may be mistaken for tuberculous or syphilitic lesions. The lesions are extensive with a raised surface, and in parts show papilliform elevations, frequently covered with a yellow crust. The diagnosis is dependent on the finding of blastomycetes in the lesions. In Castellani's and Chalmers's [5] work four types of organisms are described as being causal agents: (1) Blastomycetoid or yeast-like, (2) cryptococcus-like type, (3) endomyces-like type, (4) hyphomycetoid type. It is also noted that yeast-like organisms may be frequently found as saprophytes on the surface of various ulcerated skin lesions which have nothing to do with true blastomycosis.

Thiroux and D'Anfreville [6] have a short illustrated paper on variolous acne, or the molluscum contagiosum of Senegal. Europeans are as susceptible to it as the natives, and children are more prone to the affection than adults. The face is the seat of selection, usually

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[1] Stevenel (April 12, 1911), "Les cro-cro de la région de Zinder et leur identification avec l'ulcère phagédénique des pays chauds et le Bouton d'orient." *Bull. Soc. Path. Exot.*

[2] Keyssellitz, G., and Mayer, M. (1909), "Über das Ulcus tropicum." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIII.

[3] Heard, G. P. (October 15, 1908), "Therapy in Yaws and in Tropical Ulcer." *Journal Tropical Medicine and Hygiene.*

[4] Phalen, J. M., and Nichols, H. J. (1908), "Blastomycosis of the Skin in the Philippine Islands." *Philippine Journal of Science*, Vol. III.

[5] Castellani, A., and Chalmers, A. J. (1910). *Manual of Tropical Medicine.*

[6] Thiroux, A., and D'Anfreville, L. (July, 1909), "De l'acné varioloforme ou *molluscum contagiosum* au Sénégal." *Bull. Soc. Path. Exot.*

Skin Diseases—*continued*

the vicinity of the eyes, nose, and mouth. It commences as a small hemispherical tubercle. In its centre is a slight depression resembling the umbilication of variola pustules. If pressure is applied to the tubercle a small quantity of sebaceous material exudes from the centre, which is sometimes replaced by pus. In Europeans there is often a narrow rim of inflammation around the base. The condition may last for a month, or as long as a year. Its contagiousness has been shown by several members of a family becoming infected from each other. The treatment is unsatisfactory; excision of the tubercles and the application of tincture of iodine or salicylic acid, etc., give the best results.

Microscopical examination of the sebaceous contents did not show anything of importance. Spherical bodies were found which have been described as gregarines, psorosperms and coccidia, but Thiroux and D'Anfreville consider that they are cell degenerations.

Mention may be made of an illustrated paper by O'Zoux [1] describing a peculiar form of depigmentation of the skin occurring in some of the inhabitants of Réunion. Both sexes are liable to the condition, but it more commonly affects adult males of any race. The depigmentation is also present in the buccal mucosa. The skin in patches assumes the colour of white paper with sometimes a rosy tint, and more rarely in reflected light is nacreous. The nervous system does not seem to be affected, but those who suffer from a very marked decoloration appear to be very susceptible to the solar rays. O'Zoux does not consider that the condition is a partial albinism.

Castellani [2] in a short paper gives the principal cultural characters and sugar reactions of the various species of endomyces that have been isolated from cases of bronchomycosis in Ceylon. Their cultural characters and morphological appearances closely resemble *Endomyces albicans* and *Endomyces lactis*. When grown on solid media they appear as globular yeast-like cells with very few short mycelial articles. Of the endomyces affecting man in Ceylon, Castellani has so far been able to isolate nine different species.

Sutherland [3] has a most useful and practical paper on the treatment of eczema in the Tropics. The chief points are :—

First and foremost, we should enjoin upon our patient that he must on no account wash the affected area, even without allowing soap to come into contact with it.

Washing with water, however, is not the only way of removing the effete epidermal cells, and as it is the way which tends to keep up the dermatitis—as the patient may be taught by carrying out parallel experiments on two portions of the affected area—washing with water must be replaced by other methods of abstersion, such as the use of alcohol (unsweetened gin does admirably) or of boiled and cooled olive oil. The use of oil has the advantage that in many cases the bath may be employed and yet the affected area runs no risk of being wetted. When the affected area is treated with alcohol the patient is often put to it to devise a method of keeping the water from this area when he bathes the rest of his body, but with a little goodwill on his part in most cases he will surmount the difficulty.

If the genitals or anal region be the seat of affection he must not use a bath-tub, but may, after soaping his body, sluice himself down with water poured from a can. Where it is very difficult, or quite impossible, to devise a method of bathing so as to protect the affected area, then the patient must use oil or alcohol abstersion for the whole body surface.

While the use of alcohol as an abstergent decreases the action of the sudoriparous glands to an appreciable extent, the use of alcohol, especially *whisky*, as a beverage increases this action. I am inclined to think that grain spirit has more effect than malt spirit in this way, but the safest plan is to veto the "peg." If the patient will not hear of this, then let him do as little harm to himself as he can, by drinking brandy instead of whisky. That the average quality of the brandy sold in the tropics is higher than that of the whisky does not appear to be so generally known as it ought to be.

Of course, all exercise that causes sweating must be tabooed ; our patient must leave lawn-tennis, hockey, etc. to those whose skin is healthy. A walk in the cool of the morning and evening is enough for him, however ardently he may have worshipped the fetish of "exercise" when well.

To dry up the sweat a dusting powder—such as one composed of equal parts of starch and oxide of zinc—should be freely used. Some are inclined to add to this time-honoured mixture some boric acid. The writer is strongly of opinion that to do this is at best to waste the acid, which might well be used for other purposes. In not a few cases the use of boric acid tends to keep up, if it does not actually increase, the inflammatory condition, and in these cases it is worse than waste to employ it.

The ordinary treatment of an eczema by local means may be summed up in the words "zinc ointment" ; but in the tropics we shall only too soon find that in many cases all salves must be eschewed as of the Evil One's invention. The epidermis, overladen with fluid as it is, cannot be made to tolerate oily matter—in the damp climate of Bengal, Madras, and Burma the epidermis is sodden in the healthiest of skins. Where salves are

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[1] O'Zoux, L.-L. (April 12, 1911), "Maladie de dépigmentation chez l'homme à La Réunion." *Bull. Soc. Path. Exot.*

[2] Castellani, A. (April 1, 1911), "Observations on Fungi of the genus Endomyces affecting man in the Tropics." *Cent. f. Bakt.*, I. Orig., Vol. LVIII., No. 3.

[3] Sutherland, W. D. (September, 1910), "The Treatment of Eczema in the Tropics." *Journal Royal Army Medical Corps.*

Skin Diseases— *continued*

contra-indicated the physician must ring the changes on powders. These may be applied by means of a castor, the powder being "peppered" over the surface; or the patient may wear muslin bags filled with powder, hung so that at every motion some of their contents are deposited on the affected area.

If the eczema be acute, nothing can be done until we have lessened the inflammatory infiltration of the part. For this purpose there is nothing more satisfactory than the use of compresses of acetate of alum solution, covered with oiled silk or gutta-percha tissue to prevent evaporation. The steadily-continued use of these compresses for one, two, or it may be three days will often help the sufferer more than any previously employed means of treatment has done. In the writer's experience it is the cases of eczema genitalium that are specially difficult to treat unless one begins with the compresses. The solution is a 1 to 3 per cent. solution of the *liquor aluminis acetici* of the German Pharmacopœia, which may conveniently be prepared thus :—

℞	Alum sulph.	30·0
	Aq. destil.	80·0
(1)	Solve et adde	
	Acid. acetici dil.	30·0
	Calcis carb.	15·0
(2)	Aq. destil.	100·0

Shake well.

Into (1) we pour (2) and leave the mixture to stand for twenty-four hours, after which it is filtered. Of the solution thus obtained a 1 to 3 per cent. solution is made with distilled water, and the compresses are wetted every three hours with this. In this connection it is as well to call attention to an axiom of dermatological practice —the more acute the dermatitis the less irritating must the application be, if it is to do good. Many skins will not stand a stronger solution than 1 per cent. at first, and to begin with a 2 or 3 per cent. solution in these cases would only bring obloquy on the physician.

In some cases the part of the body affected is, so to speak, inaccessible for this compress treatment. In such a case we may derive benefit from painting on the part, twice or oftener in the day, the zinc cream which, is prepared thus :—

℞	Zincii oxidi	40·0
	Glycerini puriss.	60·0
	Aq. rosæ.	150·0

Mix well, shake, stand for three days, decant the supernatant liquid and use the residual cream.

Only once daily the precipitate formed on the affected area so treated is to be removed by means of pledgets of cotton-wool soaked in oil or spirit, used as gently as possible, and then the cream is to be again applied. Where the affected surface is very moist we must make shift to powder it, whatever be its situation. The action of the powder is to dry up the moisture and cool the part by abstracting heat from it. The powder should be applied at night, care being taken that the patient is as lightly clothed as is compatible with the prevailing temperature, else he will pass a restless night, even if he has no itching, and as he tosses about in bed will tend to make the powder come on every part save that to which it was applied.

In the hot weather and rainy season he should sleep in light clothing. "Viyella" is an excellent material for sleeping suits, and it should be insisted upon that he does not lie on a mattress. If he does, then that part of his body that is in contact with the mattress will, of necessity, be bathed in perspiration, and when he turns round in bed it will be exposed to the draught of air created by the punkah and undergo rapid cooling; whereas if he sleeps on a sheet all the surface of his body is exposed to nearly the same temperature, and no chilling of the surface will take place from change of position. Thin clothing and fairly rapid motion of the air in the room will obviate sweating during the daytime as well as night. The reader may with advantage study the article on "Ventilation in the Tropics" which appeared in the *Lancet* (1909). The lines laid down in that article, which was, the writer believes, written by a well-known Indian engineer, if they be carefully followed, cannot but have a good effect on our patient's health, while at the same time giving ease at night to those who have eczema.

If we can use salves for our patient, then the best of these will probably be found to be this :—

℞	Zincii oxidi		
	Amyli	āā	20·0
	Vaselini		40·0

Mix well together.

Vaseline does not tend to undergo decomposition, as does lanoline or benzoated lard, even when it is spread on notoriously unfavourable areas, such as the perinæum, the axilla, etc.

This salve must be spread *thickly* on the part with cotton-wool, the part being bandaged, or by means of a glass rod and covered with a thick layer of powder—*e.g.* eczema of the face or neck.

As the case progresses, to the salve may be added some oil of cade (not more than 1 per cent. to begin with), in order to promote healthy action of the skin. If we have been using powder instead of a salve then we may paint the area with Wright's liq. carbonis detergens, which is far and away superior to any of the numerous imitations of it that are on the market. The solution used should be at first a 1 per cent. solution of the liquor in rectified spirit, but even this may be found to cause too much irritation in some cases. As the treatment goes on, the proportion of oil of cade or tar is increased, a little at a time, until at last a 50 per cent solution of tar is well-borne. When there are signs of irritation being caused by the tar its use should be intermitted for a day or two, and then resumed, a solution slightly weaker than that last employed being applied. In this way the distressing itching which is so prominent a symptom of eczema of certain regions is controlled, and in time entirely removed. In order to hasten this consummation, before all things it is necessary to observe two rules: the tar should never be employed until the affected area has ceased to weep, and the patient must refrain from keeping up the condition by scratching.

The hard thing is to refrain from scratching at night, during the times of sleep and slumber. To aid him in his endeavours to carry out orders the patient should have his hands tied at night. A good way of doing this is to have attached to the head rail of the bed two stout tapes. These are of such a length that when the patient's wrists are in the slip-knots at their ends he cannot, as he lies on his back or his side, reach the affected area with his fingers without putting such a strain on the wrists as will waken him.

Skin Diseases—*continued*

Where the skin is cracked the tar will cause so much burning that its use is for this reason contra-indicated, not to mention the fact that when the skin is still cracked the disease has not advanced towards healing far enough for the tar to be of any service as an exciter of keratosis.

When we have at last brought about a cure of the eczema, how best may we avoid its return ?

For long after the last signs—itching and redness—have disappeared, the use of the tar-spirit should be continued, and the parts, which are painted once daily with, perhaps, pure liq. carb. detcrg., should be kept well-powdered ; this even when things have so far advanced that the general use of water has been resumed.

The use of alcohol as an abstergent should be resumed when the cold season is at an end, the part that was affected should be lightly touched with a small pledget of cotton-wool soaked in unsweetened gin once a day, although the daily bathing of the part is carried out.

In the cold weather—especially when the dry winds blow—the part may conveniently be anointed from time to time with "fetron," or this substitute therefor: vaselin puriss., 50·0; lanolin, 46·0: ceræ alb., 4·0; all these to be melted together and allowed to cool, and stored.

Additional Notes

Castellani [1] has some further remarks to add concerning the cultural characters of *Endodermophyton concentricum* and *E. indicum* :—

If rubber caps be applied to the cultural tubes containing cultures of *E. indicum* and *E. concentricum* these fungi take on a beautiful red colour. If, however, subcultures are made from these, using tubes closed in the ordinary way with cotton wool plugs, without rubber caps, the fungi show again after a time the same appearance I have described in my papers. Various changes in the cultural character of the fungi take place, as it was to be expected, also when they are exposed for a long time to strong light, lower or higher temperature than usual, etc.

I may take this opportunity to state that the further inoculation experiments have amply confirmed that the malady can be easily reproduced in human beings by inoculation of pure cultures of the fungi, as described in my previous publications.

Raebiger [2] reports very satisfactory results from the use of "Nikotian" soap in the treatment of ringworm in German East Africa.

The soap is prepared by C. Mentzel, Bremen, and is made by mixing tobacco extract with precipitated sulphur and superfatted soap ; the makers state that it contains 0·35 per cent. of nicotin. The soap is rubbed into the affected parts morning and evening till a lather is formed, which is then allowed to dry on the skin. Before each fresh application the skin is well washed. In some cases a certain amount of irritation is produced ; in these cases the soap is washed off at the end of two or three hours. The patients were cured in from four to eight days. The soap may also be used to relieve the itching which may occur in other skin diseases, *e.g.* scabies, pruritus, etc.

Fink [3] has recently published a paper entitled "Leucoderma in Burma." He describes three varieties—(1) The ordinary leucoderma, which is not very common in Burma. (2) *Melung* or *Beta*, a variety of leucoderma affecting almost entirely the flexor aspects of the hands and feet, and described by Ziemann [4] as affecting the negroes on the West Coast of Africa. (3) Syphilitic leucoderma, which consists more or less of a dappling of the skin.

Sleeping Sickness. The papers mentioned under this heading are those of more or less general interest. For an adequate treatment of the subject we must refer the reader, as has been done under Trypanosomiasis, to the Bulletins of the Sleeping Sickness Bureau.

Some light is shed on the possible reservoir for infection which may determine the continuance of human trypanosomes, after the segregation of the affected populace, by the following extract :—

It is known that the tsetse flies (*Glossina palpalis*) around the northern shores of the Victoria Nyanza still retain their infectivity for sleeping sickness, in spite of the fact that the native population was removed from the lake shore some three years ago.

A series of experiments was therefore carried out to ascertain if the antelope, which are fairly common along the uninhabited shores of the lake, were capable of acting as hosts of the parasite of sleeping sickness.

Eleven antelope of the water-buck, bush-buck and reed-buck species were obtained from a district where tsetse flies and sleeping sickness did not exist. Blood from these animals was first inoculated into monkeys to ascertain if they were already naturally infected with trypanosome disease. They proved to be healthy in this respect. Tsetse flies (*Glossina palpalis*) that were known to be infected with the virus of sleeping sickness were then fed upon each of the eleven antelope. After about eight days the blood of these animals was again inoculated into susceptible animals, with the result that the latter became infected with *Trypanosoma gambiense* in every case.

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[1] Castellani, A. (May 15, 1911), "Remarks on some Cultural Characters of the Fungi of Tinea Imbricata." *Journal Tropical Medicine and Hygiene.*

[2] Raebiger, A. (October, 1910), "Über Nikotianaseife als Heilmittel gegen Ringwurm." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIV., No. 20. Quoted in *Journal Royal Army Medical Corps*, June, 1911.

[3] Fink, L. S. (May, 1911), "Leucoderma in Burma." *Indian Medical Gazette.*

[4] Ziemann, H. *Arch. für Derm. und Syph.*, Bd. 74, Heft 2, No. 3. Quoted in *British Medical Journal*, May 13, 1905.

Sleeping Sickness—*continued*

In eight out of the eleven buck under experiment *Trypanosoma gambiense* appeared in their blood for a few days only (some seven to twelve days) after they had been bitten by infected flies.

Flies that were hatched out in the laboratory, and had never fed before, were now fed upon the infected antelope, and subsequently upon monkeys. After an interval of about thirty days required for the development of trypanosomes within the fly, monkeys were infected with sleeping sickness from the antelope by the agency of *Glossina palpalis* in sixteen out of twenty-four experiments.

On dissecting the flies which had been fed upon the infected antelope it was found that 10·8 per cent. of them were infected with *Trypanosoma gambiense*. The highest percentage of infected flies in any one of the positive experiments was 21 per cent.; the lowest was 1·3 per cent.

Nine of these antelope infected with *Trypanosoma gambiense* were under daily observation for over four months. They remained in perfect health.

Two of them (a water-buck and a bush-buck) never showed trypanosomes in their blood although examined every day. Both these antelope infected flies fed upon them, one of them as long as fifty-five days after its infection.

No wild antelope inhabiting the lake shore has yet been found to be naturally infected with *Trypanosoma gambiense*.

It is hardly possible to overestimate the importance of these observations.

These same observers (Bruce and others) [1] have proved by experiments that cattle may act as a reservoir of the virus of sleeping sickness, and that healthy animals may be infected from them by means of *G. palpalis*.

They have also proved that cattle in the fly area do naturally harbour *Trypanosoma gambiense*.

It is, therefore, possible that the cattle and antelope living in the fly area may act as a reservoir and so keep up the infectivity of the *Glossina palpalis* for an indefinite period, but there is no proof up to the present that this actually takes place in nature.

Probably the most important communication of the recent Uganda Sleeping Sickness Commission was on the work done to ascertain if the antelope can act as a reservoir of *T. gambiense*. Now the investigations of Bruce and his colleagues [2] have shown that though man and his domestic animals have been removed from the shore of Victoria Lake (mainland) for some two and a half years, yet a proportion of the *G. palpalis* captured in this area has been shown to be harbouring the infection of *T. gambiense*, as demonstrated by the ability of the flies to infect susceptible animals with sleeping sickness. The effect of the depopulation has been practically to convert a two mile area along the northern shores of the lake into a game preserve in which all sort of buck and game abound.

The Commission have proved to the hilt that the antelope can be a potential host; the only link missing in the chain of evidence is that, up to the present, a naturally infected antelope has not been found. Some points are very worthy of note; one that the antelope do not appear to suffer in health from the effect of this form of trypanosomiasis certainly at least for over four months. They are described as remaining "apparently in perfect health." It was also noticed that trypanosomes appeared in their blood only perhaps for two or three days at a time, and then might never be found again. Also that with a certain percentage trypanosomes were never seen in the peripheral blood, yet in every case the results obtained by feeding laboratory-bred flies on susceptible animals were positive. The general conclusions arrived at by the Commission are as follows:—

(1) Water-buck, bush-buck, and reed-buck can readily be infected with a *human strain* of the trypanosome of sleeping sickness by the bites of infected *Glossina palpalis*.

(2) One exposure to the bites of infected flies is sufficient to infect an antelope with the virus of sleeping sickness.

(3) Though the blood of an antelope may be proved to be infected with *Trypanosoma gambiense*, careful and continued examinations over prolonged periods may fail to reveal the presence of the parasite in the blood.

(4) The incubation of the disease (sleeping sickness) in antelope is probably seven days.

(5) Antelope of the water-buck, bush-buck, and reed-buck species, when infected with the virus of sleeping sickness, can transmit the infection to clean laboratory-bred *Glossina palpalis*.

(6) This transmission of the infection to clean laboratory-bred flies may occur at least eighty-one days after the last feed of the infected flies on a buck.

(7) *Glossina palpalis*, when infected with the virus of sleeping sickness obtained from the blood of infected antelope, are capable of transmitting the virus to susceptible animals.

(8) An appreciable percentage of *Glossina palpalis* will become infected with the virus of sleeping sickness should these flies feed on antelope suffering from this disease.

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[1] Bruce D., and others. S.S. Commission of the Royal Society, Uganda, 1908–10.

[2] Bruce, D., and others (January, 1911), "Experiments to ascertain if Antelope may act as a Reservoir of the Virus of Sleeping Sickness." *Proceedings of the Royal Society*, B., Vol. LXXXIII.

(9) It follows from the above conclusions that antelope living in the fly-areas are "potential" reservoirs of the virus of sleeping sickness. Sleeping Sickness—*continued*

(10) No antelope up to the present has been found naturally infected with *Trypanosoma gambiense.*

The whole paper is an exceedingly interesting and instructive one, and should be studied in the original.

The occurrence of an extraordinary number of birds of various species on the shores of Lake Victoria caused the Commission [1] to make experiments on the infectibility of the domestic fowl with *T. gambiense;* the results, however, were entirely negative.

Martin and Ringenbach [2] have shown that *T. gambiense* can penetrate intact mucous membrane and produce an infection; their experiments have some bearing on the supposed transmission of sleeping sickness by coitus. They experimented with guinea-pigs, and state that

the *T. gambiense* can transmit by the simple direct contact of virulent blood on the skin of a guinea-pig which has been shaved the day before and by the contact of the virus with the wall of the vagina. A mucous membrane, a skin more or less healthy, showing very minute intervals of continuity or scratches, will easily let the *T. gambiense* penetrate into the organism.

Symptoms.—Perhaps as instructive an article though of a less important nature is the appreciation by Kerandel [3] of his own case. The auto-observations of a scientific mind afford considerable light on symptoms and effects of treatment which it is difficult to elicit from the ordinary sufferer.

The principal points of interest in the symptomatology are as follows:—

After noting the resemblance of the onset to that of malaria, and speaking of a "pseudo-furuncle" on the neck, which might have been the spot where he was bitten by the infecting insect, he speaks of the extreme weariness experienced after a walk of a hundred yards or so associated with which was "*pain at the level of the seventh cervical vertebra,*" which he appears to believe to be important from a symptomatic standpoint.

Cramps, limited more particularly to the legs, were a very painful and early symptom, and came on often after sleep, to avoid which he was accustomed to sleep with the lower limbs flexed.

"Formications," affecting chiefly the face and sides of the fingers, came on about the same time. "*Deep hyperœsthesia*" in his case was well-marked.

What he lays most stress on, however, is the nervous asthenia. Every physical or intellectual effort was painful. And beyond all there was a special and permanent sensation of general malaise which he has called *dysphoria.* It was present continuously till its sudden disappearance under treatment, which is referred to under that heading.

He speaks of a dysenteric syndrome which he refers to the invasion of trypanosomiasis.

The erythemata were of two kinds: at first they exhibited irregular marbling, disappearing under atoxyl; ten months later they reappeared more definite and circinate.

He writes at some little length about the periodicity of the fever, and found that the auto-agglutination of his red cells appeared to increase at the end of a bout of fever and then gradually diminish; a remark throwing some light on the diagnostic value of this sign. He was much worried with nightmares and troubled sleep and found a marked tendency to a melancholic state. He ascribes these nerve affections to affinity of trypanosome toxines for the nervous system, supposing of course that they exist.

Heckenroth,[4] in discussing symptoms, has drawn particular attention to the occurrence of local œdemas as a sign of diagnostic value. He gives 76 per cent. at least as the proportion in which these œdemas occurred in his clinical experience. They are manifest most particularly on the face, then on the legs, and least on the trunk and arms.

The facial œdemas are in his opinion among the symptoms of a commencing attack, those on the limbs and trunks appearing at a more advanced stage of the disease; he particularly noticed a suborbital œdema. The symptom is worth noting, as the occurrence

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[1] Bruce, D., and others (January, 1911), "Experiments to Ascertain if the Domestic Fowl of Uganda may act as a Reservoir of the Virus of Sleeping Sickness." *Proceedings of the Royal Society,* B, Vol. LXXXIII.

[2] Martin, G., and Ringenbach (July 13, 1910), "Pénétration de *T. gambiense* à travers les téguments et les muqueuses intacts." *Bull. Soc. Path. Exot.*

[3] Kerandel, J. (November, 1910), "Un cas de trypanosomiase chez un médecin" (auto-observation). *Bull. Soc. Path. Exot.*

[4] Heckenroth (May, 1909), "Les symptômes de la trypanosomiase humaine." *Ibid.*

Sleeping Sickness— *continued*

of a facial œdema is one that would be at once noticed in a most cursory examination of large numbers of natives.

The following résumé of fifty cases of sleeping sickness in whites is given by Bagshawe[1] in the September number of the *Sleeping Sickness Bureau Bulletin* for 1910.

The value of the clinical signs is here concisely indicated :—

Method of diagnosis.—In all the cases but five trypanosomes were found; the history, symptoms, and post-mortem findings in these five seem sufficient to establish the diagnosis. In the remaining forty-five the parasites were found in thirty-two instances in the blood, in fresh or stained films, and once after centrifugation; six times by gland puncture; five times by lumbar puncture; and once by animal inoculation.

One may estimate the value of blood examination in the detection of this disease from the fact that diagnosis was furnished five times more often by the examination of blood films than by gland puncture.

Glands.—The information about the cervical glands is much wanting in precision. In thirty-nine cases they are variously described as enlarged, slightly enlarged, palpable, palpable but very small, hypertrophied, swollen, visible, with polyadenitis, etc. In four it is definitely stated that there was no enlargement, and in seven there are no data; in these last, gland enlargement, if present, would probably have been slight.

Other symptoms.—An analysis of the other symptoms gives the following results :—

Fever recorded	40 times	Incontinence of urine or fæces	10 times
Erythema of the skin	31 „	Enlargement of liver	9 „
Loss of strength	29 „	Eye symptoms	9 „
Increased frequency of heart beat	25 „	Delusions	7 „
Somnolence	23 „	Insomnia	6 „
Œdema	22 „	Vomiting	5 „
Large spleen	19 „	Melancholia	4 „
Anæmia	18 „	Epistaxis	4 „
Headache	18 „	Pains in the feet	4 „
Epileptiform fits	17 „	Paresis of the lower limb	3 „
Tremor	15 „	Dermatographia	3 „
Change of character	12 „	Painful swelling on the ankle	2 „
Itching	11 „	Sexual impotence	2 „
Hyperæsthesia	10 „	Hemiplegia	2 „

Giddiness, diarrhœa, deafness, loss of hair, phlebitis, facial paralysis, localised œdema like Calabar swellings, and orchitis, are each noted once. Auto-agglutination was recorded in six instances.

In such a list as this the relative position of the symptoms is partly determined by the relative numbers of early cases which did not progress or were lost sight of, and advanced cases. When the advanced cases are many, somnolence, epilepsy, tremor, and incontinence will rank high.

Of the cases in which somnolence was noted, all but three ended fatally. The headache was in most instances more than would be associated with malarial or other fever; it is usually described as intense or severe. When epileptiform convulsions occurred death always followed. The change of character took various forms; in three instances the patient became irritable, and in two, causeless fits of rage were noted; in one he is described as irritable and apathetic; in two he performed irrational actions; in two others he became emotional and wept; in one he was morose. Deep hyperæsthesia (Kerandel's sign) was in most cases where it is recorded well-marked. Incontinence of urine and fæces was a symptom preceding death, except in Cases 29 and 41. Of eye symptoms, in Case 4 there was choroidal atrophy, which may have been syphilitic. In Cases 5, 20, and 43, iritis. In Case 12 a markedly congested disc was seen. In Cases 24 and 35 there were symptoms which may have been due to atoxyl; they did not, however, progress. The vomiting accompanied fever in two instances; in two others it was of cerebral type, and attended by severe headache; in the fifth there was also profuse diarrhœa and delirium. The paresis of the lower limbs amounted in two instances to paraplegia. Sexual impotence has been rarely recorded in Europeans.

In six instances the patient stated that a painful swelling, the result of a bite, had preceded the first symptoms. These bites were in most cases attributed to flies; in one to a scorpion.

The following leucocytic count is given by Nattan-Larrier and Allain[2] for sleeping sickness :—

Polymorphs.	40·52 per cent.	Basophiles	0·38 per cent.
Large mononuclears	7·91 „	Turk's cells	0·31 „
Lymphocytes	38·37 „	Myelocytes	1·22 „
Eosinophiles	11·79 „		

Martin and Lebœuf give :—

Polymorphs.	49·04 „	Eosinophiles	6·24 „
Large mononuclears	6·36 „	Transitionals	0·76 „
Lymphocytes	37·60 „		

Prophylaxis. Sir Patrick Manson has noticed that a large proportion of the European women affected with trypanosomiasis appear to have been infected with bites on the leg. Dr. Bagshawe[3] points out (1) that it is the habit of *Glossina palpalis* to elude observation; it

[1] Bagshawe, A. G. (September, 1910), "Sleeping Sickness in Whites." *Sleeping Sickness Bureau Bulletin*, Vol. II., No. 20.

[2] Nattan-Larrier, L., and Allain (June 10, 1908), "L'équilibre leucocytaire chez les noirs atteints de trypanosomiase." *Bull. Soc. Path. Exot.*

[3] Bagshawe, A. (December 6, 1909), "Personal Prophylaxis of Sleeping Sickness." *Sleeping Sickness Bureau Bulletin*, No. 12.

prefers dark to bright spots ; it is therefore not unlikely to get under a petticoat. (2) The fly can easily bite through a thin stocking. . . . Every woman who is likely to be exposed to the bites of *G. palpalis* should therefore wear leggings of some sort, or at least puttees. Dr. Graham has called the writer's attention to the frequency with which women are bitten in railway carriages through neglect of this precaution. Sleeping Sickness—*continued*

Treatment. The intravenous injection of tartar emetic has, as is well known, produced such favourable results as to warrant its extended use, and Thiroux [1] has advised the previous injection of caffein subcutaneously in order to combat the depressing effects which are occasionally produced by the administration of the antimony salt.

His plan was to inject 20 c.g. of caffein subcutaneously, and he found that this proceeding had most excellent results in combating the cardiac depression, with occasional fainting fits, vertigos, and profuse sweats, that is sometimes seen ; he gave the dose twenty minutes before the injection of the emetic.

With reference to treatment Kerandel [2] in his auto-observation speaks of the effects of atoxyl as very ephemeral ; the drug, however. of which he took altogether about 70 grammes, appears to have had no toxic effects, and he believes that the trypanosomes became atoxyl-fast.

Both orpiment and tartar emetic by ingestion he dismisses in a few words, but to the antimony salt administered by intravenous injection he ascribes his cure, or at any rate the remarkable good health and freedom from any sign of illness which he has experienced up to writing the article—a period of over two years.

He had four series of daily injections of 10 c.m. of tartar emetic ; the four series consisting of 17, 15, 15, and 8 doses respectively.

Hc ascribes the beneficial result entirely to the first series, when all the symptoms at once ameliorated. The fourth series was badly borne, and discontinued.

The special sensation of malaise disappeared "as if by enchantment" with the first series of doses, and he speaks of a feeling of well-being, which was in fact the sudden cessation of a long period of illness. His case entirely points to the efficacy of treatment by an intravenous antimony method.

The following extract from the *Sleeping Sickness Bureau Bulletin*, No. 14, Vol. II., will interest those who are familiar with the action of the arsenic and antimony salts on trypanosomiases. We may say that the usual supposition is that the antimony salts act directly, while the arsenical act after the formation of a derivative product known as trypanotoxyl. One of the grounds for this idea is because antimony salts are very highly trypanocidal *in vitro*, arsenic salts little if at all.

Yamamouchi [3] has repeated the work done by Levaditi and himself on the formation of trypanotoxyl. For the experiments the trypanosomes of Nagana were used. The following are his conclusions :—

(1) The organs freed from blood, especially the liver, kidneys. and the muscles, have no action on atoxyl ; they do not produce a trypanocidal substance.

(2) A trypanocidal substance is produced by the red corpuscles of the blood as well as by their solution in water.

(3) The red corpuscles washed in physiological saline and treated with carbonic acid, or reduced by the tissue or by different bacteria, have a greater power of producing an active body than the red corpuscles not so treated, and merely washed in physiological saline. Red corpuscles treated with oxygen do not form any active substance.

(4) The leucocytes, the blood serum, the stroma of the red corpuscles, the catalasa of the blood and pure recrystallised hæmoglobin are not capable of producing the active substance.

(5) Blood dialysed in water on a collodion membrane or warmed to 80° for thirty minutes loses its power of producing with atoxyl a trypanocidal substance.

(6) The active body is soluble in alcohol ; it is thermostabile and free from proteid matter.

(7) The trypanocidal principle combined with the various albumens becomes inactive. *In vivo* after an injection of atoxyl the active body originates in the blood circulation and afterwards combines with the trypanosomes and the other albuminous matters in the blood.

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[1] Thiroux, A. (June, 1909), "Des accidents d'intoxication consécutifs aux infections intra-veineuses d'émétique." *Bull. Soc. Path. Exot.*

[2] Kerandel, J. (November, 1910), "Un cas de trypanosomiase chez un médecin" (auto-observation). *Bull. Soc. Path. Exot.*

[3] Yamamouchi, T. (January, 1910), "Action de l'atoxyl sur les trypanosomes dans l'organisme." *C. R. Soc. Biol.*

Sleeping Sickness—*continued*

Regarding this matter it is necessary to state that Levaditi and McIntosh [1] are not in agreement with Yamamouchi, and have come to the conclusion that the substance which transforms atoxyl is a cell derivative soluble in water, thermostabile, becoming spontaneously weaker *in vitro*, and needing an optimum temperature for its action.

Deviation of complement. Levaditi and Mutermilch [2] have done work on the Bordet-Gengou reaction in trypanosomiasis infections. According to these observers, the complement can be fixed by using as antigen an extract of pure trypanosomes or trypanosomes separated from blood cells. They regard this as specific in nature. Wassermann's reaction, an antigen such as alcoholic heart extract being used, is also positive in trypanosome infections, but this reaction is, of course, not specific.

Additional Notes

A good account of the symptoms of the disease, as seen in Togoland by von Raven, is given in No. 27 of the *Sleeping Sickness Bulletin.* The disease is divided into the prodromal stage ; the first stage of gland swelling ; the second of infection of the central nervous system ; and the third, the terminal or sleep stage. The further researches on the development of *T. gambiense* in *G. palpalis* carried out by Bruce [3] and his colleagues in Uganda is detailed, with illustrations, in No. 28 of the above *Bulletin* (July 20, 1911). The conclusions may be quoted :—

(1) In the course of the development of *Trypanosoma gambiense* in *Glossina palpalis* the proboscis does not become involved, as in the case of some other species.

(2) A few days after an infective feed the trypanosomes disappear out of the great majority of the flies, but in a small percentage this initial disappearance is followed by a renewed development.

(3) After a very short time the flies which have been fed on an infected animal become incapable of conveying the infection by their bites, and this non-infectivity lasts for some 28 days, when a renewed or late infectivity takes place.

(4) A fly in which this renewed or late infectivity occurs can remain infective for at least 96 days.

(5) An invasion of the salivary glands occurs at the same time as this renewal of infectivity, and without this invasion of the salivary glands there can be no infectivity.

(6) The type of trypanosome found in the salivary glands when the fly becomes infective is similar to the short stumpy form found in vertebrate blood, and it is believed that this reversion to the blood-type is a *sine qua non* in the infective process.

Tsuzuki [4] has dealt with the treatment of trypanosome infections in a memoir which contains an historical account of trypanosome therapy. A translated extract and recent work on the treatment of sleeping sickness, still unfortunately far from satisfactory, is given in *Bulletin* No. 28, which, like all the numbers, contains an interesting section on Sleeping Sickness News, that permits one to follow the progress of the disease and to note the steps taken for dealing with it on a large scale. Though outside the Review limit, one must record the announcement made by Bagshawe at the last (1911) meeting of the British Medical Association, to the effect that Taute working at Tanganyika had successfully transmitted a human trypanosome to monkeys by means of *G. morsitans.* As Bagshawe remarks in *Bulletin* No. 29 (August 17, 1911), the success of such a laboratory experiment does not prove that the like is of common occurrence in nature. Kleine expresses the hope that the transmission of *T. gambiense* by *G. morsitans* is an exceptional occurrence, a hope which will be shared by all familiar with the extensive distribution of the latter.

Small-pox. Ziemann [5] has a practical and instructive paper entitled "Protective Inoculation against Small-pox in the Colonies," which may be read with advantage by lay officials as well as medical men in the Tropics. He recommends the advisability of having an institute for the preparation of calf lymph in every colony. Healthy calves three to six months old should only be used, and he suggests that the best plan is to vaccinate a human subject with lymph freshly imported from Europe, and then to use this humanised vaccine with which to

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[1] Levaditi, C., and McIntosh, J. (April, 1910), "Mécanisme de la Transformation de l'Atoxyl en Trypanotoxyl." *C. R. Soc. Biol.*

[2] Levaditi, C., and Mutermilch, S. (July, 1909), "Rechercher sur la méthode de Bordet et Gengou appliquée à l'étude des trypanosomiases." *Zeit. f. Immunitäts f.*

[3] Bruce, D., and others (May, 1911), "Further Researches on the Development of *Trypanosoma gambiense* in *Glossina palpalis.*" *Proceedings Royal Society.*

[4] Tsuzuki, M. (May, 1911), "Die Kombinationstherapie der Trypanosomeninfektionen." *Zeit. f. Hyg. u. Infekt.*, Vol. LXVIII., No. 2.

[5] Ziemann, H. (1908), "Protective Inoculation against Small-pox in the Colonies." *Berl. Klin. Woch.*, No. 3. Quoted in *Journal Tropical Medicine and Hygiene*, May 15, 1908.

inoculate the calf. Where calves are not available, other animals should be employed. The important points in his paper may be summed up as follows :— Small-pox —*continued*

(1) Small-pox prevails endemically in nearly all the tropical colonies, and should therefore be combated by every means, with the mutual assistance of the neighbouring colonies.

(2) In order to facilitate this combat, verbal and written instructions on the symptoms of small-pox and protective inoculation are necessary. The natives should be instructed at the congresses of the chiefs.

(3) It is necessary to have laws similar to those in Europe : (*a*) for the prevention of small-pox by means of protective vaccination ; (*b*) for combating small-pox when it has broken out ; (*c*) universal compulsory vaccination when there are no particular political objections.

(4) In addition to the doctors, officials and their assistants have to give help on demand in performing vaccinations in affected districts.

(5) In every colony, according to its dimensions, one or several travelling doctors should be appointed, who, in addition to combating other diseases, should undertake the systematic vaccination of the population (especially on caravan routes), and they should likewise instruct native assistants.

(6) Independent wholesale vaccinations by native coloured assistants should never be permitted.

(7) Technique of vaccination as in Europe. The incisions should, in the case of natives, be made on the left upper arm. The operation should by preference be performed in the cool season and in the coolest hours of the day. Vaccination is successful if one well-developed pustule ensues.

(8) One institute at least, for the production of vaccine, should be established in every colony, and should be under the direction of the Principal Medical Officer.

(9) Where sufficient calf lymph is not available, arm to arm vaccination may be effected where there is no medical suspicion as to infection through relapsing fever, sleeping sickness, etc. Vaccine should only be taken from healthy children up to about eight years old.

(10) The greatest care must be exercised to use only vaccine which is as free from bacteria as possible, to prevent infection of the wound and thereby lessen the native dread of vaccination.

(11) The experiments to obtain vaccines that will keep, and which will not lose their virulence if exposed to a high temperature, must be continued. (Dried vaccines, addition of vaseline instead of glycerine, etc.)

(12) Likewise the experiment to obtain vaccines from other animals, such as rabbits, in districts where few or no calves are available.

(13) The protection by vaccination of the coloured races is mostly less than in Europeans. Repetition of vaccinations is therefore necessary.

(14) Every European holding an official position in a colony for the first time, must be vaccinated before starting on the voyage out, in case he has not been vaccinated with results within the previous two years, or had an attack of small-pox.

Robertson [1] has an interesting paper dealing with an outbreak of small-pox in Leith, where the disease was evidently spread by direct infection from person to person. In this paper he also quotes several instances of small outbreaks by small-pox due to the disease being conveyed by contact with infected persons, and the evidence collected in his paper is certainly not in favour of the aerial diffusion theory of the spread of small-pox.

Corbin [2] has called attention to the occurrence of sporadic cases of small-pox from time to time among workers in cotton mills at Stockport. From careful inquiries made there was evidence of the possibility of the infection being carried through the medium of raw cotton from parts of the world in which small-pox was endemic, for the chain of evidence connecting cases of small-pox in Lancashire with cases occurring in Egypt and the States has been followed out very completely. Corbin points out, however, that even if a native engaged in gathering the cotton were actually suffering from small-pox, the probability of the infection being conveyed is extremely slight, for there must be considerable attenuation of the virus before the material reaches the hands of the workers in England. Further, persons employed in piecing only occasionally use the saliva as a means to facilitate the process, and the probability of the strands requiring to be pieced just at the point where infected material occurred is very small. Corbin urges the necessity for the vaccination and re-vaccination of all cotton workers.

An interesting paper by Vaughan [3] contains many practical hints on the treatment of small-pox. The points to be aimed at in the treatment of the eruption are—(1) to soothe the irritation ; (2) to check the fœtor ; (3) to check local infection, and thus prevent or minimise the subsequent formation of boils ; (4) to check the tendency to pitting. These objects can be attained by the use of Lewentaner's preparation (starch 30 parts, salicylic acid 3 parts, glycerine 70 parts) applied freely to the whole body every three or four hours, but applied direct, and without the mask recommended by Lewentaner. As the cost of the glycerine made this preparation too expensive, a substitute was found in the following :—Acid salicylic

[1] Robertson, W. (January, 1909), "Lessons from an Outbreak of Small-pox." *Public Health.*

[2] Corbin, H. E. (October, 1909), "Small-pox from Imported Cotton." *Ibid.*

[3] Vaughan, J. C. S. (October, 1909), "Clinical Notes on Small-pox." *Indian Medical Gazette.*

Small-pox —*continued*

2 drms., thymol 2 drms., menthol 4 drms., eucalyptol 2 drms., and Ol. Arachis Hypogea 1 lb. This preparation, according to Vaughan, mixes well, is very soothing, and is just as efficacious as Lewentaner's, while it is cheaper. It should be applied from the very first, if possible, at the papular stage. By its use pitting is almost certainly prevented.

Vaughan recommends warm or tepid sponging of the skin as soon as the patient can stand it, to be followed later on by baths. Both for the sponging and for the baths he advocates the addition of salicylic acid to the water in a strength of 1 grain to the ounce for the first week or so, while later on the addition of a little soda assists in getting the scabs off. In the final stage a lotion of calamin with oxide of zinc is strongly indicated.

With regard to the eye complications they can, as a rule, be prevented by the application of eye drops consisting of medicinal methylene blue (1 grain to the ounce of distilled water) applied thrice daily as a routine treatment. Vaughan strongly recommends the use of oxygen inhalations when the rate of respiration rises out of all proportion to the pulse rate, usually about the eighth day of the disease. To be of any avail the oxygen must be given continuously for not less than two or three hours at a time.

Würtzen [1] has some practical suggestions in a paper entitled the "Treatment of Small-pox in Red Light and in the Dark." After considering the light transmitting properties of different varieties of red glass, he draws attention to certain conditions which must always be present if the treatment is not to disappoint expectations.

In the first place, the arrangements ought not to be limited to the sick-room, but account should be taken also of the adjoining rooms, passages, etc., so that no great quantity of injurious daylight should be thrown on the patient in opening the door of the sick-room. All sources of artificial light must be covered with red lamp-glasses, such as photographers use, and when doctors and nurses in their rounds think it necessary to use ordinary light, it ought only to come from a stearine candle, of which the flame contains so few chemical rays that no harm is done, if used only for a short time. It therefore follows as a matter of course that even for a short time, and in order to see the exanthem better, daylight ought not to be admitted freely.

Finally, there is the question as to how the red light affects the patients—apart from their illness—and the staff generally. Nothing is known of its remote effects, but the reaction to it seems to be somewhat different. Some do not seem to be appreciably influenced, while others find it rather unpleasant in the long run, and some get an absolute aversion to it. It often produces a feeling of heaviness and headache, and it is always found, exhausting and tiring for reading; on the other hand, we have not noticed any mental excitement or increased sensuality, as is said to have been the case elsewhere. Naturally the red light produces a strong sensitiveness in the retina to ordinary daylight. This hypersensitiveness is very troublesome and confusing to the nurses, who of course are obliged to go backwards and forwards between the red-room and the daylight. To mitigate these drawbacks—and in a red-room the light on bright days is very intense—coloured spectacles may be used with advantage. Green and blue glass each in their own way considerably modify the light and produce different shades, of which some will prefer one, others another; and with smoked glasses a chiaroscuro is obtained, which gives great relief. Contrary to what might be expected, neither the blue, the green, nor the smoked glass, provided they are not very dark, cause any considerable weakening of the light in a red-room.

Hanna [2] has collected a series of 75 cases of small-pox with a concurrent vaccination which will be of interest to those engaged in public health work. The series of cases are divided into (*a*) Cases unvaccinated before infection with small-pox; (*b*) Cases with primary vaccination before infection with small-pox; (*c*) Cases of concurrent variola and vaccinia. The practical inferences to be drawn from these records are as follows:—

(1) That vaccination performed subsequently to infection with small-pox will "take" up to date of onset.

(2) That protection is afforded against small-pox by vaccination when performed within three days after infection; but this may not be absolute in cases vaccinated for the first time; the course of the disease will, however, be exceedingly mild.

(3) That there is abundant evidence of the value of vaccination in mitigating the severity of the disease when performed at any time after infection up to the day of onset, and even afterwards.

As regards the etiology of small-pox nothing is as yet definitely known. A good deal of work has been carried out by various observers, but uncertainty still exists as to the exact nature of the vaccine bodies *Cytoryctes variolæ* of Guarnieri, which are present in vaccine and variola vesicles, and in the lesions caused by inoculation of the cornea with vaccine or variola virus.

Elmassian [3] has studied these vaccine bodies in the cornea of an inoculated rabbit, and concludes that they are pathogenic *chromidia*, and differ from normal chromidia, in being

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[1] Würtzen, C. H. (August 6, 1910), "Treatment of Small-pox in Red Light and in the Dark." *British Medical Journal.*

[2] Hanna, W. (July, 1910), "Observations on the interaction of concurrent Variola and Vaccinia." *Public Health.*

[3] Elmassian, M. (1909), "Contribution à l'étude microscopique de la cornée vaccinée chez le lapin." *Cent. f. Bakt.*, I. Orig., Vol. XLVIII., No. 2.

richer in plastine and poorer in chromatin in taking on a metachromatic staining, and in giving a clear blue colour with hæmatoxylin and a very bright violet with gentian violet. He considers that the "initial bodies" of Prowazek are small chromidia in the early stages of the lesion. Elmassian's paper is illustrated with a coloured plate showing these vaccine bodies stained with hæmatoxylin. Their exact nature still remains an open question, judging from the different views held by Prowazek, Beaurepaire-Aragao,[1] Casagrandi,[2] Pascher [3] and others. Small-pox —*continued*

Meirelles [4] has rather a suggestive paper in which he considers the flea as a transmitting agent of the virus of variola. According to this observer the epidemics of variola in Rio de Janeiro spread rapidly during the dry weather, which is the breeding season of the fleas *P. penetrans* and *P. irritans*. During the rains these insects are killed, except those that infest the interior of the houses. As further evidence in support of the flea theory, he noted that at the commencement of an epidemic the benign cases of variola predominated, but as the epidemic spread the benign cases diminished and the severer type of the disease prevailed. This he attributes to the fact that at the commencement of the epidemic there were fewer infected fleas, and that as the epidemic spread a larger number of fleas became infected, and those exposed to their attacks received a larger dose of the virus and developed confluent and hæmorrhagic small-pox.

He concludes his paper by recommending that the prophylactic measures adopted in an epidemic of variola should also include a campaign against fleas.

Keysselitz and Mayer [5] have a note on the lesions which occurred in the internal organs in a case of confluent small-pox. In the liver, spleen, lung, kidney, and bone-marrow, there were lesions resembling the cutaneous pustules that were present. There was a marked infiltration of leucocytes. In the cells that had not undergone necrosis they found the bodies of Guarnieri present both in the plasma and in the nuclei. These bodies were also present in the endothelial cells of the blood-vessels in the vicinity of the lesions, and in the cells in the medulla of the kidney, in the pulmonary alveoli and in the endothelial cells of the vessels in the spleen.

Musgrave and Sison [6] present a paper on the bone lesions of small-pox. They have noted in eight cases which had contracted small-pox during their childhood, certain deformities affecting the bones of the upper extremities due to destructive lesions in the epiphyses of the bones.

Mention may be made of an article by Carini [7] describing an epidemic of benign variola in the state of San Paulo. Locally the disease was known as *alastrim*, or milk-pox. Although Carini considered it to be a benign variety of small-pox, it differed from variola in certain distinctive features, as (1) It caused a very low mortality. (2) Infants were attacked to a lesser degree than adults. (3) There was no secondary fever, pustulation was more rapid, and the pus in the pustules was less fœtid than in variola pustules. (4) Persons recently vaccinated against variola did not appear immune to *alastrim*.

Cameron [8] has a very useful paper on the most important points to be considered in the examination of suspected cases of small-pox. Many practical hints are given, and it is a paper to be read with advantage by those interested in the subject. It is too long to be quoted in full, but a few of the salient points may be mentioned. They are considered under the various headings in his paper. With regard to temperature he notes that :—

In cases which have been under observation during two or three days of a feverish illness, a fall in temperature, associated with the appearance of "spots" on the skin, however few and widely scattered the lesions may be, is an indication of the highest importance.

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[1] Prowazek, v. S., and Beaurepaire-Aragao (1909), "Weitere Untersuchungen über Chlamydozoen." *Münch. Med. Woch.*, No. 13.

[2] Casagrandi, O. (1910), "L'etiologia del variolo umano." *Ann. Ig. Sperim.*, t. XX. Quoted in *Bull. de l'Inst. Past.*, September 15, 1910. Also (February, 1911), "Zur Ätiologie der Menschenpocken." *Cent. f. Bakt.*, I. Orig., Vol. LVII., No. 2.

[3] Pascher, E. (December 1, 1908), "Untersuchungen über die Variola." *Münch. Med. Woch.*, No. 48.

[4] Meirelles, Z. (February 9, 1910), "Epidémologie de la variole." *Bull. Soc. Path. Exot.*

[5] Keysselitz, G., and Mayer, M. (April, 1909), "Über Zellveränderungen in inneren Organen bei Variola." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIII.

[6] Musgrave, W. E., and Sison, A. G. (December, 1910), "The Bone Lesions of Small-pox." *Philippine Journal of Science*, B.

[7] Carini, A. (January 11, 1911), "A propos d'une épidémie très bénigne de variole." *Bull. Soc. Path. Exot.*

[8] Cameron, A. F. (April 1, 1911), "The Examination of Suspected Small-pox." *British Medical Journal.*

Small-pox —*continued*

The cutaneous signs of small-pox are gone into fully. Small-pox is capable of producing three distinct types of eruption: (1) Erythema, (2) Purpura, (3) Vesicle (the pock). In discussing the erythematous rash he states that the position which this rash occupies as a differential test for small-pox may perhaps be most easily indicated if the following features are taken to represent the type :—

(1) It has no definite unit, but consists of patches which are irregular in contour and vary much in size.

(2) It is haphazard in distribution.

(3) It is not a raised rash.

(4) It does not affect the face.

This negative method of setting out the characters of the rash may serve to indicate that in a considerable proportion of its examples the erythema is in itself of little assistance in diagnosis, but acquires importance only from being associated with a purpuric or vesicular eruption, present at the time of examination or superimposed on the erythema during a short period of observation.

He notes that the collective features of the lesions have the greater value in diagnosis :—

The unit of the rash is a gross inflammatory focus, which passes through several stages in the course of its life history. Appearing first as a macule, which very rapidly becomes a papule, the typical lesion advances steadily through vesicular and pustular stages to the formation of a crust, which on separating leaves a scar, *This quality of continuous change inherent in the lesion is of considerable assistance in diagnosis.* It is very useful in many difficult discrete eruptions which may be under observation on suspicion of small-pox. But the lesions are subject to accidental disturbances—for example, to injury by the patient himself, a factor which may have considerable influence on the very discrete rash. Their evolution is influenced by a lowering of the general physical condition of the patient—for example, by old age or previous ill-health, and it is affected also by the presence in the patient of a degree of immunity against the disease.

On the other hand, the more important of the collective features of the lesions depend much less closely on the personal factor in observation. They begin to appear with the beginnings of the eruption. They become fully established when efflorescence is completed, and they must remain as unchanging evidence as long as the rash lasts.

Additional Note

Millard [1] has recently published an interesting paper entitled "Are Unvaccinated Persons a Danger to the Community?" He points out that small-pox occurring in unvaccinated persons is generally present in such a typical form that its diagnosis is rarely missed, whereas if it occurs in patients who have been vaccinated it very often assumes such an atypical or modified form that the diagnosis is "missed," and such a patient is a danger to the community. As an instance he quotes an outbreak of small-pox in the Mile End Infirmary which was traced to a girl who had been previously vaccinated and had suffered from such a modified form of small-pox that the diagnosis was "missed." Millard states that there is a large and increasing volume of evidence as to the large part which these "missed" cases play in the spread of the disease, and many instances could be quoted from the experience of almost every epidemic. These "missed" cases are more likely to occur in the vaccinated than in the unvaccinated.

Snake-Bite. To those interested in the poisonous snakes of India, or to workers in India in whose practice cases of snake-bite occur, the second edition of Major Wall's [2] book can be thoroughly recommended. It is well illustrated, and pays special attention to differential snake diagnosis, a subject of growing importance now that anti-venin is being more generally used.

A brief but comprehensive paper on the differentiation of the poisonous snakes of India is one by Green-Armytage.[3] He states that it is largely compiled out of Major Wall's book, but recommends its condensed form for use as a ready reference, to be hung up in hospitals and dispensaries, and its object is to save time which would otherwise be spent in hunting through works of reference.

A monograph on snakes and snake poisoning in the United States is one by Prentiss Willson.[4] The communication consists of about sixty pages, and is divided into two parts. The first part is almost an epitome of all the important and practical facts connected with

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[1] Millard, C. K. (June, 1911), "Are Unvaccinated Persons a Danger to the Community?" *Public Health.*

[2] Wall, F. (February, 1909), *The Poisonous Terrestrial Snakes of our British Indian Dominions, and how to Recognise them.* Reviewed in *Indian Medical Gazette.*

[3] Green-Armytage, V. B. (March, 1911), "An Aid to Diagnosis of Poisonous Snakes." *Indian Medical Gazette.*

[4] Prentiss Willson (1908), *Snake Poisoning.* Reviewed in *British Medical Journal*, November 7, 1908.

Snake-Bite —*continued*

the crotalin snakes and the two dangerous columbrine species. The second part is devoted to the pathology, symptoms, complications and sequelæ, duration, cause of death, diagnosis, prognosis, and treatment of snake-bite in the United States. In his paper he states that the majority of patients will undoubtedly recover, for the simple reason that the amount of venom injected is not a fatal dose. The only hope lies in local treatment which will limit the absorption of venom from the wound. He recommends the uses of a series of ligatures (*vide infra*), free incision or amputation. With regard to specific anti-venin, no serum is obtainable commercially in the United States, nor is it likely that it ever will be, the difficulties of production being so formidable and the morbidity and mortality from snake-bite in the United States insufficient to encourage the preparation of an effective antivenomous serum.

A new variety of horned viper found in Tunis has been described under the name of *Cerastes subcornuta* by Millet-Horsin.[1] The article describing it contains useful notes by Doumergue for differentiating between the other Tunisian vipers, with an addition by the author.

The *Echis carinata* is perhaps of special interest, owing primarily to its extended distribution, and secondarily to the frequency with which serious results follow its bite.

Besides being found in India it occurs in both Egypt and the Sudan; its occurrence in Africa is, however, not common, and the African variety does not seem to be so venomous as the Indian.

Many articles have appeared on *Echis carinata*, and a composite extract from four of these [2] may be of interest, dealing merely with symptoms and treatment.

The symptoms generally do not set in for 10 to 27 hours, and are usually heralded by pain and swelling of the bitten part. Hæmorrhages occur about this time from the gums, nose or rectum, and there is nearly always oozing of sero-sanguineous fluid from the bite itself. Faintness comes on, but unconnected with the hæmorrhage. There is some fever and diarrhœa.

This condition may persist for a long time and the patient may recover or death may occur; sometimes even fifteen days after the bite.

Internal hæmorrhages have been noted in some cases.

The treatment is still *sub judice*.

Anti-venin, though employed in a great many of the reported cases, is not supposed to be of any use.

Wide and deep incision with dissection in the direction of the venous and lymphatic return is perhaps the best treatment, followed by washing with potassium permanganate solution, or the rubbing in of potassium permanganate crystals.

The remainder of the treatment is merely symptomatic, consisting in stimulation and the administration of hæmostatics.

Ligature (*vide infra*) above and below the bite was employed in nearly every case.

Snake venoms have received much attention during recent years with regard to their probable composition and physiological action.

To attempt to deal with venom composition would take up too much space and would not be of interest to many. An extremely interesting work on venom hæmolysis [3] is well worthy of note, and the summary of the paper is given here.

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[1] Millet-Horsin, M. (1910), "Notes sur les serpents venimeux de Tunisie. Au sujet d'une variété non encore décrite de la vipère à cornes." *Arch. de l'Inst. Past. de Tunis*, III.

[2] (*a*) Fraser, F. C. (November, 1910), "Two Cases of Snake poisoning—Recovery." *Indian Medical Gazette.*

(*b*) Reinhold, C. H. (November, 1910), "A Fatal Case of Snake-bite by *Echis carinata*." *Ibid.*

(*c*) Moncrieff, W. E. (March, 1909), "Bites of the *Echis carinata*." *Ibid.*

(*d*) Owen, C. A. (December, 1908), "The Bite of *Echis carinata*." *Ibid.*

[3] Preston Kyes (March 1, 1910), "Venom Hæmolysis." *Journal Infectious Diseases.*

Snake-Bite —*continued*

(1) That there is present in all venoms a hæmolysin, existing as one of a number of distinct toxins.

(2) That this hæmotoxin effects hæmolysis only in conjunction with a so-called complementary substance which, however, may be found within the erythrocytes.

(3) That so far as at present recognised the activating substances are lecithins.

(4) That the reaction between hæmotoxin and lecithin is essentially a chemical reaction resulting in the formation of a complete lysin.

(5) That this complete lysin is a true toxin, in that it stimulates the production of a specific antitoxin.

The physiological action of snake venoms is of more general interest.

In an article by Arthus [1] comparing the action of cobra venom and curare, he points out that in rabbits the intravenous injection of cobra venom acts primarily on the respiratory centre, and only through it on the cardiac and vasomotor centres. In this action it resembles curare, except that the incubation period of the poison action is briefer with curare. In both, prolonged artificial respiration may have good results, while the poison is being eliminated. Meanwhile the specific antivenin may be administered, and he states that even late injection is of great value if artificial respiration and the general body temperature have been kept up.

Lamb [2] in an interesting article on Indian snake venoms and antivenomous sera, deals with the physiological action of the common Indian species of snake venoms.

From observations of animal experiments he concludes that the following symptoms should occur :—

In the case of the Cobras and Kraits.

Locally there is considerable pain at the site of injection, soon followed by swelling, tenderness and redness. The patient feels intoxicated, sleepy, and weak in the legs. Nausea and vomiting are often early symptoms. Paralysis increases till he is unable to stand, and the tongue and larynx become affected. The breathing becomes slower and ultimately stops, the heart often going on beating for some time. Convulsions may precede the ultimate dissolution. Should the patient survive the paralytic symptoms, he returns quickly into a state of complete health, except perhaps in intoxication with the venom of *Bungarus fasciatus*, in which case a chronic nervous illness may supervene.

Viperine Venoms. *Daboia russelli* and *Echis carinata.*

Locally there is much swelling and ecchymosis, which often extends a considerable distance from the site of puncture; there is often serious hæmorrhage from the wound, which may last for several days. The general symptoms are marked collapse, a small thready pulse, cold sweats, nausea and vomiting, pupils dilated and insensitive to light, and often complete loss of consciousness. The patient may recover temporarily from the general symptoms only to fall into a deeper state of collapse than before. If recovery takes place from this state of depression the local condition extends, while there may be hæmorrhages from the anus and other orifices of the body. Extensive local suppuration and sloughing, malignant œdema or tetanus may supervene.

Albuminuria and hæmorrhage from the kidneys is a constant symptom. Death may be delayed for several days, and recovery is not uncommon.

In the treatment of snake-bite we meet with great advances since the publication of the first Review. It will be to some perhaps rather refreshing, as the treatment is not altogether in the hands of the bacteriologist, a line which all treatment has tended to follow since the introduction of vaccine and serum-therapy and the better grasping of the laws of immunity. The anti-venin treatment, however is yet in a healthy infancy, and a combination of drug and anti-venin treatment gives perhaps the best results.

Lamb (*loc. cit.*) also gives a good compendium of the treatment of the bites of poisonous snakes and says :—

In cases of poisonous snake-bite our efforts to influence the result should take two directions.

(1) To prevent absorption of the poison.

(2) To counteract or lessen its effect on the organism.

(i) Apply a ligature immediately on the limb above the situation of the bite. It must be lightly applied, and where there is only one bone, not on the forearm or lower leg.

Make a deep and free incision right down to the bone if possible, and wash out the wound with a strong solution of potassium permanganate. Wall considers the application of any destructive agent to a single incision through the wound as almost useless.

The ancient idea of sucking the wound is of no value.

(ii) Antivenomous sera are highly but not strictly specific. Only the specific anti-serum will be of use in a case of snake venom intoxication.

He recommends that the following instructions should be followed :—

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[1] Arthus, M. (July, 1910). "Venin de cobra et curare." *C. R. Acad. Sciences.*

[2] Lamb, G. (1909), "Snake Venoms and Antivenomous Sera." *Transactions Bombay Medical Congress.*

Snake-Bite —*continued*

They are based on (*a*) The neutralising power of the serum—that is, the exact amount of serum which can neutralise a given amount of venom; (*b*) The amount of poison which a snake can inject; and (*c*) The quantity of venom the injection of which a man can survive.

(1) The serum should be injected as soon after the bite as possible.

(2) The injection should always be made intravenously.

(3) At least 100 c.c. of the serum should be given.

As regards the treatment of snake-bite, other than by antivenomous serum, little or nothing can be done beyond keeping the patient quiet and warm. Small doses of alcohol may be beneficial, but the employment of enormous doses cannot receive too strong condemnation. Strychnine has the same action as alcohol.

In cases of viperine intoxication, adrenalin chloride should be given to countcract the paralytic action of the venom on the vasomotor apparatus.

Wall lays stress on the incomplete way in which many cases of snake-bite and snake poisoning are reported, frequently only one or two of the symptoms being mentioned, which are not necessarily symptoms of *ophitoxæmia* at all, to the exclusion of others which, though less obvious, are perhaps of greater importance in establishing a diagnosis. He points out that cases of snake-bite are often reported as snake poisoning. He shows the importance of fright and has no doubt that many cases of snake-bite by non-poisonous snakes are reported as snake poisoning.

He quotes examples showing how the bites of non-poisonous snakes, lizards, skunks, and other small animals cause death by fright alone. He gives the differential diagnosis between snake poisoning and fright. He states that it is impossible even for an expert to say by the appearance of the bite whether it was caused by a harmful or harmless variety of snake.

He shows, by a series of very interesting experiments, the uselessness of ligatures. Animals died after being bitten by poisonous snakes, although ligature had been applied as tightly as possible before the bite. Esmarch's rubber band, however, is said to be of use, but it has not been sufficiently experimented with. (These are extremely interesting facts, as ligatures have been used almost universally from time immemorial.)

He points out that alcohol is contra-indicated where anti-venin has been used, recommends artificial respiration as a method of treatment, and suggests the employment of intravenous injection of potassium permanganate. (*Vide infra.*)

In a paper by Brunton [1] the nature and mode of action of venoms is considered. This author also describes the lancet set in a hollow wooden handle which contains permanganate of potash crystals. The instrument was introduced by him and recommended to be sold at a reasonable price to Indian natives. After the reading of a paper by Rogers [2] at the "Bombay Medical Congress Transactions," the use of Brunton's lancet was discussed, and it was considered by some not sufficiently large to allow of free incision, necessitating dissection about the part bitten before the application of potassium permanganate.

Rogers stated that he tried intravenous injection of potassium permanganate, but found it too poisonous, while the sodium salt was precipitated by the boiling necessary for sterilisation. He stated that the intravenous injection of anti-venomous serum was of use in animals even after paralysis had set in. With regard to the suggested intravenous injection of potassium permanganate, the following extracts from Bannerman's [3] paper are of importance and interest.

He warns the medical profession against this method of treatment. In attempting to inject 50 c.c. of a 5 per cent. solution of potassium permanganate intravenously into a dog, after 10 c.c. had been injected, death resulted. The post mortem showed intravenous clotting. Further experiments proved that even 5 c.c. was sufficient to cause death in 63 seconds. Even experiments with a ·5 per cent. solution caused slow death after injection.

Local injection of a 5 per cent. solution of potassium permanganate is not unattended with danger; 10 c.c. of this produced local gangrene and extensive sloughing when injected under the skin of a dog.

In the Third Report of these Laboratories mention was made of a curious habit of spitting or the squirting of fluid from the mouths of some snakes, such as *Naia nigricollis*, one of the Sudan cobras.

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[1] Brunton, L. (1909), "On Snake Venom, and the Means of Preventing Death from it." *Transactions Bombay Medical Congress.*

[2] Rogers, L. (1909), "Further Results of the Local Permanganate of Potassium Treatment of Snake Bite." *Ibid.*

[3] Bannerman, W. B. (June, 1910), "The Treatment of Snake-bite Cases with Potassium Permanganate." *Indian Medical Gazette.*

Snake-Bite —*continued*

A writer [1] noting this states that a common South African snake, the "ring-hals," has this power of squirting fluid even as far as 4 to 6 feet. Combined with this spitting power they can also jump a considerable distance. The writer has seen one jump about 6 feet. Further information on this subject will be found in the Fourth Report of these Laboratories, Vol. B.

Much attention has recently been paid to the peculiar methods employed by Indian snake charmers in treating cobra bites by the use of snake root and snake stone.

Two papers [2&3] have appeared in recent literature and they are both curious and interesting.

Spirochætes and Spirochætosis (including **Relapsing Fever**). It is by no means easy to group the numerous papers dealing with this huge subject, because so many of them deal each with different aspects of the spirochætal diseases, and one frequently finds the same observer working with different strains of spirochætes. As a matter of convenience, however, it has been thought well to separate human from animal spirochætosis.

Human. Under this it seems advisable to consider papers of a general nature in the first place, *i.e.* those dealing with geographical distribution, accounts of epidemics, the clinical aspect of cases, methods of transmission, and prophylaxis, the determination of the spirochætes concerned, and conditions due to spirochætes as distinct from the spirochætal fevers; then to review articles devoted to experimental work and questions of etiology, and finally to group those papers devoted wholly to questions of treatment, whether experimental or in the course of medical practice. Spirochætosis of animals will be considered separately and as briefly as possible, but it must not be forgotten that it is an important subject calculated to throw light on the various types of the human disease, so that it cannot be lightly dismissed. The reader's indulgence is requested if he finds the various divisions of the subject somewhat mixed up, for this is not a text-book where one can proceed in a more or less orderly manner. Some allusions may be made to syphilis and yaws, but these diseases have special sections devoted to them, as have the chief skin lesions associated with the presence of spirochætes. We may start conveniently with a paper by Mackie,[4] which is indeed a review of our knowledge of the spirillar fevers during the period immediately preceding the middle of 1908. It is not easy to review a review, but it may be said that *Sp. obermeieri* (*recurrentis*), *Sp. duttoni*, *Sp. novyi*, and *Sp. carteri* are mentioned separately, and he considers each in some detail, dealing with morphology, relation to human disease, experimental and natural transmission, immunity, and the morbid anatomy of the disease caused by each species. As most of the information he supplies has now found its way into the text-books, there is no need to be discursive, but one may quote Swellengrebel's scheme of classification, which he gives in full:—

Cells with rounded extremities forming a part of a spiral. Cell division is transverse, and is generally brought about by transverse cleavage, previous to which the cell increases in length. Sometimes division is accompanied by nipping in of the mother cell. After division the daughter cells remain for some time united by an unbroken filament. The flagella, when present, take their origin from a periplastic sheath cap (calotte), and are themselves prolongations of the periplastic appendage.

The *calotte* gives the cell a pointed appearance.

First Subfamily.—Spirillaceæ (new family). Cells not flexible.

Genera. Spirillum and vibrio (of Migula).

Second Subfamily.—Spirochætaceæ (new family). The cells are flexible.

First genus.—Spirochæta (Ehrenberg). Cells without flagella, with a well-developed periplastic appendix, and often showing an alveolar structure. Sometimes there are myonemes in the appendage. Types—*Spirochæta plicatilis* (Ehrenberg); *Spirochæta Balbiani* (provisionally).

Second genus.—Treponema (Schaudinn). Cells with a flagellum at one and sometimes at both extremities, which is the prolongation of the sheath cap. A periplastic appendage has sometimes been demonstrated. Types: *Spirochæta buccalis dentium*; *Treponema pallidum.*

Personally I believe a good many of Swellengrebel's statements as to morphology will require revision, so one need not quote further from the extracts which Mackie supplies. Papers by Strong [5] may be consulted by those who wish information regarding precipitin and agglutination tests, and the employment of such methods for differentiating the various

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[1] B. G. B. (May, 1909), "The Spitting of Snakes." *Journal Tropical Medicine and Hygiene.*

[2] Reichwald, W. F. (April, 1911), "The Absorbent Stone: A Day with Cobra-Hunters." *Journal Royal Army Medical Corps.*

[3] (April 1, 1911), "Snake Root and Snake Stone." *Lancet.*

[4] Mackie, F. P. (1908), "A Review of Recent Work on Spirillar Fevers." *American Society of Tropical Medicine. Collected Papers.*

[5] Strong, R. P. (1908), "The Diagnosis of African Tick Fever from the Examination of the Blood." *Arch. f. Schiffs-u. Tropen-Hyg.*

species of spirochætes. Strong finds that neither of these methods are of value for this differentiation or for diagnosis. The latter must be made from the clinical signs, examination of the peripheral blood, splenic and hepatic puncture if considered justifiable, and the inoculation of such susceptible animals as white mice, white rats and monkeys. A general paper by Carter [1] on the pathogenic spirochætes of the mammalia contains a good deal that is interesting and useful, but the rapid advance of our knowledge has rendered some of it out of date, more especially perhaps the section headed the cytology of the life-cycle. There is an extensive list of references. A paper of special value from the clinical standpoint is that in which Choksy [2] deals with the relapsing fever of Bombay. Speaking of the parasitic infection in human beings, he says :— Spirochætosis—*continued*

> The presence or absence of the spirochætes in the blood during infection is variable in the different varieties of the fever. Whilst in the European type infection is heavy, in the African it is sparse, and in the Indian variable. The *Sp. obermeieri* are present in the blood stream from the onset of the fever until the crisis, when they suddenly and totally disappear ; it is presumed that they then collect in the spleen (Metchnikoff). They are never found in the secretions. *Sp. duttoni* is very sparse and much less in evidence than the other varieties. Heavy infection is, however, met with in the Arabian type (Markham Carter). *Sp. carteri* are found in the blood during the acute attack, become more frequent as the crisis approaches, when they completely disappear. They are not to be seen during the secondary rebound, nor always during a relapse. And even in undoubted cases, with all the characteristic clinical symptoms, they may not be present. Vandyke Carter sometimes came across immense numbers, often incalculable except by hundreds of millions. They were often so crowded as to offer mechanical impediment to the circulation, as evinced by dusky lividity of the countenance.

He mentions the grave bilious typhus relapsing form in which the infection may be very heavy, one spirillum to every three or four red cells. He further states that—

> The disappearance of the spirilla during the apyrexial interval was supposed to be due to their congregation in the spleen. Lamb, however, has found that spleenless monkeys did not suffer to a greater extent than normal ones. He thinks that the crisis is determined, not by phagocytosis, but by the increase of spirillicidal substances in the blood ; the former being of subordinate importance. According to his idea, spirilla escape by finding areas protected from the full spirillicidal pressure of the blood, and remain there until such pressure has been reduced by excretion or by the production of anti-spirillicidal bodies. They then are able to recultivate themselves in the blood stream and so produce a relapse. (Mackie.)

One cannot enter here into all the clinical signs which Choksy describes, but he gives a useful table differentiating the European, Indian, American, and African types. Owing to the discovery by Sergent and Foley [3] of a new North African species (*Sp. berbera*) which is the cause of relapsing fever in South Oran, one has found it advisable to add to Choksy's table, and also to a table drawn up by Mackie (*loc. cit.*), which sets forth the differences in morphology, etc. of the different species of spirochætes. These will be given immediately, as such an arrangement saves much space and time, and presents in a small compass the essential points of, as will be seen, half-a-dozen papers. Bousfield [4] described cases seen in Egyptian soldiers at Khartoum, and Balfour [5] studied and carried out some experimental work on the spirochæte obtained from these cases. The infection appeared undoubtedly to be transmitted by lice, but this Egyptian form is also included in both the comparative tables, and its main features can be studied there. In all probability it is due to *Sp. berbera*, which may be the cause of all the relapsing fever occurring in North Africa. Although it carries us beyond the limit set for this Review, it is perhaps advisable in this place to direct attention to a very recent paper by Stott,[6] who suggests that there are two distinct kinds of human spirochætal fevers in India. He gives an account of cases which he considers and compares under the headings, place of origin, symptomatology, morphology of causative parasites and agglutination reactions. As he had only two cases to contrast, no very definite conclusions can be drawn from his results, but he certainly presents some evidence in support of his hypothesis. His work with monkeys went some way to show that in the second of his cases, bed-bugs may have played a part as transmitting agents, but here again he was unable to obtain indubitable proof. It is, however, more than likely that several varieties of spirochætal fever exist in India.

We now submit the differential tables to which allusion has just been made.

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[1] Carter, R. M. (1909), "Pathogenic Spirochætosis in Mammalia." *Transactions Bombay Medical Congress.*

[2] Choksy, N. H. (1909), "Bombay Relapsing Fever." *Ibid.*

[3] Sergent, Edm., and Foley, H. (May 25, 1910), "Recherches sur la fièvre recurrente." *Ann. de l'Inst. Past.*

[4] Bousfield, L. (October, 1910), "Observations on Human Spirochætosis in the Sudan." *Journal Royal Army Medical Corps*, and *Fourth Report, Wellcome Tropical Research Laboratories*, 1911, Vol. A.

[5] Balfour, A. (October, 1910), "The Spirochæte of Egyptian Relapsing Fever. Is it a Specific Entity ?" *Ibid.*

[6] Stott, H. (August, 1911), "On Two Varieties of Relapsing Fever. Spirochætal Infection in India." *Indian Medical Gazette.*

Spirochætosis—*continued*

	Egyptian *Sp.* (?) possibly *berbera.*	Algerian *Sp. berbera*, nov. sp.	European *Sp. obermeieri* (*recurrentis*).	African *Sp. duttoni.*	American *Sp. novyi.*	Asiatic *Sp. carteri.*
Minimal length	13·5 μ, but possibly some coiled forms only 12 μ	12 μ	12 μ	13 μ	7–9 μ ..	12 μ .. ..
Shape	Irregular open flexures	Irregular open flexures	Spiral	Open flexures	Regularly spiral	Open flexures
Flagella ..	?	?	Peritrichous ..	Peritrichous ?	Terminal (Novy); Peritrichous (Frænkel)	?
Animals susceptible	Gerbils, but only slightly; monkeys (*Cercopithecus*)	Rats and mice with difficulty; monkeys (*Macacus; Cynocephalus*)	Small rodents only after passage through monkeys	Small rodents and many animals very susceptible	Small rodents very susceptible	Small rodents infected with difficulty
Course in animals	Very mild ..	As a rule, mild	Mild	Very severe ..	Severe ..	Very mild ..
Sub-inoculations in animals	Gerbil to gerbil positive; monkey to monkey probably negative	Rat to rat or mouse to mouse with difficulty; monkey to monkey negative	Monkey to monkey and mouse to mouse positive (Fülleborn and Meyer)	Monkey to monkey positive; same for most animals (Breinl, Kinghorn and Garrett)	Monkey to monkey and mouse to mouse positive	Monkey to monkey and mouse to mouse positive (Mackie)
Course in man	Fairly severe	Fairly severe	One, sometimes two, relapses	Severe, four or five relapses	?	Severe, one or two relapses
Parasites in human blood	Variable ..	Variable ..	Heavy infection	Very sparse ..	?	Variable ..
Natural transmission	By lice ? ..	By lice ? ..	?	By ticks ..	?	By lice ? ..
Serum-reaction	?	Immune serum possibly without effect on *Sp. recurrentis* (Russian strain)	Immune serum without any effect on *novyi* and *duttoni*	Immune serum without effect on *novyi* or *obermeieri*	Immune serum without effect on *obermeieri*, *duttoni* or *carteri*	Immune serum without effect on *novyi*

	Egyptian *Sp.* (?) possibly *berbera.*	Algerian *Sp. berbera*, nov. sp.	European *Sp. recurrentis.*	African *Sp. duttoni.*	American *Sp. novyi.*	Asiatic *Sp. carteri.*
Incubation period in man	Doubtful; possibly more than 12 days	Not stated ..	5–7 days ..	7–10 days ..	5–7 days ..	7 days .. ..
Duration of first attack	2–8 days ..	5–7 days ..	5–6 „ ..	Average 3 days (rarely 4–5).	5–6 „ ..	5–7 days ..
Duration of apyrexia	2–9 days: 6 apparently the most common	6–16 days: usually 7–8 days	7–10 „ ..	1–8 days (occasionally 10–18)	7–10 „ ..	5–13 days; occasionally up to 19 days
Number of relapses	One or two, possibly three	One or two certainly, possibly others, but very slight	1–2 ..	3–5 (sometimes up to 11)	One (rarely 2–5)	1 relapse in 40 per cent., 2 in 7 per cent. and 3 more in 3 per cent.
Relapses absent	In one case ..	?	?	..	Not uncommon	In 50 per cent.
Rigors and sweating	Present; rigors only in one case	Rigors not mentioned; sweating marked	Present ..	Rigors in 50 per cent. only, sweating present	Present ..	Very frequent
Pains in limbs, muscles, etc.	Present ..	Frequent ..	„ ..	Frequent ..	„ ..	„ „
Toxæmia (bilious-typhus type)	Possibly in one case	Absent ..	Mentioned ..	?	Mentioned ..	Present in 10–20 per cent.

Spirochætosis—*continued*

	Egyptian *Sp.* (?) possibly *berbera.*	Algerian *Sp. berbera,* nov. sp.	European *Sp. recurrentis.*	African *Sp. duttoni.*	American *Sp. novyi.*	Asiatic *Sp. carteri.*
Low pulse rate after crisis	Apparently not noted	No mention ..	Present ..	?	Present ..	Almost invariably present
The tongue ..	White and furred	Moist, white and furred in centre	Large and moist, except in grave infection	?	Large and moist, except in grave infection	Large, flabby and moist, except in grave infection
Appetite ..	Not mentioned: probably therefore never voracious	Not mentioned: probably therefore never voracious	Poor, sometimes voracious	?	Poor	Poor, rarely voracious
Jaundice ..	Absent ..	Exceptional and slight	Mild, except in grave infection	Infrequent in Uganda	Mild, except in grave infection	Present in 70–80 per cent.; grave in toxæmia
Vomiting of bile	Not mentioned; vomiting present	Not mentioned: vomiting present	Not uncommon	Not usual ..	Not uncommon	Present in 70–80 per cent.
Diarrhœa ..	Absent ..	Rare.. ..	Of brief duration	Always in the Congo; infrequent elsewhere	Moderate ..	Present in 12 per cent.
Tympanites ..	Not mentioned	Common ..	Grave in toxæmia	?	Grave in toxæmia	Invariably associated with toxæmia
Hiccough ..	„ „	Not mentioned	Present ..	Mentioned ..	Present ..	Often present
Hæmorrhage from stomach and intestines	„ „	„ „	Not frequent	?	Not frequent	More frequent than in the other varieties
The liver ..	Tender, but not markedly enlarged	Enlarged and tender	Enlarged ..	Enlarged ..	Enlarged ..	Enlarged and tender
The spleen ..	Enlarged and tender	„ „	„ ..	„ ..	„ ..	„ „
Parotitis ..	?	?	Mentioned ..	?	?	Present in about 10 per cent.
The urine ..	No albuminuria	Dark; excess of urobilin; slight albuminuria	High coloured, scanty	?	High coloured	High, bilious, scanty
Hæmaturia ..	Absent ..	Absent ..	?	?	Present ..	?more frequent than other hæmorrhages
Epistaxis ..	Mentioned ..	Mentioned ..	Mentioned ..	Mentioned ..	More frequent than other hæmorrhages	Present in 10 to 15 per cent.
Pulmonary symptoms	„ ..	„ ..	„ ..	„ ..	Present ..	Present; more so in toxæmia
Delirium (violent)	Absent ..	Absent ..	„ ..	Infrequent ..	„ ..	Not uncommon; also maniacal
Facial paralysis	„ ..	„ ..	?	Mentioned ..	?	Not observed
Eye affections	„ ..	Slight conjunctival injection	Mentioned ..	Frequent (Moffat, Harrord, and Cook)	Mentioned ..	Present in about 1 per cent.
Herpes labialis	May occur ..	May occur ..	Not uncommon	?	?	Not uncommon
Mortality rate	*Nil* (8 cases)..	*Nil* (42 cases)	Very low, under 5 per cent. except in grave infection	13·6 per cent. (?); about 50 per cent. on the Zambesi (?), probably lower	2 to 4 per cent., rarely 10 per cent. higher in toxæmia	30 to 40 per cent. in all cases; if toxæmic cases are excluded 15 to 20 per cent.

Spiro-chætosis—*continued*

More work on the Egyptian form has been done by Graham-Smith,[1] whose thesis, however, is in the main a useful compilation. It is impossible to review it in the small space available, but it is mainly concerned with the possible conveyance of infection by different kinds of domestic vermin, and will be found valuable by those carrying out laboratory work in this direction. He concludes that relapsing fever in Europe and in North Africa, India, and Indo-China is, in all probability, transmitted by body-vermin (louse or flea) in the act of feeding, and the available evidence is as favourable to Mackie's hypothesis (lice transmission) as it is opposed to that of Tictin (bed-bug transmission).

A word or two as regards the form of spirochætosis met with in Arabia, and described by Carter [2] seems advisable, as it resembles the African rather than the Indian type. It is characterised by a short incubation period, headache and boneache together, with enormous œdema at the site of tick bite (for ticks of the Ornithodoros type play the part of vectors), intense prostration, lack of mental activity, increase in the size of the spleen, terminal copious greenish diarrhœa, and a slow return to comparative health. He describes the spirochætes found, some of which were peculiar in that they presented globose thickenings. These he illustrates and explains as possible stages in the life-cycle of the parasite. Strong [3] compares the Indian relapsing fever with African tick fever. He finds that for the study of these and the other forms, white mice are the only suitable experimental animals, as they alone are susceptible to all the species of spirochætes.

Strong took rats (his stock of white mice being exhausted) to India. These rats had previously been immunised separately against the African, European, and American strains of spirochætæ. He succeeded in getting a few cases of Indian relapsing fever, and inoculated his rats with spirochæte-containing blood from them. He states that—

> Twenty-four hours after the injections were made a microscopic examination of the blood of the animals showed that no spirochætæ were present in those immunised with the American and with the European strains, but that spirochætæ were present in the blood of all those animals immunised against the African strains as well as in the blood of the control normal animals. Forty-eight hours after infection the spirochætæ were still present in the blood of one of the animals immunised against the African species, and, as might be expected, in one of the control normal animals; in all of the others the spirochætæ had disappeared. An examination seventy-two hours after infection showed the blood of all the animals negative for parasites, and the organisms did not appear or reappear again in any, as was evidenced by repeated careful examinations.

He therefore concludes that—

> These experiments seem to show that Bombay spirillum fever is distinct from African tick fever, but that it constitutes a form of relapsing fever very closely related, if not identical, with the forms of relapsing fever encountered in Europe and the United States.
>
> Finally, from a consideration of the work performed by other investigators and from my own experiments, carried on with all these different strains of spirochætæ, including a study of the morphological characteristics, serum reactions, and animal inoculations, it appears to me that the African and European strains of spirochætæ are distinct species. However, it does not yet seem clearly demonstrated that the American and Indian strains are distinct from the European; if not identical, these strains must certainly be very closely related to one another.

One need merely mention the occurrence of human spirochætosis in Abyssinia as noted by Brumpt [4] and Doreau,[5] in Tangiers, as signalised by Breeze,[6] in Nyasaland, as recorded by Hearsey,[7] who shows that its range there is much more extended than was thought to be the case, and speaks of the iritis complicating it. Chisholm [8] found it present in the neighbouring district of North-Eastern Rhodesia, and mentions a case where complete deafness set in during a relapse. Cases have been reported from places so wide apart as Tonkin and Colombia Mathis and Leger [9] worked at the disease in Tonkin, but were unable to classify the spirochæte

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[1] Graham-Smith, U. (1909), "On some Cases of Relapsing Fever in Egypt, and the Question of Carriage by Domestic Vermin." *Thesis.* London.

[2] Carter, R. M. (October, 1908), "A Preliminary Note on Spirochætosis occurring in Southern Arabia and the Morphology of the Parasite." *Indian Medical Gazette.*

[3] Strong, R. P. (June, 1909), "Relation of the Indian Form of Relapsing Fever to African Tick Fever." *Philippine Journal of Science,* B.

[4] Brumpt, E. (October 14, 1908), "Existence de la Fièvre des Tiques en Abyssinie." *Bull. Soc. Path. Exot.*

[5] Doreau, P. (1909), "Notes de géographie médicale sur l'Abyssinie." *Ann. de Hyg. et de Méd. Col.*

[6] Breeze, G. R. (April 1, 1909), "Relapsing Fever in Tangier, Morocco." *Journal Tropical Medicine and Hygiene.*

[7] Hearsey, H. (October 2, 1909), "Tick Fever in Nyasaland." *British Medical Journal.*

[8] Chisholm, J. A. (February 19, 1910), "Tick Fever in Nyasaland." *Ibid.*

[9] Mathis, C., and Leger, M. (January 9, 1910), "Recherches sur le spirochète de la fièvre récurrente du Tonkin." *Bull. Soc. Méd. Chir. de l'Indochine.*

causing it. Robledo [1] describes the recurrent fever of Colombia, and concludes that (1) The spirochæte which produces it does not differ markedly from *Sp. duttoni*. (2) It is usually transmitted by the bite of *Argas americanus*. (3) The symptoms approach those of African tick fever. Of greater importance is Darling's [2] paper on the form met with in Panama. His conclusions are given here, though I am of opinion that some of them will require modification in the light of recent work :— Spirochætosis—*continued*

The relapsing fever of Panama is distinct from the analogous fever of Africa, Europe and Asia, although belonging to the same general class.

The micro-organism causing the local relapsing fever belongs to the group containing *Sp. obermeieri*, *Sp. duttoni*, and *Sp. carteri*.

This spirochæte causes a recurring infection in man, monkeys (genus *Macacus*), and white mice, and single paroxysms in white and wild rats.

The animal reactions are similar to those obtained by Norris, Pappenheimer, Fleurnoy, Novy and Knapp, with the organism erroneously identified by the latter two as *Spirillum obermeieri*.

The blood of animals very recently recovered from an infection, and that between paroxysms, where spirochætes are apparently absent from the peripheral blood, is infectious, and by analogy this affords a valuable means of diagnosis of the fever in man during the afebrile period, by the inoculation of susceptible animals, mice and rats, with patient's blood.

There is considerable variation in the morphology of the spirochete in the same strain, and sometimes in the same smear.

Identification of spirochetes cannot be made with certainty on morphological grounds.

The mechanism of defence is largely that of phagocytosis by hepatic endothelium.

Infected animals sacrificed at different stages of the infection show, as the disease advances, an increasing number of fragmented spirochetes, engulfed by endothelial cells of the liver.

In animals which had recently recovered from an infection a liver emulsion is more infectious than heart's blood. This suggests the probable vitality and unity of fragments.

Infection by one strain of spirochetes is followed by a considerable degree of active immunity for that strain, but such immunity is not potent against another strain from a different source, although of the same species and from the same locality but from a different human host.

For the production of preventive and curative serums, polyvalent sera derived from all the strains will probably be necessary.

The blood, in moderate amounts, of subjects which have recovered, is of no value in preventing infections in white mice and white rats.

Relapses may be explained by the multiplication of spirochetes in out-of-the-way places where they do not enter the portal circulation and cannot be engulfed by liver endothelium.

Agglutination of spirochetes occurs at least twenty-four hours before the crisis in rats *in vitro* and *in vivo*.

This spirochete is probably a spiral ribbon and not a spiral cylinder.

The group of spiral-shaped micro-organisms needs reclassification on a basis of morphology, pathogenicity and habitat.

This spirochete is more closely related to bacteria than to protozoa.

The rôle of the spleen is similar to that observed in anæmia.

With suitable emulsions of liver substance and immune serums it should be possible to demonstrate specific opsonins.

The natural mode of infection is probably by means of an intermediary host—some suctorial insect or acarid, either directly or by means of an alternate host, such as a wild rat or other susceptible animal.

The most recent article on the European variety is one by Fehrmann,[3] who deals with an epidemic in St. Petersburg. He mentions that in the case of Mohammedan Tartars who shave both head and pudenda, cephalic and pubic lice cannot be vectors, and that the blame must be laid on clothes lice. His notes on the methods of getting rid of vermin by disinfection are interesting. Lice, bed-bugs, and fleas have all to be dealt with, and disinfection is required (1) of the clothes and linen, (2) of the premises or locality, and (3) of the patient. As regards (1) the use of xylol, xylol and turpentine or petroleum is effectual, but the method is troublesome and expensive. Formaldehyde disinfection and treatment in a Clayton apparatus proved unsuccessful, for lice apparently dead revived the next day. Ordinary steam disinfection is not recommended, but the "Helios" system gave good results. The apparatus is not expensive, and can be managed by a man without special technical training. It is described by Schumberg in the *Zeitschrift für Hygiene und Inefktionskrankheiten* for 1902 (Vol. XLI., Part 2). With respect to (2), bed-bugs and fleas have chiefly to be killed, for lice do not often leave their hosts.

[1] Robledo, E. (March 10, 1909), "Fièvre récurrente de Colombie." *Bull. Soc. Path. Exot.*

[2] Darling, S. T. (August, 1909), "The Relapsing Fever of Panama." *Archives of Internal Medicine.*

[3] Fehrmann, E. (1910), "Das Rekurrensfieber in St. Petersburg." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XIV., No. 21.

Spirochætosis—*continued*

A dry cleaning of the room is not so good as a wet one, because in the former, fleas get hidden in the sawdust. Boiling water, steam, or the flame of a benzine lamp may all be employed with success under suitable conditions. So may the Clayton method. So far as (3) is concerned one has to deal with pubic and head lice. Balsam of Peru gets rid of the first, but the latter present a problem. Xylol may be used, but the danger of fire must be remembered. Its inflammability may, however, be lessened by the addition of sal-ammoniac, styrax, or turpentine. Afterwards thorough washing with soap and water is indicated.

Moellers[1] has worked at the transmission of *Sp. duttoni* by *Ornithodoros moubata*. He found, working with 110 ticks to start with, that ticks are able in the course of a year and a half to infect successively ten healthy monkeys. The eleventh and twelfth monkeys of the series did not become infected. By the end of this time his 110 ticks had become reduced to 7. He also proved that the virus can be transmitted hereditarily to several generations of ticks. By far the most important work on transmission, however, is that of Leishman,[2] who made the important discovery that in *O. moubata* the spirochæte of African tick fever breaks up into granules which are found for the most part in the Malpighian tubes of the tick, but occur also in the walls of the intestinal sac, oviduct, ovary, eggs, and more rarely in the salivary glands, and spermatozoa. In the Malpighian tubes the distribution of these granules is irregular, the parts affected being apparently those which lie in close contact with the alimentary diverticula. One cannot here give an account of Leishman's interesting experiments. The chromatin granules are found in larvæ derived from infected ticks, and in the ticks themselves under special temperature conditions have been found to develop into forms which seem to be young spirochætes. The discovery is so important, and has already had such far-reaching results, that we give Leishman's summary :—

(1) In nymphs of various ages and adults, which have been kept for a week or ten days at a temperature of 34° C., spirochætes have, in some instances, been seen to reappear in various situations, chiefly in the Malpighian tubes and in the walls, not the lumen, of the intestinal sac and diverticula. These spirochætes, however, did not resemble *Sp. duttoni*, as encountered in the blood; they were shorter, more homogeneous, and less regularly curved. They occurred, too, as far as could be observed, not free in the fluids, but actually in the cytoplasm of the cells lining the tubules and the intestinal diverticula.

(2) The above change is preceded or accompanied by an alteration in the character of the granules so constantly found in the Malpighian tubes; these become more coccoid or spherical in form, and many are enlarged beyond the usual limits of size.

(3) Control material in the shape of ticks of the same batches, which had always been fed at the same time and on the same animal, but which had been kept at a temperature of 24° C., showed on dissection no trace of spirochætes, but only granules of the usual types and in the usual situations.

(4) Spirochætes which have reappeared in ticks under the above conditions of temperature, etc., may persist in such ticks for some months after they have been replaced at the lower temperature, and are found in the same situations, though in smaller numbers.

(5) Young nymphs newly hatched from infected parents, when kept at a high temperature, show the same changes in the character of the granules as older ticks and adults, but spirochætes have never been noticed. This would suggest that a feed of blood may be another factor in inducing the change into spirochæte form.

(6) A comparative study has been made of newly hatched nymphs whose first meal consisted of spirochæte blood, and which were subsequently divided into three lots and kept at three different temperatures. For this purpose nymphs of each group were examined daily up to three or four weeks after feeding.

(*a*) In nymphs kept at the lower temperature of 24° C. the ingested spirochætes were found to undergo speedy segmentation of the chromatin and, after a period of ten to twelve days, were found to have disappeared completely from the stomach; later than this, no spirochætes could be detected in any situation in the nymph's body. An increase in the number of granules in the Malpighian tubes appeared to coincide with the disappearance of the spirochætes from the gut, but this point was difficult to verify in view of the constant presence of the granules in almost all ticks, and the variable numbers encountered in different individuals.

(*b*) Nymphs kept at a temperature of 34° C. showed similar changes in the ingested spirochætes, but such changes and the disappearance of the spirochætes from the gut occurred more rapidly than in those kept at 24° C. A few days after the spirochætes had disappeared, they *re*-appeared in the tissues and fluids of the nymph, but in greatly altered form, most being very much shorter than any of those usually seen in the blood, and some little larger than cholera vibrios. While the smallest forms of *duttoni* as seen in the blood are about 16 μ to 19 μ in length—Dutton and Todd mention one of 13 μ—many of these "young" forms, as I may call them, are no more than 8 μ to 9 μ. These young spirochætes persisted as long as the ticks were kept at this temperature, but rapidly disappeared when they were replaced at 24° C. In some situations it was apparently possible to trace the origin of the young spirochætes out of the granules.

(*c*) Nymphs kept at a temperature of 37° C. showed a similar condition as regards the spirochætes to those kept at 34° C.; the young spirochætes appearing after the ingested ones had disappeared from the gut, but in this case they were not so abundant, doubtless on account of the impaired vitality of the ticks which, at this temperature, will not moult, and eventually die in about three or four weeks.

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[1] Moellers, B. (1908), "Experimentelle Studien über die Übertragung des Rückfallfiebers durch Zecken." *Zeit. f. Hyg. u. Infekts.*, Vol. LVIII.

[2] Leishman, W. B. (January, 1910), "Observations on the Mechanism of Infection in Tick Fever and on the Hereditary Transmission of *Spirochæta duttoni* in the Tick." *Transactions Society Tropical Medicine and Hygiene.*

(7) Attempts made with a view to the detection of spirochætes in the eggs laid by infected parents. Out of many hundred eggs examined, it is only recently that spirochætes have been encountered, and this in four eggs only. Two of these were eggs laid by a tick which had been heated for five days at 37° C. some months before, but which had subsequently been kept at 24° C. In this case the spirochætes were scanty and of the usual adult form. The two remaining eggs were dissected out of the ovary of a tick which, after feeding on normal blood, had been placed at 34° C., and kept at this temperature for nearly four weeks before dissection. In this instance the spirochætes were extraordinarily abundant; they occurred in great tangles, and many of them appeared to be in process of development out of the granules. Spirochætosis—*continued*

It may be noted that Leishman thinks it possible that infection takes place not from the salivary glands of the ticks, but through the wounds inflicted by their mouth parts becoming bathed in the fluid copiously secreted from their coxal glands during the act of feeding, and which may contain the virus, either in the form of infective granules or of young spirochætes. The paper requires careful study by all interested in the life history of the pathogenic spirochætes. The author mentions the confirmatory work of Balfour in the case of the Sudan fowl spirochætes and *Argas persicus* (*vide infra*), and that of Darling, who has seen granular forms in the tissues of animals infected with the spirochæte of the relapsing fever of the Isthmus of Panama. Brumpt [1] found that *Sp. duttoni* can be transmitted by *O. savignyi*, as well as by *O. moubata*, and that the latter tick can transmit *Sp. gallinarum* (*marchouxi*), but fails to act as a vector for *Sp. novyi*, and *Sp. berbera*. The same observer [2] has noted the presence of *Sp. duttoni* in the menstrual blood of an infected monkey. In his former experiments he used monkeys (*Macacus sinicus*, and *M. cynomologus*). Schellack [3] has only had negative results in his attempts to transmit *Sp. obermeieri* (*recurrentis*) to the rat by means of *Argas reflexus*, and to the rat, the monkey, and man by using bed-bugs. He is inclined to think that lice carry the European disease.

There are some German papers on the possible rôle of the bed-bug, and on the survival of spirochætes in these insects. They need not be quoted, but will be found in the later volumes of the *Centralblatt für Bakteriologie*, etc. Mention may, however, be made of a recent paper by Nattan-Larrier,[4] who set himself to find out if blood containing spirochætes were ingested by ordinary (house ?) flies, how long the parasites would remain living in the alimentary tracts of the insects, and for how long they would retain their pathogenic action. He places the time for both at something over twenty-four hours, but from experience in this class of work I am inclined to think that erroneous ideas are obtained so far as the first question goes, unless the dark field method is employed. Curiously enough the author does not state the species of spirochæte with which he worked, but it seems to have been *Sp. recurrentis*. Neumann [5] found that the rat louse, *Hæmatopinus spinulosus*, could transmit *Sp. duttoni*, and has some notes on the transmission of spirochætes by ticks. Butler [6] pointed out that when *Sp. duttoni* is kept alive outside the body

small nodules, generally about the hind portion of the organism, but occasionally towards one end, are a common occurrence. The nodule is organically part of the spirochæte, and measures from 1 to 3 μ, and many contain one or more granules taking the chromatin stain. It appears that these nodules show chromatin ducts, proving that the spirochæte must be a protozoan and not a bacterium. The nodules referred to are not spores.

This reminds one of the globose swellings seen by Carter in the Arabian spirochæte (*loc. cit.*). I have seen appearances of this kind in *Sp. granulosa* of Sudan fowls when studied by the dark field method.

Papers on the power of spirochætes to traverse the unbroken skin and mucous membrane are not lacking, though perhaps most of them deal with *Sp. gallinarum* (*marchouxi*). Nattan-Larrier,[7] employing a Russian strain of *Sp. recurrentis* and the white rat, found that the spirochæte can easily and rapidly traverse the unbroken skin of the white rat, but only at points where the skin is fine and very vascular. The mucosa and the conjunctiva are very easily traversed, the male genital mucosa alone seeming to present any difficulty.

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[1] Brumpt, E. (November 11, 1908), "Transmission du *Spirochæta duttoni* par l'*Ornithodorus savignyi*.—Transmission du *Spirochæta duttoni* et du *Spirochæta gallinarum* par l'*Ornithodorus moubata*, non-transmission des Spirochètes de la fièvre récurrente américaine et algérienne par ce même parasite." *Bull. Soc. Path. Exot.*

[2] *Idem* (November 11, 1908), "Passage du *Spirochæta duttoni* dans le sang menstruel." *Ibid.*

[3] Schellack, C. (April, 1909), "Versuche sur Übertragung von *Spirochaeta gallinarum* und *Spirochaeta obermeieri*." *Arb. a. d. Kais. Gesundheitsamt*, Vol. XXX., No. 2.

[4] Nattan-Larrier, L. (May 10, 1911), "Spirilles de la fièvre récurrente et mouches." *Bull. Soc. Path. Exot.*

[5] Neumann, R. O. (1909), "Über das Verhalten der Spirochäten des Rückfallfiebers im Tierkörper und die experimentelle Übertragung der Parasiten durch Zecken und Läuse." *Münch. Med. Woch.*, No. 9.

[6] Butler, C. S. (October, 1908), "A Peculiar Characteristic of *Spirochæta duttoni*." *United States Naval Medical Bulletin*, quoted in *Journal Tropical Medicine and Hygiene*, May 15, 1909.

[7] Nattan-Larrier, L. (May 12, 1909), "Pénétration du Spirille de la fièvre récurrente à travers les téguments et les muqueuses intacts." *Bull. Soc. Path. Exot.*

Spirochætosis— *continued*

Spirochætosis resulting from such invasion is of a mild type, doubtless on account of the small number of parasites gaining access to the circulation. A recent and important paper is that by Gózony,[1] who, working chiefly with *Sp. recurrentis*, came to the following conclusions—(1) That infection by way of the skin is possible. (2) That the mucous membranes of the alimentary tract are not impassable for spirochætes. (3) Spirochætes can traverse the conjunctiva of the mouse. (4) The intact mucous membrane of the genital tract permits the passage of *Sp. recurrentis* through it. The question of hereditary transmission is an important one. The latest contribution to this subject is made by Nattan-Larrier,[2] who in three short papers discusses both hereditary transmission and congenital immunity in the case of rats infected with *Sp. obermeieri* (*recurrentis*), and *Sp. duttoni*. He points out that in the case of the latter spirochæte Breinl and Kinghorn showed that infection could be transmitted from the mother to the fœtus. The conclusion to each of his three papers may be given shortly as follows :—

First. (1) Both *Sp. recurrentis* and *Sp. duttoni* can be transmitted from mother to fœtus. It cannot be said if this phenomenon constantly occurs, as it has not so far been observed in more than 80 per cent. of cases. (2) The number of spirochætes penetrating the placental tissue is never great. This explains the character of the fœtal infection (long incubation, small blood infection, short persistence of parasites in the blood). The virulence of the spirochætes transmitted to the fœtus does not, however, appear to be attenuated. (3) In some cases it seemed that the fœtal infection occurred more readily when the maternal infection was intense and prolonged. When the pregnancy is near its end, the fœtal spirochæte infection is greater, and may cause serious illness and death of the fœtus *in utero*.

Second. (1) The young born of a mother infected a short time before their birth do not possess any immunity during the first days following birth even though there has been a passage of spirochætes from the mother to the fœtus. Immunity, always slow, is not acquired until after the hereditary contagion has determined a spirochætal infection in the new-born. (2) When inoculation is practised on a female at the beginning of gestation the fœtus acquires a spirochætal infection which develops before birth and confers a slight congenital immunity. (3) The newly born of a female spontaneously refractory to the spirochæte of relapsing fever are not protected from spirochætal infection.

Third. (1) Spirochætes can pass from mother to fœtus in the absence of any placental lesions. The fœtal infection does not seem more intense in the rare cases where areas of the placenta exhibit necrosis. (2) The spirochætes are apt to penetrate into the protoplasm of the ectodermic elements of the placenta, and they accumulate in certain situations from which they find their way into the fœtal capillaries. (3) The spirochætes, especially at the beginning of the pregnancy in the rat and the mouse, seem to spread by means of the omphalo-mesenteric vessels. In the case of females at term the migration is more limited, *i.e.* by way of the vessels of allantoid origin (afferent capillaries of the umbilical vessels).

A good deal has been written one way and the other on the modes of division of spirochætes, and there has been a good deal of discrepancy in the observations recorded. One of the latest utterances on the subject is by Fantham and Porter,[3] who, as the result of work on *Sp. recurrentis*, *Sp. duttoni*, *Sp. anodontæ* and *Sp. balbianii*, reached the following conclusions :—

(1) The observations recorded in this paper were made on living spirochætes. We have previously examined much fixed and stained material. It is very necessary to examine living material, as results based only on stained preparations are not always reliable.

(2) Both longitudinal and transverse division occur in spirochætes, as seen in *S. recurrentis*, *S. duttoni*, *S. anodontæ*, and *S. balbianii*.

(3) Longitudinal division of *S. recurrentis* and *S. duttoni* is best seen when there are but few spirochætes in the blood. This is the case at the onset of infection and at its close. In longitudinal division, rapid waves pass down the body of the spirochæte. At one end a split occurs, which gradually widens. Waves travel down each of the diverging daughter forms, which ultimately lie at an angle of 180° with one another. The daughter spirochætes then separate. Organisms about to divide longitudinally are slightly stouter than the others.

(4) Transverse division of *S. recurrentis* and *S. duttoni* also occurs. It is initiated by the appearance of waves passing from both ends towards the centre of the organism (which centre acts as a node). These waves meet and die out, and return waves pass rapidly from the centre towards each end. These processes are repeated many times, the frequency of the waves increasing and the nodal region becoming thinner. Finally, after a succession of very rapid waves, division occurs at the node, and two complete daughter organisms result.

(5) There is periodicity in the direction of the division of *S. recurrentis* and *S. duttoni*. At the onset of infection longitudinal division occurs. This is followed by transverse division of the spirochæte when the infection is at its height, while, with the diminution in numbers of the parasite as the infection draws to an end, there is reappearance of longitudinal division. Naturally, there are times when both forms of division occur together. Our observations relating to periodicity were made on peripheral blood of the host.

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[1] Gózony, L. (February 13, 1911), "Die Infektionswege und natürliche Immunität bei Spirochätosen." *Cent. f. Bakt.*, I. Orig., Vol. LVII., No. 6.

[2] Nattan-Larrier, L. (March 3, 10, and 17, 1911), "L'hérédo-contagion des spirilles. Spirilloses héréditaires et immunité congénitale. La pathogénie des spirilloses héréditaires." *C. R. Soc. Biol.*

[3] Fantham, H. B., and Porter, A. (1909), "The Modes of Division of *Spirochæta recurrentis* and *S. duttoni*, as Observed in the Living Organisms." *Proceedings of the Royal Society*, B., Vol. LXXXI.

Spiro-chætosis—*continued*

Mackinnon [1] made interesting observations on *Sp. recurrentis*, and found that in two cases apparent longitudinal division was seen in *Spirochæta recurrentis;* in eleven cases the division was apparently transverse. It is not possible to say with absolute certainty, except in one instance, that these transverse divisions were not the final act in a longitudinal division. I am nevertheless inclined to think *that both forms of division may take place, transverse being the more common.* Breinl and Dutton and Todd have expressed the same opinion with regard to *S. duttoni*, and Fantham also states that in *S. balbianii* both modes of division occur.

It is no easy matter to cultivate spirochætes, at least on artificial media. Duval and Todd [2] describe a special egg medium, by the use of which they ascertained that (*a*) *Sp. duttoni* can be maintained virulent for wild mice in artificial media for forty days. (*b*) *Spirochæta duttoni* will multiply, and can be successfully transferred in artificial media. The egg medium is rather complicated, and takes long to prepare, while the method of determining the multiplication of the parasites is a special one; hence this short note, and the reference must suffice. Karwacki and Szolkaski [3] have succeeded in cultivating *Sp. obermeieri* in the body of the leech. The parasite survives for 44 days on an average in the leech. The shortest time was 10 days, the longest 102 days. Apparently the vitality of the parasite does not diminish with the length of duration of the febrile attack as has hitherto been supposed to be the case. Leeches fed on a patient towards the end of an attack harboured parasites for from 22 to 95 days.

A few papers dealing with treatment now come under review. Salmon [4] mentions attempts at treatment by antimony, but in the light of the results obtained with salvarsan ("606") it is not necessary to consider his paper in detail. The good results recorded by Uhlenhuth and Manteufel [5] in syphilis and fowl spirochætosis point to atoxylate of mercury possessing powerful spirillicidal properties, but, so far as one knows, it has not been employed in the special spirochætal fevers. As already indicated the discovery of salvarsan has revolutionised the treatment of the spirochætal fevers which until recently had merely been symptomatic. Now the Ehrlich-Hata preparation may be regarded as a specific in relapsing fever, at least in the European variety.

For those to whom German presents difficulties there is Emery's [6] French version of Ehrlich and Hata's valuable monograph. It is beyond the scope of this review to discuss a work of this kind, but it may be said that the treatment of recurrent fever, not only by "606"—and here we have the records of successfully treated Egyptian cases by Bitter and Dreyer—but by certain aniline colours, by atoxyl, arsacetin, arsenophenylglycin, arsenophenol, atoxylate of mercury, and other less well-known combinations is fully discussed. The Yakimoffs [7] record their experience with salvarsan, and also with benzidine dye in the case of mice inoculated with *Sp. duttoni*. They gave the "606" in a 0·5 per cent. solution in normal sodium hydrate, freshly prepared, and administered 0·12 gramme per kilo of mouse weight. Briefly put, they found that the drug rapidly drove the spirochætes out of the blood, and if given in sufficient doses prevented relapse. If administered twenty-four hours before inoculation it prevents infection, and if given at the same time as the virus it would seem that, provided the dose is sufficient, infection does not take place. While spontaneous cure immunises, cure as the result of giving salvarsan does not do so, and animals which have been treated and recovered can be re-inoculated. The results with benzidine were by no means so favourable.

Iversen's [8] work on human recurrent fever with the hydrochloride of diamido-arseno-benzol, to give salvarsan its full chemical title, is quoted in Ehrlich and Hata's monograph, but as it is important and decisive, a few notes on it may find a place here.

The solutions employed were 1 per cent. aqueous solutions. Intramuscular injections of from 0·05 to 0·4 gram were used. In all 52 patients were subjected to the treatment. Of these, 37 received the injection during

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[1] Mackinnon, D. L. (September, 1909), "Observations on the Division of Spirochætes." *Parasitology.*

[2] Duval, C. M., and Todd, J. L. (March 20, 1908), "A Note on the Multiplication of *Spirochæta duttoni*." *Lancet.*

[3] Karwacki, L., and Szolkaski, C. (1910), "The Culture of *Spirochæta obermeieri* in th Body of the Leech." *C. R. Soc. Biol.*

[4] Salmon, P. (December 9, 1908), "L'antimoine dans les spirilloses pathogènes. Note préliminaire." *Bull. Soc. Path. Exot.*

[5] Uhlenhuth and Manteufel (1908), "Über die Wirkung von atoxyl-saurem Quecksilber bei Spirochätenkrankheiten, insbesondere bei der experimentellen Syphilis." *Med. Klin. Berl.*

[6] Emery, E. (1911), *La Chimiothérapie expérimentale des spirilloses* (Ehrlich and Hata). Paris.

[7] Yakimoff, W. L., and Kohl-Yakimoff, N. (October 25, 1910), "Contribution à la chimiothérapie de la 'tick-fever' avec '606' et la couleur de benzidine." *Ann. de l'Inst. Past.*

[8] Iversen, J. (April 12, 1910), "Über die Wirkung des neuen Arsenpräparates Ehrlichs bei Rekurrens." *Münch. Med. Woch.*, quoted in Epitome, *British Medical Journal*, January 28, 1911.

Spiro-chætosis—*continued*

the first attack, 11 during the second attack, and in 4 the injection was given intravenously during the first attack. In all these patients the fever ceased critically and the spirochætes disappeared from the blood. The fall of temperature occurred between seven and fourteen hours after the injection in the greater number. In two cases a second attack took place after the injection had been given on the first day. The longest interval between the interval and the fall of temperature, save in these two cases, was twenty hours. In 92 per cent. of the cases no recurrence took place. A single injection had sufficed to kill off all the spirochætes. Four patients had recurrences; in three of these the attacks were very short. In two the injections had been carried out on the first day of a second attack, when the spirochætes were sparse and difficult to find. He next attempted to determine whether the arseno-benzol injected in the interval could prevent a recurrence. This was tried in one case on the third day after the attack. No further attack took place. He concludes that the sodium salt of dichloride of diamido-arseno-benzol is able to check an attack of recurrent fever within twenty hours and to prevent a recurrence in 92 per cent. of the cases. A single injection suffices for this purpose. A therapeutic dose is from 0·2 to 0·3 gram. The substance injected intramuscularly in the gluteal regions causes some pain and a little infiltration, but this is variable. On the other hand, the intravenous injection is painless, and does not cause any untoward symptoms. No pathological constituents appeared in the urine of any of his cases.

In a later paper the Yakimoffs [1] record further results in the case of rats and mice infected with *Sp. duttoni*. They find salvarsan to be the best of known remedies at the present time, but note that in the rare cases where relapse occurs two successive injections seem indicated. This is of special interest in view of recent work on granule-shedding in spirochætes, occurring both naturally and under the influence of drugs. This phenomenon will be found mentioned under fowl spirochætosis (*vide infra*) and under the heading "Syphilis" (*page* 355). Nattan-Larrier and Salmon [2] find that in experimental spirochætosis the milk of an infected female treated by salvarsan does not possess any preventive or curative property.

Before considering the spirochætoses of animals, certain human pathogenic conditions due to spirochætal infection, but quite distinct from the spirochætal fevers, must receive very brief consideration. For example there is the bronchitic condition associated with the presence of spirochætes in the sputum. Waters [3] recognised it in India, and found it accompanied by fever. The sputum is thin and mucoid, and only a few rhonchi are present in the chest. He realised that the presence of parasite was not merely accidental. Castellani [4] has found the same condition in Ceylon, and mentions that Jackson has seen it in the Philippines. Castellani terms it bronchial spirochætosis. He

recognises two types of the disease, one acute the other chronic. At times the chronic supervenes upon the acute form, but frequently the acute stage is wanting. The patient has a chronic cough, which is frequently more severe in the morning; expectoration is not abundant; it is muco-purulent in character, but not nummular. At times blood stains the expectoration, or one or two teaspoonfuls of blood are coughed up. Fever may or may not accompany the condition, or it may occur occasionally and very irregularly; in some cases a true hectic fever may be present, with rapid wasting. Beyond a few dry or moist râles in the lung, little else is to be made out by examination of the chest. The diagnosis is apt to be mistaken; and malaria, influenza, phthisis, or infection by *Paragonimus westermanii* (*Distoma ringeri*) must be excluded. Amongst the many spirochætes found in the expectoration Castellani recognises four types: (*a*) A thick variety with irregular coils; in length it is 15 to 20 μ. (*b*) Spirochætes resembling *S. refringens* (Schaudinn), presenting graceful waves and pointed ends. (*c*) The most commonly seen is a thin spirochæte, with many coils; the ends taper, or one may be blunt. (*d*) A very thin spirochæte, with a few irregular coils. Castellani is of opinion that spirochætes probably play an important part in the bronchitic cases he describes.

A fuller account with references will be found in Castellani's and Chalmers' *Manual*. It seems worth while mentioning a paper by Werner [5] which deals with the morphology of spirochætes encountered in the human intestinal tract. As is well known there is a spirillary form of dysentery described by Le Dantec, and this is mentioned in Werner's article.

Spirochæta aboriginalis is the name given by Bosanquet [6] to the parasite found by Cleland in the ulcerative granuloma of the pudenda of Australian natives. It is not at all like *Treponema pallidum*, the spirals being quite irregular.

Animal. Pride of place may be given to the monkey. Thiroux and Dufougere [7]

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[1] Yakimoff, W. L., and Kohl-Yakimoff, N. (March 8, 1911), "Nouvelle communication relative au traitement de la maladie du sommeil et de la 'tick-fever' par le '606.'" *Bull. Soc. Path. Exot.*

[2] Nattan-Larrier, L., and Salmon, P. (April 7, 1911), "Spirillose expérimentale et allaitement." *C. R. Soc. Biol.*

[3] Waters, H. G. (March, 1909), "Presentation of Specimens of Spirocheta believed to be Pathogenic to Man, causing Fever and Bronchitis, with thin Mucoid Expectoration." *Transactions Society Tropical Medicine and Hygiene*, Vol. II., No. 4.

[4] Castellani, A. (August 16, 1909), "Bronchial Spirochætosis." *Journal Tropical Medicine and Hygiene.*

[5] Werner, H. (1909), "Über Befunde von Darmspirochäten beim Menschen." *Cent. f. Bakt.*, I. Orig., Vol. LII., No. 2.

[6] Bosanquet, W. C. (December, 1909), "A Note on the Spirochæte present in Ulcerative Granuloma of the Pudenda of Australian Natives." *Parasitology.*

[7] Thiroux, A., and Dufougere, W. (January 12, 1910), "Persistance de l'infection des méninges chez un singe guéri sans médication d'une infection sanguine à spirilles naturelle." *Bull. Soc. Path. Exot.*

described a spirochæte in the blood of *Cercopithecus patas* in Senegal, and named the parasite *Spirillum pitheci*. They found it to be of the *Sp. duttoni* type, and to cause an irregular fever. Laveran and Pettit [1] have studied this spirochæte. Of the ordinary laboratory animals they found only rats and mice susceptible. Spirochætosis—*continued*

Carter (*loc. cit.*) in his paper on pathogenic spirochætosis in mammalia gives a good review of the subject generally and mentions *Sp. equi*, *Sp. theileri* (in cattle), and *Sp. ovina*. He also cites spirochætes found in the blood of monkeys, of the camel, the elephant, and in several species of antelope. Bats are known to harbour spirochætes, and so do some species of rats, *i.e. Mus decumanus* in India and America, and *Nesokia bandicota*. *Mus musculus* also may be infected. He has also notes on the spirochætes of the buccal cavity, and on spirochætes found in skin lesions. The paper is useful, though our knowledge has increased since it was written. Under the name of *Sp. bovis caffris*, Nuttall [2] has described what he took to be a new and peculiar species of blood spirochæte in the African buffalo. It is very broad, tapers at both ends, and stained preparations may show transverse achromatic bands. Balfour [3] found similar forms in Jackson's hartebeeste in the Sudan, and they were also seen by Cummins, in a goat. The former believes they may be in reality contaminations derived from the intestinal tract, but the point is not yet settled. Schein [4] found a spirochæte in the blood of calves in South Annam. It seems to be allied to that noticed by Heanley in cattle at Hong-Kong and also to *Sp. theileri*. It appeared to be connected with the occurrence of epistaxis, and to render a co-existing piroplasmosis more severe in type. Theiler [5] finds that the adults and larvæ both of *Boophilus decoloratus* and of *Rhipicephalus evertsi* transmit *Sp. theileri*. In addition to the animals already cited as harbouring spirochætes Mathis, and Leger [6] mention Macacus monkeys, the otter, the gondi, (a North African rodent), the pig, the zebra, and finally the rabbit, in which at Tonkin they recently found what they have called *Sp. raillieti*. They describe long and short forms, and regard it as a specific entity. A new locality for the small spirochæte of *Mus decumanus* is Brazil, where it has been seen by Carini.[7] Leaving aside the avian spirochætes for a moment, we note that Neumann [8] has described and figured two species of spirochætes in sea fish, while Henry [9] has also found a spirochæte in a species of cod. It is interesting to note that this observer saw what may prove to be spirochætal inclusions in the red cells of the infected fish. The spirochætes of molluscs are of especial interest, as owing to their large size it is comparatively easy to study their morphology. One cannot enter into this interesting and important subject here, and we rest content with giving references to useful papers by Fantham,[10] Bosanquet,[11] and Dobell.[12] The last named is a highly suggestive article, and contains a good bibliography. Bosanquet's paper describes the mussel spirochæte breaking up into granules or coccoid bodies when placed under artificial surroundings. Coming a little way up the scale we find Mackinnon [13] gives a list of insects in which spirochætes have been found, *i.e.* mosquitoes and mosquito larvæ, *Glossina palpalis*, the larvæ of *Chironomus*, and the larva of *Ptychoptera contaminata*. She adds to the list the larvæ of *Trichoptera* (caddis-flies). We now come to the avian spirochætes, the most important of which are those of the domestic fowl, for there can be little doubt several species exist in different parts of the world.

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[1] Laveran, A., and Pettit, A. (July 13, 1910), "Contribution à l'étude de *spirillum pitheci*." *Bull. Soc. Path. Exot.*

[2] Nuttall, G. H. F. (April, 1910), "On Hæmatozoa Occurring in Wild Animals in Africa." *Parasitology.*

[3] Balfour, A. (September, 1910), "Note Regarding the New Buffalo Spirochæte." *Ibid.* See also *Fourth Report, Wellcome Tropical Research Laboratories*, Vol. A.

[4] Schein, H. (February 9, 1910), "Spirillose des Bovidés dans le Sud Annam." *Bull. Soc. Path. Exot.*

[5] Theiler, A. (June 9, 1909), "Transmission des spirilles et des piroplasmes par différentes espèces de tiques." *Ibid.*

[6] Mathis, C., and Leger, M. (February 17, 1911), "Spirochète du Lapin." *C. R. Soc. Biol.*

[7] Carini, A. (1910), "Sobre uma espirillose do rato." *Revist. da Soc. Scien. de S. Paulo.*

[8] Neumann, R. O. (1909), "Studien über protozoische Parasiten im Blut von Meeresfischen." *Zeit. f. Hyg. u. Infekts.*

[9] Henry, H. (April, 1910), "On the Hæmoprotozoa of British Sea-Fish (a Preliminary Note)." *Journal Pathology and Bacteriology*, Vol. XIV.

[10] Fantham, H. B. (February 9, 1910), "The Spirochætes found in the Crystalline Style of *Tapes Aureus*. A Study in Morphological Variation." *Parasitology.*

[11] Bosanquet, W. C. (February, 1911), "Brief Notes on the Structure and Development of *Spirochæta Anodontæ*, Keysselitz." *Quarterly Journal Microscopical Science.*

[12] Dobell, C. C. (April, 1911), "On *Cristispira veneris*, nov. spec., and the Affinities and Classification of Spirochætes." *Ibid.*

[13] Mackinnon, D. L. (September, 1910), "New Protist Parasites from the Intestine of Trichoptera." *Parasitology.*

Spirochætosis—*continued*

Gareitschnoff [1] in 1907 described a case of fowl spirillosis in Bulgaria, a new locality for the disease, which is much more widespread than was originally thought to be the case.

Galli-Valerio,[2] in a preliminary note, signalised the production of spirochætosis in fowls at Lausanne by means of ticks (*Argas persicus*) which had been fed on infected fowls in Tunis.

Later [3] he returned to the subject, having carried out numerous experiments. As a result, he came to the conclusion that there is a single form of avian spirochætosis, and that therefore the spirochæte with which he worked is *Sp. marchouxi* (*gallinarum*).

Of special interest here is the fact that in a fowl bitten by *A. persicus*, and which succumbed nearly a month afterwards without showing spirochætes, the red cells were found to harbour pyriform bodies which Galli-Valerio thinks resemble the "afterphase" bodies described in the Sudan disease. Spirochætes were not found in sections of the organs stained by the Levaditi-Volpino method. Other forms, even more similar, were discovered in the erythrocytes of a rat inoculated from an infected fowl, and which also died. The author is doubtful as to what interpretation to put upon them, but thinks they may be evidence of a feeble infection passing into a chronic state.

Comte and Bouquet [4] observed a spirochætal disease of fowls in the oasis of Degache and in the neighbourhood of Tunis, and found that it was transmitted by *A. persicus*. Bats were not susceptible, but geese and ducks could be infected. Brumpt has named the infecting agent *Sp. nicollei* n. sp., as, from its peculiar immunity reaction, he believes it to be a distinct species. It does not protect against itself.

Simond, Aubert, and Noc [5] described a fowl spirillosis at Martinique, which they believed to be identical with that originally found in Brazil. They say it probably exists in Guadeloupe and French Guiana.

Mezincescu and Calinescu [6] met with the condition in Roumania, where *A. persicus* was common. Ducks and geese were also affected.

Brumpt and Foley [7] in 1908 gave a short account of *Sp. gallinarum* in fowls in South Oran.

The former author at a later date [8] produced a very interesting paper on a fowl spirochætosis in Senegal. He has named the parasite *Sp. neveuxi*, as he found that it could infect fowls which had acquired immunity to *Sp. gallinarum* infection and, conversely, fowls inmune to *Sp. neveuxi* contracted the Brazilian septicæmia.

A point of special importance, and one which from personal experience I believe to be true, is cited by Brumpt. He finds that while chicks are easily inoculated with different species of spirochætes, certain adult birds exhibit a natural immunity conferred apparently by age. Thus he found one very old fowl (five years) which could neither be inoculated by the bites of *Argas* ticks nor by inoculation with *Sp. neveuxi*. He believes this peculiarity to be shared alike by rats as regards the spirochæte of African tick fever (Abyssinian strain). The duck, goose, Java sparrow, sparrow and chaffinch are susceptible to *Sp. neveuxi*. He did not experiment with the pigeon. The infection seemed somewhat less virulent than that produced by *Sp. marchouxi*, but like the latter is conveyed by *Argas persicus*.

Still later, the same author [9] found that the Somaliland infection was due to *Sp. marchouxi*, or, as he calls it, *Sp. gallinarum*, and was conveyed, like the other, by *Argas persicus*.

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[1] Gareitschnoff, G. (July, 1907), "Ein Fall von Hühnerspirillose in Bulgarien." *Veterinaria Shirka.*

[2] Galli-Valerio, B. (1908), "Spirochétiase des Poules déterminée à Lausanne avec *Argas persicus*, Fischer, Tunisie." *Cent. f. Bakt.*, I. Orig., Vol. I., No. 46, 4.

[3] *Idem* (1909), "Recherches sur la Spirochétiase des Poules de Tunisie et sur son agent de transmission: *Argas persicus*, Fischer." *Cent. f. Bakt.*, I. Orig., Vol. I., No. 50, 2.

[4] Comte, C., and Bouquet, H. (1909), "Recherches expérimentales sur la spirillose des Poules en Tunisie." *Arch. de l'Inst. Past. de Tunis.*, p. 163.

[5] Simond, Aubert, and Noc, F. (April 20, 1909), "Sur l'existence de la spirillose des Poules à la Martinique." *C. R. Soc. Biol.*, Vol. LXVI., p. 714.

[6] Mezincescu, D., and Calinescu, J. (1909), "Spirillose des Poules et *Argas persicus* en Roumanie." *Bull. Soc. Path. Exot.*, Vol. II., p. 292.

[7] Brumpt, E., and Foley (July 18, 1908), "Existence d'une Spirochétose des Poules à *Spirochæta gallinarum*, R. Bl., dans le Sud Oranais. Transmission de cette maladie par *Argas persicus*." *C. R. Soc. Biol.*, Vol. LXV., p. 132.

[8] Brumpt, E. (June 9, 1909), "Sur une nouvelle Spirochétose des Poules du Sénégal produite par *Spirochæta neveuxi* n. sp." *Bull. Soc. Path. Exot.*, Vol. II., p. 285.

[9] *Idem* (July 17, 1909), "Existence d'une Spirochétose des Poules *Spirochæta gallinarum* dans les pays Somali." *C. R. Soc. Biol.*, Vol. LXVII., p. 174.

Spiro-chætosis—*continued*

Bouet [1] encountered a fowl spirillosis in the French Sudan. By inoculation experiments he apparently proved the identity of this Sudanese spirochæte with *Sp. marchouxi*, and further found it the same as the Senegal virus which Brumpt named *Sp. neveuxi*.

This then would tend to support Galli-Valerio's view. Bouet found my "afterphase" bodies in the red cells, but would not commit himself to an opinion regarding their nature.

Mohn [2] found the disease in the German Cameroons, but of more importance is the work of Blaizot.

In 1909 he presented two papers [3&4] dealing with the effects of the Somali virus (*Sp. gallinarum*) on chicks of from five days to three months old, comparing the disease in them as produced by tick bite and by inoculation, and contrasting the condition caused by spirochætes taken from birds early in a series of inoculations and those taken late.

In the case of tick bite the disease was found to be of great severity, the chicks often dying before spirochætes had time to appear in their blood. In the case of inoculation everything depended on the time when the virus was obtained. If early in the successive passages, from chick to chick, a lengthy illness resulted, and there was a marked reaction of the organism against the virus; if late, the disease was shorter and there was no reaction.

In a later paper Blaizot,[5] working with the same strain, pointed out the curious fact that while successive passage of the virus through chicks greatly increased its virulence for chicks, it at the same time lessened its virulence for adult fowls.

Balfour [6] at an earlier period communicated a paper on further work with the spirochæte of fowls in the Anglo-Egyptian Sudan. This is merged in and corrected by later articles.

Prowazek,[7] working at Rio de Janeiro with *Sp. gallinarum*, discovered that this parasite passes through a regular cycle of development in the cœlemic fluid, and finally in the salivary glands of *Argas miniatus*.

He figured dividing and resting forms, and concluded that the tick is a true host for the spirochæte. His paper is important, and requires early confirmation.

Dschunkowsky and Luhs,[8] at the Veterinary Congress at the Hague, dealt with the spirillosis of geese due to *Sp. anserina*. They managed to cultivate the parasite in a special manner, and found atoxyl to be a specific against the disease. Further, they succeeded in preparing a preventive and curative serum from the blood of treated geese.

The same authors [9] mention the occurrence of what theyconsider to be my intra-corpuscular bodies in altered red cells of sick and healthy fowls examined at Elizabethpol and at Surnabad in Transcaucasia. In geese they found two forms, one recalling the "bodies," the other in geese suffering from spirillosis and formed of paranuclear bodies included in unchanged red cells.

They ask if the occurrence of these forms in healthy birds does not throw doubt on their parasitic nature, and suggest they may merely be endogenous deformities like Kurloff's bodies or Ferrata's plasmosomes.

One would like to see their specimens before expressing an opinion on the nature of their findings.

Schellack [10] has continued the researches mentioned in our Third Report. He finds that

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[1] Bouet, G. (June 9, 1909), "Spirillose des Poules au Soudan Français." *Bull. Soc. Path. Exot.*, Vol. II., p. 288.

[2] Mohn (1909), "Über Hühnerspirochätose in Kamerun." Quoted in *Briefk. des Inst. f. Schiffs-u. Tropen-Hyg. zu Hamb.*, No. 5.

[3] Blaizot, L. (October 23, 1909), "Études sur la Spirochétose des Poules produite par *Sp. gallinarum* (Virus Somali). La maladie chez les poussins—(1) Modifications de la virulence du parasite par passages directs." *C. R. Soc. Biol.*, Vol. LXVII., p. 421.

[4] *Idem* (October 30, 1909), *loc cit.*, Vol. LXVII., p. 447.

[5] *Idem* (June 15, 1910), "Études sur la Spirochétose des Poules produite par *Sp. gallinarum* (Virus Somali)—Une propriété de la race cultivée sur poussins." *C. R. Soc. Biol.*, Vol. LXVIII., p. 29.

[6] Balfour, A. (October 1, 1909), "Further Observations on Fowl Spirochætosis." *Journal Tropical Medicine and Hygiene*, Vol. XII., p. 285.

[7] v. Prowazek, S. (August, 1909), "Contribuição para o estudo do desenvolvimento de '*Spirochæta gallinarum*.'" *Mem. do Inst. Oswaldo Cruz*, Vol. I., No. 2.

[8] Dschunkowsky, E., and Luhs, J. (1909), "Prophylaxis and Pathology of Protozoan Diseases." Quoted in *Journal Tropical Medicine and Hygiene*, Vol. XII., p. 292.

[9] *Idem* (1910), "Sur l'Étude des Maladies Protozoaires des oiseaux domestiques en Transcaucasie." *Rev. Gén. de Méd. Vét.*, Vol. XIV., Nos. 163-4.

[10] Schellack, A. (1909), "Versuche zur Übertragung von *Spirochaeta gallinarum* und *Spirochaeta obermeieri*." *Arb. aus d. Kaiserl. Gesundheitsamte*, Bd. 30, H. 2, S. 352.

Spiro-chætosis—*continued*

Argas miniatus, *A. reflexus* and *A. persicus* are all efficient as vectors, while *Ornithodoros moubata* can also transmit *Sp. gallinarum*. *Dermanyssus avium* is not a carrier. The rôle of other ecto-parasites of the fowl as carriers has not been demonstrated. If the hen-house is infected, he says that infection *per os* can take place.

Tedeschi [1] by the use of abrin killed *Sp. gallinarum*, and thus produced a vaccine which protected canary birds. It is worth noting that he found that *Sp. duttoni*, in experimental animals during fever-free periods, remained in the blood as endoglobular forms, both in the erythrocytes and the leucocytes.

Dodd [2] has a paper on fowl spirochætosis in Queensland. He describes the symptoms well, but there is not much that is new in his account. He did not find the "afterphase" bodies despite careful search.

Blaizot [3] contributed a paper on relapses in the fowl spirochætosis of Tunisia (virus de Degache). He cites the work of Comte and Bouquet already mentioned, and also the facts as regards recurrence discovered by Bouet and myself. The object of his research was to discover if relapses, characterised by the presence of spirochætes in the blood, occurred in the Tunisian spirochætosis.

This he found to be the case, and he points out that so far as we know at present only a heavy, acute infection is capable of conferring a permanent immunity. He indicates the close relationship existing in this direction between African fowl spirochætosis and the spirochætal fevers of mammals. He puts forward the ingenious suggestion that both relapses and absence of immunity may be due to a premature crisis occurring before there has been time for saturation with anti-bodies, and thereby preventing the first infection being sufficiently severe to ensure a complete immunity. From the study of this question of immunity Blaizot believes that it may yet be possible to affirm that Africa is the original country whence avian spirochætosis spread. His paper is interesting, suggestive, and will repay careful perusal.

Quite recently, Jowett [4] has discovered fowl spirochætosis in the vicinity of Cape Town. Moreover, along with the disease, he has found intra-corpuscular bodies exactly like those in Sudan fowls. *A. persicus* is the vector, and, judging from the preliminary paper, this spirochætosis of South Africa is identical with our Khartoum form.

Gilruth [5] describes the disease from Victoria in Australia, but did not find endoglobular forms.

Dschunkowsky [6] has recently treated the spirillosis of geese successfully with "606," which he finds to be much more active than atoxyl.

Blaizot [7] in yet another paper returns to the subject, and deals with the subsequent cachexia, the question of intracerebral inoculation, and the susceptibility of fowls to second infections.

Gózony (*loc. cit.*), in a highly interesting paper, shows that spirochætal infection can take place through the unbroken mucous membrane, and believes that leucocytes play a great part in the production of natural immunity, not however by phagocytic action, but by the production of substances injurious to the parasites.

Balfour [8] has carried out further work on the Sudan strain, and tabulates the new features ascertained and conclusions reached as follows :—

1. In all probability the avian spirochætosis of the Sudan is due to a special spirochæte distinct from *Sp. marchouxi*, and most, if not all, other species hitherto described with the exception of that recently discovered

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[1] Tedeschi, A. (1910), "Experimenteller Beitrag zur Erforschung der Spirochäte des africanischen Recurrensfiebers (*Spirochaeta duttoni*)." *Cent. f. Bakt.*, I. Orig., Vol. LIV., No. 1, p. 12.

[2] Dodd, S. (March 31, 1910), "Spirochætosis in Fowls in Queensland." *Journal Comparative Pathology and Therapeutics*, Vol. XXIII., Part 1.

[3] Blaizot, L. (1910), "Note sur la récurrence dans la Spirochætose des Poules en Tunisie (virus de Degache)." *Arch. de l'Inst. Past. de Tunis*, Part 2, p. 53.

[4] Jowett, W. (December, 1910), "Fowl Spirochætosis, Note on the Occurrence of, at the Cape." *The Agricultural Journal of the Cape of Good Hope*, Vol. XXXVII., No. 6.

[5] Gilruth, J. A. (1910), "Note on the Existence of Spirochætosis affecting Fowls in Victoria." *Proceedings Royal Society, Victoria*, Vol. XXIII.

[6] Dschunkowsky, E. (January 5, 1911), "Heilversuche mit Ehrlich-Hata '606' bei der Gänsespirillose," etc. *Berl. Tierärztl. Woch.*

[7] Blaizot, L. (1910), "Nouvelles Recherches sur la Spirochétose des Poules." *Arch. de l'Inst. Past. de Tunis.*, Part 4.

[8] Balfour, A. (1911), "Spirochætosis of Sudanese Fowls." *Fourth Report, Wellcome Tropical Research Laboratories*, Vol. A.

by Jowett in South Africa. The chief points which have led me, somewhat against my own inclination, for the multiplication of species is to be deprecated, to adopt this view are :— **Spiro-chætosis—** *continued*

(*a*) Its peculiar tendency to break up into "infective granules" in the internal organs. These granules, which are discharged by the still living spirochætes from one or other end of its periplastic sheath or cell membrane, would appear to constitute a stage in the non-sexual life-cycle of the parasite, for they seemingly enter the red cells, develop in them, undergo a process akin to schizogony, and regain the *liquor sanguinis* as tiny merozoites which vary in number and slightly also in size.

(*b*) The course of the disease in fowls and in chicks. This it is true somewhat resembles the spirochætosis of fowls in Senegal, due to *Sp. neveuxi* (Brumpt), and which Bouet found in the French Sudan. If it is the same disease, and there are points of difference, the spirochæte of the Anglo-Egyptian Sudan was first discovered and has priority in nomenclature. Our fowl spirochætosis would appear to differ in some respects, notably as regards the "granule-phase," from the Tunisian and Somaliland strains.

(*c*) The peculiar sexual (?) life-cycle, partly worked out in the tick, *Argas persicus* (Fischer), and which seems in most respects comparable to that described by Leishman for *Sp. duttoni* in *Ornithodoros moubata.*

(*d*) The absence of any cycle in the tick corresponding to that described by Prowazek for *Sp. gallinarum* (*marchouxi*) in *Argas miniatus.*

(*e*) The fact that lice (*Menopon* sp. ?) have been shown capable of transmitting the disease may be another distinguishing factor.

(*f*) The insusceptibility of pigeons to the disease. The fact that gerbils cannot be inoculated with it may also serve to separate it from other forms of avian spirochætosis.

He considers it justifiable to regard this fowl spirochæte as a specific entity, and has proposed for it the name *Sp. granulosa* with the word *penetrans* as a sub-species title if required. Moreover, he has found that chicks fed on ticks containing either spirochætes and granules, or granules alone, become readily infected. In one case nearly three months had elapsed since the ticks fed to the chick had ingested spirochætal blood, and yet the incubation period was less than two days.

Others beside domestic birds are known to harbour spirochætes, but considerations of space prevent any reference to them. Neither can we consider papers on auto-agglutination in spirochætosis or the action of pyocyanase upon the parasites, both points of interest which can merely be mentioned. There are also papers on the treatment of avian spirochætosis by "606" well worthy of study, but these and other matters are referred to either directly or indirectly in one or other of the numerous papers reviewed, and the line must be drawn somewhere. Notes on staining, another subject untouched here, will be found under the section bearing that title. Though many of the observations here recounted will undoubtedly be amplified, and possibly in some instances discredited, in the immediate future, it is hoped that a fairly complete and coherent account has been given of recent work on one of the most important divisions of tropical medicine and protozoology.

Additional Note

The latest research work on *Sp. duttoni* has been carried out by Hindle,[1] who amongst other things has found that a certain proportion of *O. moubata* are immune to infection with this spirochæte. He summarises his interesting observations, which serve to confirm those of Leishman (*loc. cit.*), as follows :—

(1) About 30 per cent. of the *O. moubata* from Uganda have been found to be immune to infection with *Sp. duttoni.*

(2) When infected ticks are kept at ordinary temperatures (about 21° C.) the following parts of the body are found to harbour the infection : gut and contents, sexual organs, Malpighian tubules, excrement.

The following parts were found to be uninfective : salivary glands, coxal fluid.

(3) When infected ticks are kept at a temperature of about 35° C. for two or three days previous to dissection, all the organs of the body, including the salivary glands, are found to be infective. Moreover, the incubation periods that elapse before the appearance of spirochætes in the injected mice are shorter than in the case of the corresponding experiments with ticks that had not been kept at a high temperature.

(4) No spirochætes have been detected in any of the organs of infected ticks that had been kept at a temperature of about 21° C. When a tick ingests blood containing spirochætes the latter persist in the lumen of the gut for periods varying from a few days up to as long as four weeks ; usually, however, they disappear from the gut in nine or ten days.

(5) When infected ticks are heated to a temperature of 35° C. for two or three days, spirochætes reappear in the lumen of the gut, and also appear in all the organs of the tick and in the cœlemic fluid.

(6) The spirochætal infection that may follow the bite of an infected *O. moubata* results from the entrance of the infective material, excreted by the tick whilst feeding, into the open wound caused by the tick's bite.

It is not the result of the inoculation of infective material from the salivary glands.

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[1] Hindle, E. (June, 1911), "The Transmission of *Spirochæta duttoni.*" *Parasitology.*

Sprue. Little has been left for us to say about this disease, since the publication of Carnegie Brown's book.[1] The work is well illustrated, and gives a mass of valuable information gleaned from all sources. The many theories of origin, cause, and treatment of the malady are fully discussed.

The question if sprue is an intestinal blastomycosis has been studied by Le Dantec.[2] He succeeded in isolating a yeast fungus from the stools of a case of chronic diarrhœa of hot countries to which he attributes an important share in the etiology of the affection. He regards sprue as a true intestinal blastomycosis following on a phase of acid diarrhœa due to paralactic bacilli. He employed for his cultivation a medium produced by placing a slice of potato in 15 c.c. of water and sterilising it at 105° to 110° C. Heated to this extent, under pressure, a portion of the starch of the potatoes changes into maltose, the latter being, so to speak, in a nascent condition, and therefore specially favourable to the growth of yeast fungi. Before insemination the medium is acidified by the addition of two or three drops of lactic acid.

The yeast fungus so isolated stains a more or less reddish-brown with tincture of iodine, and ferments bouillon with glucose, but will not liquefy gelatine. Under anærobic conditions it grows mainly by cell proliferation, but as an ærobe it grows as a mycelium.

Macy [3] has described a spirillum found in the fæces of cases of sprue, and an extract from his paper is given here :—

> If a very thin, even smear of sprue fæces be made, and stained when dry with one of the ordinary stains, such as an alkaline, watery solution of methylene blue, there will be seen an exceedingly tenuous and faintly blue spirillum which differs from those common to other and normal fæces in size, shape, and staining reaction. This organism is more closely coiled, often barely visible even in the dyed spread, is much more slender, and will not grow on any media which I have yet used. It is present in great numbers, especially in the small, white, mucous threads that abound in some specimens, and is quite variable in length but not in breadth. In shape it is spiral, and the longer forms are sometimes bent so as to resemble three sides of a rectangle. Certain of them appear to have divided transversely, the apparently new cell so formed lying invariably at an obtuse angle to the parent cell. They are not distinguishable in unstained fæces, and since they have not been cultivated, it is impossible to describe any motility they may possess. They have been constantly and certainly found abundantly in every case of sprue which I have examined since I first noticed them, and so far I have never observed them in any other fæces, either normal or from other diseases. Cases admitted with a diagnosis of chronic diarrhœa, or some form of enteritis, have occasionally shown them, but careful examination of their histories as given by themselves and as furnished by previous attendants, has, with one exception, revealed the occurrence of sprue in the past, while others showed symptoms of the disease at the time of the examination. The single exception cited is a doubtful case. While he gives some evidence of sprue at the present time, it is not so positive as to preclude all doubt.
>
> As I have only recently noticed the presence of this organism, I shall have to defer a more detailed description of it and an opinion of its etiologic importance until another time.

Le Dantec,[4] arguing on the lines that sprue is an advanced stage of the chronic diarrhœa of tropical countries,* and taking as a basis that it is a blastomycotic affection, recommends in the treatment the suppression of the carbohydrate articles of diet, which will cause death of the blastomycetes by inanition.

In his treatment he gives albuminoids till the motions are solid, and then crowds the intestine with lactic acid bacilli, using for this purpose Bulgarian milk.

Patients who cannot take the milk, owing to its acidity, are given the serum of the milk in a cup of broth, which masks the acidity.

He recommends a line of treatment for children with milk serum, as the clotted milk is so likely to cause *per se* intestinal disorders in the young.

Montgomery,[5] in a very excellent paper on sprue, describes amongst the many other methods of treatment one by means of argilla, which is a finely powdered desiccated white clay. It is said to relieve the symptoms of diarrhœa in sprue, and indeed in other forms of diarrhœa. The dose is large, viz. 3 to 6 ounces of argilla stirred up with 10 ounces of water, and taken slowly, during the day. The patient fasts for the first 24 hours, and never takes food till at least three hours after having taken the argilla mixture.

It is inexpensive, and keeps well in any climate.

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[1] Brown, C. W. (1908), *Sprue and its Treatment.*

[2] Le Dantec, A. (April 1, 1909), "The Presence of a Yeast Fungus in Sprue, and its Pathological Significance." *Journal Tropical Medicine and Hygiene.*

[3] Macy, F. S. (1909), "Notes on Tropical Diarrhœas." *Transactions Bombay Medical Congress.*

[4] Le Dantec, A. (June 10, 1908), "Nouveaux traitement des diarrhées chroniques des pays chauds." *Bull. Soc. Path. Exot.*

* *Note.*—Authorities are still at great variance as to whether sprue is a definite disease, or only a stage of tropical diarrhœa.

[5] Montgomery, H. J. (May, 1910), "Sprue : Its Diagnosis and Treatment." *China Medical Journal.*

Sprue—*continued*

He mentions the treatment by means of saverin, which is a culture of lactic acid bacilli. When taken with milk this passes almostly directly to the small intestine and colon, and there produces large quantities of lactic acid, with consequent coagulation of the milk and neutralisation of intestinal toxins. Cases treated by this method are stated to have done well, but it is only on trial, and no judgment can be pronounced. A few notes from the recent journals [1] on the santonin treatment of sprue are of interest.

There are a few points which must be carefully attended to if we hope to obtain the good results that have been ascribed to the use of this remedy.

To begin with, the white santonin is said to be valueless, and it is the yellow santonin or chromosantonin which alone has the curative power.

The method of preparing the drug is :—

White santonin crystals are spread out in the sun (preferably in the Tropics), and the crystals are turned over from day to day ; the preparation is complete when on crushing a single crystal there is no large proportion of white colour.

The solution when made up should be of a deep yellow colour. It is given in five-grain doses twice daily, in castor oil, olive or almond oil, otherwise it does not reach the part of the intestinal tube where its germicidal action is required. Chromosantonin is said to be a new drug, and not santonin. It is more valuable in early cases of the disease.

Staining. In dealing with a subject as large and as progressive as staining, it is impossible in this Review to attempt to cope in detail with the wide field of work it presents.

Attention, however, will be drawn to recent methods and improved modifications of older methods. An attempt will also be made to group the subject under special headings, though some overlapping is unavoidable.

Blood Staining. Two new combined fixing and staining solutions for blood films have recently been introduced by Marco del Pont.[2]

Their compositions are :—

1. Azure II.	0·30 gramme	2. Borrel Bluc	0·30 gramme
Eosin (Höchst)	0·20 gramme	Eosin (Höchst)	0·20 gramme
Aqueous Solution Carbonate of Potassium, 10 per cent.	0·3 c.c.	Aqueous Solution Carbonate of Potassium, 10 per cent.	0·3 c.c.
Methyl Alcohol (absolute)	150 c.c.	Methyl Alcohol (absolute)	200 c.c.

The method of preparation and use is the same in both cases, but the second formula is less costly than the first.

Dissolve separately the azure and the eosin in a small quantity of alcohol ; work up the mixture with the remainder of the alcohol ; now add the alkaline solution and let stand for 48 hours. The slide is flooded with the solution, which is allowed to act for 1½ to 2 minutes, then an equal quantity of distilled water is added, and after 2 minutes the slide is washed in distilled water and dried with filter paper.

General Staining. Some explanation should perhaps be given for such a heading. Under it, however, will be found methods of routine work for the staining of bacteria, protozoa and sections, in contradistinction to special stains which will be given under separate headings.

In Leishman's staining fluid, methyl alcohol is the solvent ; this deteriorates in a few weeks, and much is lost by evaporation, especially in warm climates.

This may be avoided by the addition of equal parts of glycerine, which keeps the stain almost indefinitely.

Another method of preparing Lieshman's stain may be noted, as methyl alcohol is sometimes difficult to obtain. It is as follows :—

A saturated solution of Lieshman's crystals is made with methylated spirit, and an equal volume of glycerine is added.

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[1] (*a*) Maxwell Preston, J. (April, 1911), " The use of Santonin in the treatment of Intestinal Affections of the Tropics." *Transactions Society Tropical Medicine and Hygiene.*

(*b*) (April 1, 1911), " Yellow Santonin in Sprue." *Journal Tropical Medicine and Hygiene.*

(*c*) Begg, C. (December 15, 1911), " Yellow Santonin in Sprue and Dysentery." *Ibid.*

[2] Del Pont, A. M. (1909), *Sobre un nuevo método para la fijación y coloración de las preparaciones de sangre.* Quoted in *Bull. de l'Inst. Past.*, January 15, 1910.

Staining—*continued*

Both these modifications [1] are used in the same way as Giemsa's stain. They leave no deposit.

Previous fixation is required, and this may be done by mixing a few drops of absolute alcohol with 3 c.c. of distilled water and applying it to the slide for half-an-hour.

Giemsa's [2] eosin-azure method of staining fresh films is described here, though it may also be employed for chromatin staining and for staining trypanosomes.

(1) Fixation of the moist cover-glass preparation in sublimate alcohol (Schaudinn's method, two parts of a concentrated watery solution of sublimate and one part of absolute alcohol), for twelve to twenty-four hours or even longer.

(2) A short washing in water, after which the preparation is placed for five to ten minutes in a solution of 2 grammes of potassium iodide in 100 c.c. of distilled water and 3 c.c. of lugol solution. Immediately after this

(3) A short washing in water, followed by ten minutes in a $\frac{1}{2}$ per cent. watery solution of sodium thiosulphate. The preparation, which previous to this appeared to be yellow, should now become bleached.

(4) Washing for five minutes in running water.

(5) The specimen is now placed in a freshly-prepared dilute solution of Giemsa's stain (one drop of the made-up stain in 1 or 2 c.c.) for twelve or more hours. At the end of the first half-hour the stain is to be thrown away and a fresh quantity poured on.

(6) Wash in water and place in the following mixtures :—

(*a*)	Acetone, 95 c.c.	Xylol, 5 c.c.
(*b*)	,, 70 c.c.	,, 30 c.c.
(*c*)	,, 70 c.c.	,, 30 c.c.
(*d*)	Pure xylol	

(7) Mount in cedar oil.

The degree of differentiation can be regulated by varying the time during which the preparation is kept in *a*, *b*, *c*.

Compared with dry preparations, this method shows up the differentiation of the structure of the nucleus to a much greater degree. It has, however, the one disadvantage that acetone cannot be used in the Tropics, as its boiling point is a very low one (56° C.).

Bonney [3] has introduced a new triple stain.

Solutions—

I. Methyl-Violet 0·25 gramme
Pyronin 1 gramme
Distilled Water to 100 c.c.

Make the solution by heat, and filter.

II. To 100 c.c. acetone add, drop by drop, a 2 per cent. aqueous solution of Orange *b* (made by heat and filtered). A flocculent precipitate slowly appears on shaking and stirring, which dissolves in excess of the Orange *b* solution. When it has just re-dissolved, filter the mixture and label "Orange Acetone."

Method—

Fix in acetic alcohol.

(1) Stain for one to two minutes in the methyl-violet-pyronin solution.

(2) Wash in water and wipe all the slide dry, except the section.

(3) Flood the slide with "orange acetone." A colour cloud comes out. Pour off and flood again. When no more colour comes out—

(4) Wash rapidly in acetone, and

(5) Transfer to xylol and mount.

When examining use a dark blue screen with artificial light.

Capsule Staining. A new method of staining bacterial capsules [4] is of interest.

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[1] Birt, C. (November 14, 1908), "Leishman's Stain." Quoted under "Royal Society of Medicine, Pathological Section." *Lancet.*

[2] Giemsa, G. (1909), "Über die Färbung von Feuchtpräparaten mit meiner Azur-Eosin-Methode." *Deutsche Med. Woch.* Quoted in *Journal Royal Army Medical Corps*, May 1910.

[3] Bonney, V. (July, 1908), "A New Triple Stain." *Journal Pathology and Bacteriology.*

[4] Rosenau, M. J. (February 11, 1911), "Capsule Staining of Bacteria." *Journal American Medical Association.* Quoted in *Journal Tropical Medicine and Hygiene*, March 1, 1911.

Staining—*continued*

A thin even smear of sputum or culture growths diluted with distilled water is made. Tissue paper will be found useful in spreading the smear. As the smear becomes nearly dry, cover for ten to twenty seconds with 5 to 10 per cent. aqueous solution of tannic acid.

Wash in water and blot. Stain with carbol [saturated alcoholic solution of gentian-violet (Grübler), 1 part; 5 per cent. phenol in water, 4 parts] or aniline gentian-violet for half a minute to one minute; heat over flame, but do not boil; wash in water again; Gram's iodine solution from half a minute to a minute, decolorise in alcohol (95 per cent.); stain for two to ten seconds, depending on the thickness of the smears, with saturated alcoholic (60 per cent.) solution of Grübler's eosin.

Wash in water and blot, clear in xylol, mount in balsam and examine. Gram-negative bacilli may be stained with Lœffler's or aqueous methylene blue.

This method works well with pneumococci, which stain a deep brown-black, the capsules pink.

It is not suitable for sputum containing tenacious mucus, and the following may be substituted.

Fix and stain simultaneously with the 2 per cent. aqueous solution of tannic acid, 4 parts, and saturated solution of gentian-violet, 1 part. The cocci decolorise easily, and the tannic acid gentian-violet may be followed by carbol gentian-violet, and then by the usual procedure. Decolorisation by this fixing method is faster than in the heat fixed films.

Chromatin Staining. This is a subject which has received much attention recently. Ordinary cytological stains are unsuitable for detailed study, as they are liable to stain the whole cell uniformly, without differentiation of the internal structure.

Bacterial Chromatin. An easy method is one recommended by Dobell.[1]

A drop of medium containing the bacteria is placed in the centre of a carefully cleaned glass slide (or cover-slip) by means of a platinum loop. A drop of 1 per cent. osmic acid or strong formol (40 per cent. formaldehyde Schering) is placed beside the first drop, the two drops are mixed and spread in a thin film on the slide. The film is then allowed to dry without heat.

The slide or cover-slip with the dried film is placed in absolute alcohol for about ten to fifteen minutes. It is then removed and the film again allowed to dry.

Now stain the film with Giemsa or Lieshman stain in the usual way.

After staining, differentiate in 30 per cent. alcohol, wash in distilled water, dry and mount in cedar oil or neutral Canada balsam. Chromatin structures are coloured bright red, the cytoplasm being blue or lilac or pink, according to the degree of differentiation.

The structure of many bacteria is revealed with remarkable distinctiveness, its chief disadvantage being that the preparations sooner or later fade, and cannot as a rule be satisfactorily re-stained.

Protozoa. Heidenhain's Iron Hæmatoxylin method can be recommended. It will be given under staining of the tissues of insects.

Sections. A new method,[2] which gives excellent results, for the staining of protozoa in tissues and for sections of the central nervous system, especially for the Negri corpuscles in rabies, is briefly as follows :—

Unna's Polychromatic Methylene Blue (Grübler), 5 minutes.

Wash in tap-water.

Chromic acid 2 per cent., 1 to 15 minutes.

Wash again.

Tannic acid 5 per cent., to differentiate till the section appears a clear blue, and takes on a reddish-violet colour.

Wash, dehydrate comparatively quickly in absolute alcohol, clear in xylol, and mount in balsam.

Trypanosomes. The staining of trypanosomes has received special attention of late, as attempts have been made to classify these parasites by their structure; the value of this method

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[1] Dobell, C. C. (April, 1911), "Contributions to the Cytology of the Bacteria." *Quarterly Journal Microscopical Science.*

[2] Krogh, M. (March 6, 1911), "Eine neue Methode zur Chromatinfärbung." *Cent. f. Bakt.*, I. Orig., Vol. LVIII., No. 1.

Staining—*continued*

of classification and differentiation cannot be entered into here. The subject, however, is of interest.

Methods of fixation are of primary importance, as a good staining method is often useless if the subject of study has been distorted by coarse fixation.

One recommended is[1] :—

A 4 per cent. solution of osmic acid is put in the bottom of a stain tube, to which two or three drops of acetic acid are added.

The slide to be fixed is placed in the tube as quickly as possible after the film has been drawn.

A fairly deep or thick glass ring in the liquid at the bottom of the tube prevents the slide from getting wet.

Leave in contact with the vapour for 20 seconds to half a minute, the shorter the time the better, particularly in the case of smears from a culture.

After fixing, the slide is placed in absolute alcohol for 15 to 30 minutes, according to convenience. If Romanowsky's stain is to be employed the slide should not be left in the alcohol for more than 30 minutes.

As regards staining, Twort's[2] stain is a good one for studying the structure of trypanosomes; it does not give show pictures, but brings out well the delicate structures. Neutral red and brilliant green are mixed, the precipitate is collected, dried, and re-dissolved in methylic alcohol with 5 per cent. of glycerine added.

For use after fixation—

Mix two parts of this solution with one part of distilled water. Differentiate with a 2 per cent. solution of Unna's glycerine-ether in water.

Staining of Trypanosomes from cultures. A useful method is—

(1) A 1 per cent. solution of Azure I., in equal parts of glycerine and methyl alcohol.

(2) A 1 per cent. aqueous solution of Methylene Blue (Höchst—an essential point), to which 5 per cent. of pure sodium carbonate is added.

This solution is kept warm at a temperature of 40° to 45° C. for a couple of days, when it is made up, after which it is ready for use.

(3) A 2 per cent. solution of Eosin (also Höchst).

In using the stain a mixture made up of four drops of each of the three solutions is added to 10 c.c. of distilled water.

Drop-bottles of equal size should be used, as the drops of the different liquids are not the same size.

Cultural forms are stained in from 6 to 8 minutes.

If any stain is deposited in the ground substance it may readily be removed with orange-tannin.

This method may also be used for staining trypanosomes in the blood; only 40 to 50 minutes is required.

Rinse well after staining with tap water. A few drops of orange-tannin poured on the slide for half-a-minute or so removes the excess of stain. If, after further washing, the parasites appear to be over-stained, either more orange-tannin or else acetone should be added.

The latter must be used with caution and quickly rinsed off, for though at first it only extracts the blue it soon begins to take out the red from the flagellum.

Eventually the slide is washed with distilled water and allowed to dry.

The Romanowsky method is unsuitable for trypanosomes, as nuclear structures and details cannot be interpreted correctly by means of this stain alone.

Spirochætæ. Some methods will be found considered under the heading of Syphilis.

Two new modifications of Levaditi's method have been introduced for films, and one for sections.

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[1] Woodcock, H. M. (November, 1910), "Studies on Avian Hæmoprotozoa." *Quarterly Journal Microscopical Science.*

[2] Minchin, E. A. (1909), "The Structure of *Trypanosoma lewisi* in relation to Microscopical Technique." *Quarterly Journal Microscopical Science*, Vol. LIII. Quoted in *Bull. de l'Inst. Past.*, January 15, 1910.

Staining—*continued*

In films.

1.[1] Fix the smear in absolute alcohol.

Place in a solution of 10 per cent. silver nitrate for one hour at a temperature of 100° F.

Reduce by means of a 5 per cent. solution of pyrogallic acid.

The treponema should stain dark brown, connective tissue cells yellow, while various histological debris are coated with metallic silver.

2.[2] The film is spread on a cover-glass, and fixed by osmic acid vapour, immersed in a saturated solution of nitrate of silver made up with 95 per cent. alcohol, and left for four hours. The solution should be in a clear glass receptacle and remain exposed to diffuse light. At the end of this time the film should be a dark brown. Wash in water and examine.

Recognition is easy, as the treponema is small and can be seen without using the oil immersion lens. The method is especially good in thick films.

In tissues. The original Levaditi method gives the best results, but it suffers from the disadvantage that the tissues become stained with the silver as well as the treponema.

A modification which is free from this disadvantage is [3] :—

Method. The tissue to be investigated may be preserved in various solutions, and is then cut into small pieces ten millimetres long and five millimetres in thickness and breadth. These are washed free from the fixing medium by rinsing in water for 24 hours, and finally in distilled water for 1 hour. Each piece is then put into ten cubic centimetres of a 5 per cent. solution of silver nitrate in a brown-coloured bottle, and kept at 37° C. for 48 hours. At the end of this time they are placed in a reducing solution containing 2 per cent. of pyrogallic acid and 1 per cent. of tannic acid in distilled water in similar brown bottles, in which they are kept for 24 hours at 37° C. It is, however, necessary to change this solution after the first half-hour since it is rendered turbid by the reduction. After this the pieces of tissue are placed in water for an hour and then washed in alcohol of increasing strength until decolourised ; they are then imbedded in paraffin or celloidin, the latter giving better results. If it is desired to counterstain the tissues, the sections should be dipped in Lœffler's methylene blue solution for a second. The celloidin is removed in the usual way and the specimen cleared by oil of origanum instead of by xylol, and then mounted in Canada balsam.

It may be mentioned here that picric thionin [4] is the best counterstain for the Levaditi method.

Tissues of Insects. Tissues like the organs of mosquitoes, bugs, and flies are best stained according to Heidenhain's Iron Hæmatoxylin method.[5] It will take effect on any material, is permanent, and it permits of the use of a large variety of counterstains. The technique is as follows :—

The sections having been fixed on the slides and the paraffin washed out with xylol, the slides are resting in 90 per cent. alcohol. It is now necessary to transfer the specimens into 80 per cent. alcohol, containing iodine and potassium iodide, in the following proportions. Make up a concentrated solution of potassium iodide in water, and of iodine in alcohol. Mix them together, and add to the mixture some 80 per cent. alcohol until the mixture becomes a dark brown colour. Leave the slides in this solution for five to ten minutes, and then pass them into 30 per cent. alcohol, and through decreasing strengths of alcohol to distilled water.

The specimens should now be immersed for about an hour in the following solution of iron-alum (eisenoxydammon, Grübler), 3 per cent. dissolved in distilled water.

The slides are then washed with water and stained in an aqueous solution of hæmatoxylin, prepared as follows :—

Hæmatoxylin (pure) ½ per cent. ; dissolved in distilled water to which a few drops of concentrated solution of lithium carbonate may be added by way of improving the stain.

The sections should be left in the hæmatoxylin from one and a half to two hours. They

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[1] De Verteuil, F. L., and Kilroy, L. (September 18, 1909), "A Method of Staining the *Treponema pallidum*." *Lancet.*

[2] Khitrovo (November, 1909), "A Simple Method of Staining Spirochætes in Films." *Arch. Méd. Belg.*, quoted in *Journal Royal Army Medical Corps*, May, 1910.

[3] Yamamoto, J. (February 27, 1909), "A Method for Staining the *Spirochætæ pallida* in Tissues." *Cent. f. Allgem. Path.*, quoted in *Lancet*, March 27, 1909.

[4] Salrazès et Dupérié (May 1, 1909), "Thionine picriquée aprés imprégnation argentique des Spirochètes." *C. R. Soc. Biol.*

[5] Hammerton, A. E. (September, 1908), "An Introduction to Methods of Studying the Morbid histology of Disease-carrying Insects." *Journal Royal Army Medical Corps.*

Staining—*continued* are then washed with water and again treated with iron-alum solution, which slowly washes out the stain.

The progress of differentiation ought to be controlled by frequent microscopical examinations under the low power, the section being removed from time to time out of the iron-alum, rinsed with water, and examined.

When a proper differentiation has been obtained, *i.e.* the nuclei appearing black and other parts of the cell fairly clear or smoky, the preparations should be washed for at least a quarter of an hour in running tap-water.

In order to make a pretty preparation with a good contrast of colour, it is advisable to counterstain in one of the following solutions. Saffranin O (Grübler), 1 gramme dissolved in 10 c.c. of absolute alcohol, and added to 90 c.c. of aniline oil in water.

After differentiation and washing in tap-water, preparations may be transferred directly into this stain, and left therein until the tissue has become sufficiently coloured.

They must then be rapidly dehydrated with alcohol, cleaned in xylol and mounted.

Orange G (Grübler). A little of the stain is put into 8 per cent. alcohol to form a saturated solution.

The slides should be passed through increasing strengths of alcohol to the 80 per cent. solution containing the stain.

They may be left in the latter for about 10 minutes.

Eosin or acid fuchsin prepared in the same way may be used as a counterstain.

Amœbæ.[1] For living preparations, the best of the vital stains is neutral red.

The ectoplasm does not take the stain, endoplasm and nucleus become faintly and diffusely pink, the nucleus being the deeper. Granules and absorbed matters in the endoplasm take a deep cherry-red tint. The preparations do not keep, as the stain fades when the amœbæ die.

Wet fixed preparations.

For these may be employed Grenacher's and Böhmer's Hæmatoxylin. Heidenhain's Iron Hæmatoxylin and Hartmann's recently recommended modification of the Iron process.

Additional Notes

Klausner [2] describes a method of rapidly staining the *Treponema pallidum*, which seems simple and efficient. A thin film of the suspected material is fixed by holding it above a 1 per cent. solution of osmic acid ; it is then stained for twenty to thirty seconds with the reagent.

The staining fluid is prepared by shaking 3 c.c. of aniline with 20 c.c. of distilled water for some five to ten minutes ; the emulsion is then filtered and the clear liquid mixed with a concentrated solution of gentian-violet in a proportion of 2 to 1.

A useful paper on special modifications of the Iron-Hæmaten stain and the Giemsa method, both in the case of sections and films, is that by Seidelin.[3] It is illustrated and must be consulted for details.

Syphilis. Some apology is perhaps required for attempting to deal in so brief a manner with such an important subject. So many advances, however, have been made during recent years, since the discovery and description of the *Treponema pallidum*, namely the application of dark background illumination for diagnostic purposes, the introduction of complement fixation and of the Ehrlich-Hata preparation that a few practical notes on these recent advances will not be out of place.

The study of syphilis is of special interest to us in Africa, and it is for those workers who cannot easily obtain access to recent accounts of methods and results that this short epitome is intended.

Microscopical diagnosis. Here in the first instance we have the choice of several methods of procedure both as regards obtaining material and examining it. We will only deal with early diagnosis, and the material for it may be obtained either from the primary sore or from enlarged glands.

Primary Sore. The best way is to take up in a fine capillary tube the serous exudation after slight scraping or incision of the indurated border.

Glandular Swelling. A small syringe such as is used for injections is employed. After

[1] Werner, H. (July, 1909), "Studies Regarding Pathogenic Amœbæ." Translated. *Indian Medical Gazette.*

[2] Klausner, E. (1911), "On a Momentaneous Method of Staining *Spirochæta pallida*." Dermatological Clinic of the University of Prague. *Berl. Klin. Woch.*, No. 4, p. 169. Quoted in *Journal Royal Institute of Public Health*, March, 1911.

[3] Seidelin, H. (June, 1911), "An Iron-Hæmaten Stain with Remarks on the Giemsa Stain." *Parasitology.*

Syphilis—*continued*

preliminary cleansing, the skin is drawn away from over the gland as far as possible so that on withdrawing the needle no superfluous exudation from the loose tissues can enter the latter. The needle is plunged in as obliquely as possible and, when it has entered the long axis of the gland, its point is moved about. Aspiration should be vigorous.

This method is very useful in those cases where there is a good deal of pus present about the initial lesion, and by its use Preis [1] has been able to demonstrate the *Treponema pallidum* in sixty doubtful cases in which clinical evidence of syphilis appeared later. It must, however, be understood that a negative result does not indicate that the patient has not acquired syphilis.

The material thus obtained may be examined in three ways :—

By staining.

By the dark background illumination method.

By the Chinese ink method.

Staining. To deal thoroughly with the various methods of staining the *Treponema pallidum* would be to write a volume, and only certain processes whose utility we have proved will be given here. Leishman's method is one of the best. Two parts of the stain are mixed with three parts of distilled water, and the unfixed film is flooded with this mixture. The stain is renewed every 15 minutes for 1 to 1½ hours and the film is then washed in distilled water and examined.

Giemsa's stain also may be used. Twenty to twenty-five drops of Giemsa's stain (Grübler's) are added to 15 c.c. of distilled water and the unfixed film is flooded with this mixture. The slide is warmed over a flame till steam rises, and the solution is then poured off, the process being repeated till all the stain has been used up. For papers describing two new rapid-staining processes, the reader is referred to the appended reference.[2]

A simple method of staining the living treponema is Meirowsky's.[3] He rubs on a primary lesion a thick coloured paste consisting of some methyl-violet in physiological saline solution. After a few minutes some of the fluid is taken up and in this the treponema may be found.

Dark-ground illumination. This is by far the best and most rapid method of detecting the treponema, though it requires special apparatus. Excellent descriptions of apparatus and technique by Harrison [4] will be found in the *Journal of the Royal Army Medical Corps* and by Coles [5] in the *British Medical Journal.*

Chinese ink method. This requires some practice, but gives good results. A drop of the suspected fluid is mixed with a drop of Chinese ink and allowed to dry on a slide. It can then be examined in daylight with a $\frac{1}{12}$th-inch oil immersion lens.

An interesting method of obtaining the treponema is by blistering the skin during the period of the secondary rash, the parasite being found in the serous fluid.

Movements of the *Treponema pallidum* according to Eitner.[6]

The organism moves in three ways :—

(1) Rotation around its long axis ; (2) by bending its body ; (3) by jerking backwards and forwards. It does not move widely or energetically, and when seen crossing the field it is always being carried in the currents of the fluid medium.

Selenew [7] has described ring and star forms, but cannot say that they are distinctive of the treponema. His star forms look rather like spirochæte agglutination.

We now pass to a very brief consideration of complement fixation, or what is known as the Wassermann reaction. There are many modifications of the original reaction which tend to simplification, and some of these give very nearly as good results, besides reducing

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[1] Preis, K. (1908), "Über den praktischen Wert der diagnostischen Drüsenpunktion bei Syphilis." *Pest. Med. Chir. Presse, Budapest,* Vol. XLIV.

[2] Klausner, E. (January 23, 1911), "Two Rapid Methods of Staining the *Spirochæta pallida.*" *Berl. Klin. Woch.* Quoted in *Lancet,* February 4, 1911.

[3] Meirowsky (July 5, 1910), "Über einfache Methoden zur schnellen Färbung lebender Spirochäten." *Münch. Med. Woch.* Quoted in *Journal Royal Institute of Public Health,* September, 1910.

[4] Harrison, L. W. (April, 1910), "Dark-ground Illumination in the Diagnosis of Syphilis." *Journal Royal Army Medical Corps.*

[5] Coles, A. C. (August, 1909), "*Spirochæta pallida.* Methods of Examination and Detection by means of the Dark-ground Illumination." *British Medical Journal.*

[6] Eitner, E. (April 16, 1907), *Münch. Med. Woch.* Quoted in *British Medical Journal,* June 20, 1908.

[7] Selenew, I. F. (1910), "Zur Morphologie der *Spirochaeta pallida ;* Ring-und Sternformen derselben." *Cent. für Bakt.,* Vol. LIV.

Syphilis—*continued* labour enormously. Different authorities have different ideas, but one of the best and simplest modifications is Fleming's. A good account of Fleming's technique is given by Gibbon.[1]

His conclusions, based on one hundred and forty-one cases; are :—

(1) The diagnosis of syphilis can readily be made by means of a reaction in which rabbit's heart extract, sheep's red blood corpuscles, and the suspected serum alone are employed.

(2) Eighty per cent. of cases of syphilis diagnosed clinically have given positive results.

(3) In 100 per cent. of non-syphilitic blood examinations the results have been negative.

(4) The reaction has not appeared in the blood of some of those patients who have undergone a prolonged course of mercurial treatment.

It must, however, be stated that there are a certain number of fallacies, as some disorders, apart from syphilis, give the complement fixation reaction such as scarlet fever, trypanosomiasis and several other protozoal diseases.

A good modification of Wassermann's reaction is one by Birt,[2] which has the advantage, that it can be practised in countries where anti-vivisection laws are in force.

A very simple substitute for the test was suggested by Porges and reported upon by de la Motte.[3] It consists in mixing equal parts of the patient's serum and a 1 per cent. solution of sodium glycocholate in a test-tube which is set aside for from 16 to 20 hours. At the end of this time, if the reaction is positive, a precipitate has appeared, which usually forms a small clump floating on the surface of the mixture. Simultaneous tests with this and the Wassermann reaction are said to show the new method to be equally reliable. It is certainly worthy of a trial.

A new venture in the treatment of syphilis, and one that opened up a great field of research, and which, moreover, has led to excellent results, was the employment of the organic arsenical compounds. Amongst the first of these to be used were atoxyl, orsudan, soamin and arsacetin, and though they did not bring about a cure of the disease they were and are still of great use in treating symptoms, especially so when given in conjunction with mercury.

The Ehrlich-Hata preparation has inaugurated a new era in the treatment, and even at present improvements on the original "606" are in progress. Ehrlich does not contend that it is certainly curative, but of its great value so much has been written that there is no necessity for me to dilate upon it here. A certain number of cases have developed toxic symptoms, and the injections give rise to a good deal of pain, but these are minor evils which will undoubtedly soon be rectified.

A simple method of injection is one by Richard Volk.[4] He points out that the injection of Ehrlich's preparation into a vein is often followed by a considerable rise of temperature, and intra-gluteal injection by very severe pain which disturbs sleep and causes the patient to be confined to bed, but that subcutaneous injection of the preparation is well borne. His method of preparing the emulsion is as follows :—The powder is ground in a sterile mortar until it is fully dry, and a little sterile liquid paraffin or olive oil is added and rubbed in under slight pressure ; 5 c.c. to 8 c.c. of paraffin oil are then added to make an emulsion, which is injected under the skin of the back in one or two places. Allowances must be made for a little of the emulsion being lost, and in order to make the loss as small as possible rather more paraffin than is necessary for emulsification must be used. The needle for the injection must be of rather wide calibre. The preparation of the emulsion takes only from three to four minutes, and solution, neutralisation, etc., are dispensed with. The painfulness of the injection varies in individual cases, but is not greater than when the emulsion is prepared by Wechselmann's method ; the patients are usually not confined to bed, nor is their sleep disturbed. The author, in a whole series of cases, has proved the efficiency of the preparation when thus administered.

During the last few years the treatment of syphilis has been carried out on a large scale in Uganda by means of mercurial injections and the first of the above-mentioned arsenical compounds. As Conseil and Fribaudeau[5] show, "606" will be very useful in treating the

[1] Gibbon, T. H. (February, 1910), "Fleming's Method of Scrum Diagnosis in Syphilis, with the Results of One hundred and forty-one Cases." *Journal Royal Army Medical Corps.*

[2] Birt, C. (October, 1910), "A simple Modification of Wassermann's Reaction." *Ibid.*

[3] De la Motte, W. (August 25, 1910), "Die Porgessche Luesreaktion." *Deutsch. Med. Woch.* Quoted in *The Prescriber*, January, 1911.

[4] Volk, Richard (December, 1910), "Simple Method of Injection of the Ehrlich-Hata Preparation." Epitome, *British Medical Journal.*

[5] Conseil, E., and Fribaudeau, J. (November 12, 1910), "Application du '606' au Traitement de la Syphilis en Pays Arabe." *Bull. Soc. Path. Exot.*

disease in semi-civilised countries, where syphilis is spread chiefly by, and is most severe in, the nomadic tribes in whom long courses of treatment are impossible. Syphilis—*continued*

A very interesting epitome of Pinard's conclusions on "Immunity in Syphilis, Syphilitic Superinfection and Reinfection," is to be found in the *British Medical Journal*, February 4, 1911. We quote it as there given :—

Pinard (*Thèse de Paris*, 1910), after giving an interesting account of modern investigations into these problems, comes to the following conclusions :—

(1) It is possible, but not proved, that certain individuals have a natural immunity against syphilis.

(2) Immunity is not always absolute during the evolution of syphilis.

(3) It is possible to produce a syphilitic lesion by inoculating with the active virus during the incubation of the primary chancre.

(4) The syphilitic chancre is auto-inoculable during the first ten days.

(5) After this interval up to the appearance of the roseola, inoculations in sub-epidermic pockets with a larger quantity of virus may produce a chancre.

(6) That the lesions produced by re-inoculation are truly syphilitic is shown by their incubation (ten to twelve days), appearance, and histological structure, and by the presence of the *Spirochæta pallida*.

(7) The lesions of re-inoculation of the primary period resembled either early chancres or secondary papules.

(8) The lesions of re-inoculation are due to the introduction of the spirochæte, and cannot be produced by traumatism alone; they last several months.

(9) The lesions of inoculation may also be produced in regions remote from, or near to, the primary chancre, and their evolution is the same. Immunity is established slowly, but does not progress from region to region.

(10) Inoculations with the patient's own virus or with other virus give similar results.

(11) During the secondary period re-inoculation is difficult, and the lesions are small insignificant maculo-papules.

(12) It is possible to produce lesions of re-infection, or rather superinfection, in tertiary syphilitics. The lesions have the typical appearance of tertiary syphilis, and have an incubation period of fifteen to twenty days.

(13) Lesions of superinfection may be observed clinically as well as experimentally, and may be due to autoinoculation or heteroinoculation. During the incubation of the chancre new contaminations may produce successive chancres, less and less developed. During the existence of the chancre new chancres sometimes develop by contact or pressure. During the tertiary period certain genital chancriform syphilides, impossible to differentiate clinically from spontaneous lesions, may be due to second infection. These cases are more common than is usually supposed.

(14) Cases of true syphilitic re-infection, with a second syphilis and more or less complete secondary lesions, may also occur.

(15) Heredo-syphilitics, not only the dystrophic but also those who have received actual syphilis, are liable to contract syphilis again.

(16) Immunity is incomplete during the primary period, very pronounced during the secondary period, reaches its acme after the disappearance of secondary lesions, and becomes weaker during the tertiary period.

(17) Early mercurial treatment, intensive or prolonged, contributes to the disappearance of immunity—that is, to cure.

(18) The Wassermann reaction, negative at first but constantly positive during the secondary period, is often negative in the tertiary stage, especially at an advanced date from the primary infection, and when the patient has been treated intensively.

(19) True lesions of superinfection and reinfection are not only possible but more frequent than is believed. The syphilitic reacts to a new inoculation according to the stage of his first attack, that is, according to the degree of his immunity.

(20) A syphilitic may after a certain time completely lose his immunity, and may then undergo true reinfection. There are undoubted examples of this.

Attention may also with advantage be directed to the description by Hermann[1] of a case of severe visceral syphilitic fever because of the difficulty of distinguishing such a febrile condition from malaria and tuberculosis. There was marked liver enlargement, but the spleen and mesenteric glands were also severely affected. The condition appeared to be a diffuse, gummatous infiltration of the viscera and terminated fatally, one of the causes of death being intestinal hæmorrhage.

At a discussion on syphilis and marriage[2] the following points were brought out :—

That gonorrhœa leads to disease and to a diminution of the population almost equal to that produced by syphilis.

Syphilis during active life does not lead to sterility, but 42 per cent. of miscarriages and abortions are due to it, and many of the children who survive are diseased.

In cases where both parents are syphilitic the proportion of miscarriages might be 70 per cent., and Fournier has stated that of 90 women infected during the first year there were 50 abortions, 38 children were born alive, but soon died, and only two survived.

[1] Hermann (1910), "Visceral Syphilitic Fever." *Wien. Med. Klin.*, quoted in Epitome, *British Medical Journal*, November 26, 1910.

[2] "Discussion on Syphilis and Marriage." *Edinburgh Medico-Chirurgical Society. Lancet*, January 15, 1910.

Syphilis—*continued*

As regards the attitude of society towards venereal disease, nothing is done as to instructing young adults, but it is left to the physician to cure or prevent contagion, and he might prevent or delay marriage. The treatment generally occupied three to four years.

With reference to the historical aspect of syphilis

In 1850 treatment for 3 to 4 months was considered sufficient.

1861 a course of 3 months' mercury and 3 months' potassium iodide.

1872 a two years' course of mercury.

1881 a four years' course.

1897 a six years' course.

In cases of pre-matrimonial syphilis it is questionable whether the syphilitic should marry. The question does not lie so much in the fact of a cure, but as to whether the risks to wife, child or self are so slight as not to enforce celibacy. In determining the question as regards (1) Risks to the wife. 75 per cent. of married women who are syphilitic have contracted it from their husbands, directly from syphilitic lesions on their husbands or conceptionally, the infected fœtus infecting the mother. (2) Risk to the offspring. The parental syphilis is communicated by infected sperms or ova, or through the utero-placental circulation during pregnancy. The mother is not invariably infected, and may later be infected from another source. Fully 28 per cent. of paternally infected fœtuses die *in utero*, or the infants die shortly after birth, and if mothers are infected the fœtal and infantile mortality is much greater.

In cases of mixed hereditary syphilis the mortality is 60 to 80 per cent. *in utero*, while one-third of those born alive die within six months.

If one parent suffers from heredo-syphilis, of 81 pregnancies there would probably be 28 abortions, 13 premature births, 7 dying soon after birth, and 52 would survive.

It is a most interesting but a difficult question to decide as to the duration of the contagion and the length of the transmissive period.

An active syphilitic may beget healthy children.

The mere fact of not finding the spirochæte does not show the case was not contagious.

There is no absolute proof of the non-contagiousness of tertiary lesions.

A safe rule to adopt is that if there have been no manifestations for 18 months, and if a period of four years has elapsed since the primary sore, and if the patient has been properly treated and is in good health, he may be allowed to marry. But there are exceptions both with regard to contagion and also transmission. Transmission persists longer than contagion.

As to treatment: without any, abortion is the rule; with treatment, healthy children are born; when treatment is stopped syphilitic children are born.

As to post-matrimonial syphilitics the question is one of infection. The husband has to be treated so as to prevent infection; he has to be instructed as to his mode of life; there is the question as to whether the wife should be told. If the wife is healthy but pregnant there is the question of treating the wife though she has no symptoms.

About 3 per cent. of all syphilitics pass into general paralysis. The greater number of syphilitics die at an early age, usually before the age of 40. Syphilis may be contracted twice.

Author's Note.—With regard to answering the question as to whether a so-called properly treated patient should be allowed to marry, a Wassermann reaction would be of value. The whole outlook may possibly now undergo a change owing to the introduction of salvarsan.

Additional Notes

Following on the lines of Alston's [1] work on yaws, Gibbs and Calthrope [2] have employed the serum derived from blistering patients who have been injected with salvarsan as a therapeutic agent. Alston used the serum from cases of frambœsia who had received salvarsan injections for the treatment of other cases of this disease. Gibbs and Calthrope utilised the same procedure in treating a case of syphilis.

In both diseases the serum appears to act in a similar manner to salvarsan itself. The method of treatment is very interesting, but nothing can yet be said regarding its use as a

[1] Alston, H. (February 18, 1911), "The Curative Effect of Salvarsan ('606') in Cases of Frambœsia." *British Medical Journal.*

[2] Gibbs, C., and Calthrope, E. S. (April 8, 1911), "The Curative Effect of Salvarsan Serum in a Case of Syphilis." *Ibid.*

substitute for "606" or as an improved method of administration. How it may act prophylactically is not known, but it should be studied in the light of the infective granule theory. It may, however, be of use in those cases of kidney disease and other conditions in which salvarsan is contra-indicated. Syphilis—*continued*

A few notes by Ehrlich [1] on the indication and contra-indication before employment of salvarsan are of interest and importance. The paper, however, is too long for review here, though it contains many other important points with regard to nervous symptoms occurring after injection, the use of salvarsan in optic cases, and his views on repeated injections as a method of treatment with a view to cure. Cumulative action and alteration of salvarsan in the tissues to toxic bodies is also dealt with.

Schamberg and Ginsburg [2] give the following contra-indications to the use of and warnings for the safe employment of salvarsan, which may be of interest.

(1) Don't use salvarsan in myocarditis, in advanced cases of tabes dorsalis and general paresis, in nerve syphilis affecting vital centres, in grave kidney disease, in cachectic and debilitated persons (unless the condition is due to syphilis), in aneurism, in optic neuritis, and in persons with lesions (such as gastric ulcer) in whom increased blood-pressure may produce hæmorrhage.

(2) Don't use intravenous injections of salvarsan until you have fully qualified yourself and possess a detailed knowledge of the technique. Deaths have occurred and more will occur from unskilful administration.

(3) In the preparation of the drug for intravenous use, do not use a solution made with common salt or undistilled water (such as is often supplied in hospitals), but use a specially prepared sterile physiological salt solution made with chemically-pure sodium chloride; otherwise you may find it impossible to obtain a clear solution.

(4) Don't under any circumstance inject into the veins a solution which is not *perfectly clear;* a flocculent or cloudy liquid may produce alarming symptoms of collapse or even death.

(5) Don't use a solution any more alkaline than is absolutely necessary to secure a clear solution.

(6) Don't inject the salvarsan into the veins without previously running in physiological salt solution; if the needle is not in the vein you will infiltrate the surrounding tissue with the salvarsan solution and cause subsequent inflammation and unnecessary pain.

(7) Don't infuse the solution into the vein too rapidly; it is best to have a needle of such a calibre as will require eight minutes to introduce 200 c.c. of fluid. With the gravity apparatus, the rapidity of inflow can also be governed by the height of the receptacle.

(8) Don't infuse a cold solution; the liquid should be about the temperature of the blood.

(9) Don't use "glass pearls" in the mixing jar, as is often recommended; we have found that minute particles of glass chip off which might cause embolism.

(10) Don't use a routine dosage of the drug; the dose should be gauged according to the weight of the patient and the character of the condition to be treated.

(11) Don't employ intravenous injections in your office or in a dispensary. The patient should be treated in a hospital and put to bed and carefully observed for a period of not less than three days.

(12) Don't persist in the intravenous injection if the patient should show signs of collapse during the administration, but stop at once.

Balfour [3 & 4] has recently described a phenomenon occurring in connection with the *Treponema pallidum*, which is probably of interest and importance. The phenomenon is that of "granule shedding" or the throwing off of highly refractive granules from the parasite, which he considers to be resistant forms or spores.

This discovery may considerably influence our treatment in the future, but as yet the difficulty of differentiating between the treponema granule, hæmoconia and leucocyte granules is so great, that we must await further investigation before venturing an opinion as to how it may affect therapeusis.

Technique. A comparatively new departure in hæmotherapy is the employment of leucocytic extract as a therapeutic agent in epidemic cerebro-spinal meningitis, endocarditis, pneumonia, empyema, osteomyelitis, chronic furunculosis, and chronic acne. The technique of the process by which the extract is obtained is very clearly and concisely put in an article by Moore Alexander,[5] and is given here:—

The author has employed throughout the method of Hiss and Zinsser for procuring the leucocytic extract from the pleural cavity of rabbits. Since it has succeeded almost invariably in producing good results, no necessity

[1] Ehrlich, P. (January, 1911), "Pro und contra Salvarsan." *Wien. Med. Woch.* Quoted in *British Medical Journal*, May 20, 1911.

[2] Schamberg, J. F., and Ginsburg, N. (February 4, 1911), "The Use of Salvarsan." *Journal American Medical Association.* Quoted in *Journal Tropical Medicine and Hygiene*, March 1, 1911.

[3] Balfour, A. (May 20, 1911), "The Effect of Salvarsan on *Treponema pallidum.*" *British Medical Journal.*

[4] *Idem* (June, 1911), "Resistant Forms of *Treponema pallidum.* A suggestion." *Journal Royal Army Medical Corps.*

[5] Moore Alexander, D. (February 18, 1911), "The Use of Leucocytic Extract in Infective Processes." *British Medical Journal.*

Technique —*continued*

was found for resorting to the perhaps more effective methods of Petterson and his followers, who use the more dangerous technique of abdominal injection.

A sterile 10 per cent. suspension of Mellin's food in distilled water was injected in amounts varying from 5 to 10 c.c., according to the size of the animal, into each pleural cavity of a rabbit. The animal was killed twenty-four hours later, and the fluid exudate removed. Difficulty was experienced at first in obtaining this perfectly sterile, until the following plan was adopted.

The skin is removed from the thorax, and the ribs laid bare by cutting away the pectoral muscles. The surface of the ribs and intercostals is lightly seared over the whole side of the thorax, a 10 c.c. syringe with a large bore needle is thrust into the pleural cavity, through an intercostal space, usually the seventh or eighth, and the fluid removed by suction. If the nearer cavity be emptied, it is easy with practice to thrust the needle through into the opposite pleural cavity, and thus the fluid from both cavities may be drawn off through the one external opening. The fluid should be pale yellow with a flocculent haze of leucocytes. Any large masses of Mellin's food must be removed by a preliminary sedimentation. Ten to 20 c.c. is the average amount of fluid obtained. The exudate is rapidly placed in sterile centrifuge tubes and centrifugalised until a thick grey deposit of leucocytes appears at the bottom of the tube. The supernatant fluid is carefully pipetted off. The leucocytes may be again centrifugalised several times with fresh amounts of normal saline to free them from the last traces of exudate fluid. This is not, however, in the writer's opinion, absolutely necessary, and is usually dispensed with unless some circumstance should arise, such as the presence of a trace of blood. Sterile distilled water is then added in equal volume to the deposited leucocytes, which are well broken up with a pipette or glass rod. The tubes are placed in the incubator at 37° C. for at least four hours. Each tube is then tested for sterility, and, if sterile, the contents of several tubes are mixed and distributed in 10 c.c. ampoules, which are placed in the ice-chest until required. Leucocytic extract so prepared will remain effective for at least three months.

The dose used in the cases described was from one to ten c.c. In some cases a dose of ten c.c. was repeated daily for three days. In a successful case of treatment, one of furunculosis, two injections of eight and ten c.c. were given at an interval of three days. The extract is injected into the flank or buttock.

Two new methods of examining blood for parasites are of special interest. One is based on solution of the erythrocytes, the other on their agglutination.[1] A drop of blood to be examined is mixed with ten to fifteen drops of acetic acid (3 per cent.) and centrifuged.

The sediment may then be examined in the fresh condition, or after drying and staining.

In the latter case the parasites and nuclei of the leucocytes are alone stained, the red corpuscles being dissolved by the action of the acetic acid.

The finding of trypanosomes, spirochætes and filariæ in specimens of blood poor in these parasites may be facilitated by the use of ricin.

It has been found that ricin has a strong agglutinative action on red blood corpuscles, but not on the above-mentioned protozoa and nematodes.

The technique is :—

Twenty or thirty drops of blood are let fall into a small centrifuge tube, and 4 c.c. of a solution of hirudin and ricin, dissolved in physiological saline solution, are added. The blood corpuscles agglutinate and fall to the bottom of the tube. The supernatant fluid is collected, centrifuged, and the sediment is slightly diluted and examined.[2]

The solution of ricin and hirudin may be conveniently made up as follows :—

0·01 gramme of hirudin is dissolved in 90 c.c. of physiological saline solution, a 1 per cent. solution of ricin is added to this so as to make up a solution 1 per cent. of ricin to 10 per cent. of the hirudin solution. Small centrifuge tubes are now taken and 4 c.c. put in each, the tubes are now sealed off and sterilised by heat at 60° C. for an hour. The tops of the tubes may be broken off when required for use.[3]

Mackinnon,[4] in an article on herpetomonads, recommends the use of iron-hæmatoxylin or other reliable cytological stain, in preference to the Romanowsky method, owing to the tendency of the Romanowsky stain to produce artifacts. The author fixes the iron-hæmatoxylin preparations by dropping lightly-smeared cover-glasses on to the hot fixative (Schaudinn's sublimate-alcohol) after the method recommended by Schaudinn.

In an article on the preparation of Endo's medium, Kastle and Elrove [5] recommend the

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[1] Stäubli, C. (December 15, 1908), "Beitrag zum Nachweis von Parasiten in Blut." *Münch Med. Woch.* Quoted in *Journal Tropical Medicine and Hygiene,* June 1, 1909.

[2] Levaditi, G., and Stanesco, V. (November 27, 1909), "Sur un procédé facilitant la recherche des trypanosomes, des spirilles et des filaires dans le sang." *C. R. Soc. Biol.*

[3] *Idem* (February, 1910), "Sur un procédé facilitant la recherche des trypanosomes, des spirilles et des filaires dans le sang." *Folia Serologica,* Vol. IV., No. 4.

[4] Mackinnon, D. L. (September, 1910), "Herpetomonads from the Alimentary Tract of certain Dung-flies." *Parasitology,* Vol. III.

[5] Kastle, J. H., and Elrove, E. (November 26, 1909), "On the Use of Anhydrous Sodium Sulphite in the preparation of Endo's Medium, together with a Note on the Preparation of Anhydrous Sodium Sulphite and its Stability under Ordinary Conditions." *Journal Infectious Diseases.*

Technique —*continued*

employment of anhydrous sodium sulphite instead of the hydrated salt, on account of its greater purity and stability. They have found it to be quite stable under ordinary conditions, especially when kept dry. An improved method (Elrove's) for the preparation of pure anhydrous sodium sulphite is also described.

Three simple methods of making lantern slides from diagrams are worthy of note. Their advantage is that the room need not be darkened when using them in the lantern, thus enabling the lecturer to see his audience.

A piece of glass,[1] thoroughly cleaned with acid, is placed over the required diagram, which is copied on the glass with process or Indian ink, a crow-quill or etching pen being used. Mistakes can be corrected by scratching with the point of a penknife when the ink is dry. The slide after washing may be used again.

Some difficulty may be experienced if the slide is not perfectly clean.

This difficulty is obviated in the second method.

A solution of equal parts of benzol and gold size is made, and well mixed. Rubber solution, a few drops (from tyre repairing outfit), is dropped in, the whole stirred till dissolved, and filtered if necessary.

The lantern slides are now flooded with this solution, and being stood on edge (with one corner lowest), put in a warm, still place to dry. When dry, diagrams may be drawn or traced on them with Indian ink by means of an etching pen.

A slide [2] can also be made by drawing on glass, blackened by the flame of a turpentine lamp. The details should be fixed by immersing the slide in a varnish made by adding 10 c.c. of castor oil and 250 c.c. pure hard white varnish to 1000 c.c. of methylated spirit.

Details of a method of marking objects on microscopical slides [3] may be of use. The object is focussed under the low power. The substage of the microscope is now lowered and an ink dot is made on the lower side of the slide corresponding to the part opposite the lens above. After the ink is dry remove the slide from the microscope, and with a diamond or other hard instrument scratch a small ring on the glass around the ink mark. Wipe off the ink, and render the mark more visible by scratching on it with lead pencil, and rubbing. The object required is now in the centre of the ring and the ring can be easily found by the low power.

A label with a sketch of the field, marking any distinctive features, as well as the outline of the ring, will further facilitate subsequent finding of the object required. Another way is, along with the ring, to make drawings of the distinctive features of these fields under low, high, and oil immersion powers.

A modification of the needle for performing lumbar puncture is one designed to prevent wounding of vessels, and to secure the needle against being blocked by skin or membrane.[4]

The point is short and conical, and consequently it has no cutting edges. There are three lateral apertures a quarter of an inch from the point, their openings facing in different directions, so that all these are unlikely to be blocked by the same cause.

A convenient staining dish, which is very useful when employing stains which precipitate, and also when prolonged staining is necessary, is one of glazed ware, and capable of taking seven slides at a time.

Along the whole length of the dish on either side run lightly raised margins, upon which the ends of the slides are supported. A shallow space is thus left between the under surface of the slides and the bottom of the dish, so that only a small quantity of stain is used. The slides are placed face downwards in the stain and the dish covered to prevent evaporation.

The preservation of rubber articles is one which generally presents some difficulty in the Tropics. A good method [5] is as follows :—

Ordinary paraffin oil is placed in a flat tin vessel of suitable size, only a small layer of oil being needed (about half an inch in depth). A tray perforated with numerous small holes is fitted into the vessel, over the paraffin, and the rubber articles are placed loosely on the top of the tray. The oil vapour passes through the perforations, comes in contact with the rubber, and keeps it soft and supple. A cover fitted to the top excludes dust.

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[1] (February, 1909), "A Simple Method of Preparing Lantern Slides." *Journal Royal Army Medical Corps.*

[2] Wanhill, C. F. (July, 1909), "Making Lantern Slides from Diagrams." *Ibid.*

[3] Albert, H. (March, 1908), "On the Technique of Blood Examination." *Bulletin State University of Iowa,* Vol. I.

[4] (October 23, 1909), "New Lumbar Puncture Needle and Staining Dish." *Lancet.*

[5] Fox, A. C. (January, 1911), "A Simple Method of Preserving Rubber Articles." *Journal Royal Army Medical Corps.*

Technique —*continued*

Turpentine soap, which is largely used both in clinical work and laboratories, may be prepared as follows [1] :—

Take two parts of soft soap, one of glycerine, and boil. Strain through muslin, and when nearly cold add one part of turpentine and mix well. Store in a wide-mouthed bottle.

Three papers which may be of use to laboratory workers are worthy of note, *i.e.*—

An article entitled "An outfit for sending bile, specimens of blood, fæces, and urine, and some results of the examination of such material." [2]

An illustrated article on a new bucket for blood clotting in serum preparation.[3] The writer states that it gives results superior to those obtained by other methods of clotting, and also to the process of centrifugation.

An article giving the plans for special laboratories and antitoxin stables.[4]

The subject of dark ground illumination is mentioned, and references are given to it, under the heading of syphilis. It has been found very useful in these laboratories for standardising vaccines, and want of space is the only reason why it has not been dealt with in this Review in detail.

Additional Notes

Coles [5] has introduced a new medium for mounting microscopical specimens which he hopes will prevent the fading that occurs in aniline stained preparations when Canada balsam is employed. He finds that specimens mounted in Canada balsam, dammar cedar oil, or media of like nature fade, owing to these media becoming acid by oxidation. The medium he recommends is parolin, or liquid paraffin, and after numerous experiments he has adopted the following :—

A small drop of parolin is placed on a perfectly clean cover-glass, which has been held over the flame of a spirit lamp to drive off any moisture on the glass, this is applied to the air-dried film, which is also held for a second considerably above the flame, just long enough to make the moisture fade off. If the amount of oil is just sufficient to reach the margin of the cover-glass so much the better. If there be too much oil the preparation is placed under a piece of blotting-paper, and the excess of oil removed as much as possible. The margin of the cover-glass is then rung round with Apathy's gum syrup made as follows : picked gum arabic, cane sugar, ordinary, not candied, distilled water of each 50 grammes. Dissolve over a water bath and add 0·05 gramme of thymol. If the reaction is tested with litmus paper and if acid a little sodium carbonate is added. The gum syrup sets quickly in a warm room in about ten to thirty minutes. A coat of Bell's cement is then applied which dries quickly and is not acted upon by the immersion oil. The specimens obtained are clearer than those mounted in balsam owing to the refactive index of the parolin.

The only drawback to this method is that it is more troublesome than the Canada balsam method, but if its results are more permanent the extra work is well expended.

Parolin cannot be used as an immersion oil with unmounted stained specimens in the same manner as cedar wood oil, as it impairs the optical performance of the lens.

A rapid and simple method of testing the hæmolytic properties of micro-organisms is one by Keith,[6] and may be performed as follows :—

(1) A citrate-saline suspension of blood cells is made in the way employed in opsonic work. The cells are washed twice in saline.

(2) An emulsion of the micro-organism to be tested is made by putting enough sterile saline solution into a twenty-four-hour agar slope culture to reach half-way up the slope. The tube is then rotated between the hands.

(3) A Wright's tube of rather wide calibre is fitted with a teat and marked with a glass pencil at a point about three (*sic*) from the mouth.

(4) Blood suspension is drawn up to the mark, and then the emulsion of the organism to the same mark with a bubble of air intervening.

(5) The blood and organism are then mixed and drawn into the pipette, which is at once sealed off in the flame.

(6) The tubes are placed in a horizontal position for twelve hours, and then placed upright for about half-an-hour. This allows the blood cells to fall to the bottom, and above is left a solution of hæmoglobin—if any has been set free. This can usually be detected, if it is present, by the naked eye ; the direct vision spectroscope may be necessary, however.

If there be no hæmolysis at room temperature in this part of the world (Singapore) after twelve hours, it may be concluded that the test is negative.

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[1] Harding, N. E. (September, 1909), "Turpentine Soap." *Journal Royal Army Medical Corps.*

[2] Stokes, W. R., and Storer, W. H. (May 20, 1910), "An Outfit for sending Bile, specimens of Blood, Fæces and Urine, and some results of the Examination of such Material." *Journal Infectious Diseases.*

[3] (1909), "New Bucket for Blood Clotting in Serum Preparation." *Journal Tropical Veterinary Science,* Vol. IV., Part 4.

[4] Aldwinckle, T. W. (October, 1909), "The Bacteriological Laboratories and Antitoxin Stables of the Metropolitan Asylums Board." *Journal Royal Institute Public Health.*

[5] Coles, A. C. (April 1, 1911), "The Fading of Aniline Stained Microscopical Preparations." *Lancet.*

[6] Keith, R. D. (April, 1911), "Note on a Method of Testing Hæmolytic Properties of Micro-organisms." *Malay Medical Journal.*

Tetanus. Tetanus is generally considered one of the best examples of a pure toxæmia, in which the infective agent is localised in the wound.

Porter and Richardson,[1] however, have reported two cases where the bacilli were found in the inguinal lymphatic glands, after injuries to the foot. This discovery has an important bearing on treatment, for if the lymphatic glands near a wound which causes tetanus prove to be frequently infected they, as well as the primary focus, should be eradicated.

Nicolle and Truche [2] recommend the following method of keeping tetanus toxin :—

The dry toxin is added in excess to equal parts of glycerine and water, in a large tube, and stored in a cold place; the mixture is shaken up at intervals for several days and then allowed to stand.

When required for use the clear liquid is first taken off with a 50 c.c. pipette which has been previously sterilised by boiling and well dried. The excess of toxin not used is replaced in the tube. Owing to the preservation of the toxic solution in glycerine, this process can be repeated very often, and the toxin keeps for several years.

Chattot

discusses the value of anti-tetanus serum—first, when used as a preventive, and, second, as a curative measure. Fifty-one cases are on record in which the preventive use of the serum appeared to fail. From these have to be subtracted fourteen cases in which an error of diagnosis was made, and a pseudo-tetanus may be very deceptive, because in it temporo-maxillary arthritis may cause trismus, vertebral arthritis may cause rigidity of the neck and vertebral column, and arthralgia may cause muscular phenomena mistaken for tetanic contractures. In another set of observations the data supplied were so inadequate as to deprive the cases of value as evidence. In other cases the dry serum was incorporated with the dressing applied to the wounds—a method which is ineffectual. Finally, passive immunity cannot be counted for longer than eight days after injection, and therefore cases which have arisen after a longer interval cannot be considered as failures. This leaves unaccounted for twelve cases in all, and it has, therefore, to be admitted that the serum given as a preventive may sometimes fail. Some of the unsuccessful cases may depend upon the variable length of the incubation period, the serum having been given too late in those in which the incubation period happened to be short. Or again, it may be that a second injection, as in suppuration at the seat of a fracture, in phlegmon or gangrene, etc., may induce a condition which is unfavourable to the preventive action of the serum. Some of the most striking figures in favour of the preventive use of the serum come from America, where, in connection with the festivities of July 4, a certain number of accidents invariably occur, with, formerly, a considerable mortality due almost altogether to tetanus. Wells reports that in 1903, before the introduction of preventive serum treatment, there were 406 such cases of death from tetanus, but that in the succeeding four years tetanus did not develop in any cases in which the serum was used. Scherk, of St. Louis, gives figures from his own practice, which are equally conclusive. Other cases which show the value of the serum are laboratory cases of accidental infection which have been successfully treated with antitoxin. The practical conclusion is that in all cases in which there is reason to fear the onset of tetanus the preventive treatment should be begun as soon as possible, large doses of the serum being given at first, and the treatment being continued until the wound has completely healed. Vallas recommends three injections of 10 c.c. to be made respectively on the first, third, and tenth day, and subsequently an injection every eighth day. The injection should be made either subcutaneously or, better, should be made directly into a vein, a method which, according to the author, avoids the danger of accidents due to the serum. As is well known, the serum treatment, begun when the disease has well developed, does not give nearly such good results; but taking all the different methods of administration together, with the exception of the intracranial method, in which the mortality is very high, the mean mortality is less when serum is used than otherwise. Only three methods of introduction are to be recommended—namely, the subcutaneous, the intravenous, and the method by lumbar puncture. The author, in conjunction with Cl. Gautier, has injected the serum into the carotid arteries of rabbits, and has had promising results.

In the treatment of tetanus, the employment of anti-tetanic serum has been largely reinforced by other methods of treatment, and in some cases these methods have been used alone.

Two cases [4 & 5] of tetanus treated by carbolic acid injection are of interest.

The solution used in the first case was a 4 per cent. solution of carbolic acid, 1 to 2 c.c. of which were injected twice daily, and in a later stage of this case a 5 per cent. solution was given in doses of 1 c.c., 5 and 4 times daily.

In the second case a 3 per cent. solution was employed, 210 minims of which were injected in doses of 20 minims at intervals of $1\frac{1}{2}$ to $2\frac{1}{2}$ hours in the acute stage of the disease.

The injections were made into the subclavian or intra-scapular regions, which did not cause so much pain as when given in the arm. No toxic symptoms resulted.

A case treated by chloretone is reported,[6] but anti-tetanic serum was also used. The

[1] Porter, C. A., and Richardson, O. (December 23, 1909), "Tetanus Bacilli in Lymphatic Glands." *Boston Medical and Surgical Journal*, quoted in *Lancet*, January 29, 1910.

[2] Nicolle, M., and Truche, Ch. (January 15, 1910), "Notes sur la conservation des 'toxines solubles.'" *Annales de l'Inst. Past.*

[3] Chattot, J. (February 19, 1910), "Tétanos et sérum anti-tétanique." *Prov. Méd.* Quoted in Epitome, *British Medical Journal*, August 6, 1910.

[4] Phillips, M. E. (December 11, 1909), "Case of Tetanus treated with Carbolic Injections: Recovery." *British Medical Journal.*

[5] Boyd, C. J. (April, 1911), "A Case of Tetanus—Treated by Bacelli's method in conjunction with Anti-tetanic serum." *Indian Medical Gazette.*

[6] Hobbs, A. R., and Sheaf, W. E. (November 5, 1910), "A case of Tetanus treated by Chloretone." *British Medical Journal.*

Tetanus—*continued*

chloretone was administered per rectum with olive oil. The author states that the indication for its use is increased rigidity.

It brings about a marked decrease in the trismus, the effect at first appearing as early as an hour after administration, but this takes longer to be produced after repeated dosage. As much as 120 grains were given in one day.

The injection of magnesium sulphate intraspinally has been recommended by many. Johnson [1] in a case reported by him used a 25 per cent. solution of the salt, and from 45 to 60 minims were injected. He states :—

> Of course one cannot say whether the ultimate cause was due to magnesium sulphate, to anti serum or to nature, but I have no doubt that the distressing spasms were at least temporarily relieved by the lumbar injections.

Magnesium sulphate has also been given subcutaneously; it acts by controlling the spasms, and it has been suggested that, by conserving the patient's strength it gives him time to form his own antitoxin.

Paterson [2] employed a 10 per cent. solution. As much as 20 c.c. were administered, 10 c.c. being injected into different parts of the body at the same time. In the case reported an erythematous rash resulted, probably from the employment of the magnesium sulphate, but it faded rapidly.

Precipitated sulphur and treacle have been employed in a case reported by Barnes.[3] He mentions that sulphur has been used in Chili, locally and internally, in tetanus, with good results.

Additional Notes

The relation of tetanus to the hypodermic or intramuscular injection of quinine is a subject that has received the attention it deserves in a monograph by Semple.[4] He states :—

> Quinine when given hypodermically to a spore-infected person would produce favouring conditions for the production of tetanus in two ways.
>
> (1) By a paralysing effect on the phagocytes when given in large doses and for some time.
>
> (2) By destroying tissues at the seat of injection, and by this means producing a suitable local anærobic focus where a stray phagocyte carrying tetanus spores might get stranded.

He deals fully with the nature of tetanus infection, and gives animal experiments showing the action of quinine on them and the result of such injection in producing favourable conditions for infection with tetanus spores. The matter is dealt with in detail and is full of interest, but as limited space forbids our consideration of them we can only quote the two last chapters of his work.

> (1) Rabbits and guinea-pigs are susceptible to the action of quinine when given hypodermically, or by the stomach. When a large dose is given to these animals it produces muscular spasms, convulsions, and death by asphyxia. When given hypodermically a certain lethal dose for a guinea-pig is 1 grain per 150 grammes of body-weight, and for a rabbit 6 grains per kilogramme of body-weight; but in some cases less would suffice. When given by the stomach a certain lethal dose for a guinea-pig is $1\frac{1}{4}$ grains per 150 grammes of body weight, and for a rabbit 15 grains per kilogramme; but in some cases less would prove fatal. Rabbits are very susceptible to small doses of quinine given intravenously. In these animals $\frac{3}{4}$ grain per kilogramme of rabbit is a certain lethal dose, and kills in most cases within one minute, asphyxia being the immediate cause of death. The fatal results of intravenous injections of quinine are not due to the acidity of the solutions, as evidenced by the fact that rabbits can withstand the intravenous injection of dilution of sulphuric or hydrochloric acid of much greater acidity than the solutions of quinine which rapidly prove fatal. $\frac{1}{4}$ grain per kilogramme of body-weight is a non-lethal dose of quinine for a rabbit when given intravenously.
>
> (2) When quinine is injected hypodermically or into muscles, it has a well-marked destructive action on the tissues at the site of injection; and in addition to producing these foci of dead tissue which would serve as suitable anærobic media for growth of tetanus spores should they by any chance become lodged there, it also gives rise to conditions favourable for infection with " washed tetanus spores " injected into other sites.
>
> (3) When quinine is given hypodermically to tetanus infected animals, tetanus germs are transferred from the original site of the tetanus infection to the site where the quinine has been injected. The experiments on this point confirm those carried out by Vincent in 1904.
>
> (4) Pure " washed tetanus spores " given hypodermically to guinea-pigs and monkeys do not produce tetanus;

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[1] Johnson, E. (August 20, 1910), " Treatment of Tetanus by Intraspinal Injections of Magnesium Sulphate." *British Medical Journal.*

[2] Paterson, P. (April 2, 1910), " A case of Tetanus treated with Subcutaneous Injection of Magnesium Sulphate : Recovery." *Lancet.*

[3] Barnes, E. (August 13, 1910), " Tetanus in a Septuagenarian : Recovery." *British Medical Journal.*

[4] Semple, D. (1911), " The Relation of Tetanus to the Hypodermic or Intramuscular Injection of Quinine." *Scientific Memoirs of the Government of India,* No. 43.

Tetanus—*continued*

but when quinine is injected hypodermically into a different part of the body, either the day before, the same day, or the day after spores are given, a large percentage of these animals contract tetanus.

(5) Pure "washed tetanus spores" when mixed with quinine, or weak lactic acid, and injected hypodermically into guinea-pigs invariably produce tetanus, but when given mixed with morphia the animals remain well. Quinine and lactic acid when injected hypodermically produce sites favourable for the development of tetanus spores; but morphia, and normal saline solution do not produce this effect.

(6) Pure "washed tetanus spores" when injected hypodermically into guinea-pigs remain latent at the site of injection for months, as evidenced by the fact that virulent tetanus bacilli may be recovered from these sites after a period of seven months, and possibly after a much longer period. The importance of this fact in its relation to the hypodermic injection of quinine is evident.

(7) Tetanus bacilli or tetanus spores are not found in the blood and internal organs in cases of acute tetanus, although they are invariably found at the original site of injection, and at the site of quinine injections given during the disease; they are also found at the site of quinine injections, when quinine has been the means of bringing about an infection with "washed tetanus spores" injected into a different part of the body.

(8) Tetanus infection was present in the intestinal tract of healthy human subjects in four cases out of ten examined. In three of these cases the tetanus bacilli isolated were virulent for guinea-pigs.

(9) Cold has an influence in producing tetanus in guinea-pigs when "washed tetanus spores" are given hypodermically; and this influence is increased by the hypodermic injection of quinine.

(10) No evidence has been obtained of the presence of tetanus infection in any of the solutions of quinine used in the experiments recorded in this paper.

(11) Some strains of tetanus spores are extremely resistant, and may remain alive and retain their virulence on a rusty nib for as long as eighteen years, when the nib is placed in a test tube capped with rubber, and kept in a cupboard at room temperature.

(12) Tetanus antitoxin is an efficient prophylactic against tetanus when it is necessary to give quinine hypodermically.

Anti-tetanic serum as a prophylactic in cases of malaria in which it is necessary to give quinine hypodermically.—Although cases of tetanus are, comparatively speaking, of rare occurrence after hypodermic injections of quinine, it is a terrible calamity when they do occur.

To avoid with certainty what the late Professor Maclean described as "something revolting in a death brought about directly or indirectly by a remedy intended to cure," the only reliable safeguard against tetanus when quinine must be injected hypodermically is a dose of tetanus antitoxin. In countries where severe forms of malaria occur, and in those cases where quinine cannot be tolerated by the stomach, or for other reasons, it may be sometimes necessary to give it hypodermically. When such a necessity arises, and especially in those localities of tropical countries where tetanus frequently occurs, it would be advisable to give a dose of anti-tetanic serum immediately before or immediately after giving quinine hypodermically. A dose of from 10 to 15 c.c. given hypodermically confers a passive immunity to tetanus for two or three weeks, and by that time the patient would probably not require any further injection of quinine.

It is well known that the principal use of anti-tetanic serum is not so much curative as preventive in its action; as a prophylactic it is most reliable. An injection of serum into the loose subcutaneous tissues of the side of the abdomen would not cause any pain or inconvenience to the patient, and this amount, for the time being, would render several daily injections of quinine safe as far as tetanus is concerned. Those who have an extensive experience in treating malaria in tropical climates assert that there are cases in which it is possible to save the patient by hypodermic injections when it would be impossible to do so by the ordinary administration of quinine. It is in such cases, and not as a routine measure in those who can tolerate quinine by the stomach, that hypodermic injections are justifiable. Given with the precautions which a dose of anti-tetanic serum would ensure, there would be no risk of tetanus ensuing and the patient would only have to contend with the local reaction caused by the quinine. The passive immunity to tetanus which is so quickly conferred by anti-tetanic serum would prevent the local effects of quinine from acting as a focus for the growth of tetanus spores, and it would also prevent any latent spore injection from giving rise to tetanus under the combined favouring influences of quinine and an attack of malaria.

An interesting case of tetanus is recorded by Fink.[1] Two relapses occurred, the first four months and the second six months after the original attack. The author considers the condition to be due to "Latent or Dormant" spores. Two other interesting features are—(1) that though the original wound was on the foot before the relapses, pain was complained of in the knee, which rather bears out Porter and Richardson's discovery (*loc. cit.*), that the bacilli may be present in the adjoining lymphatic glands down the course of the lymph circulation. (2) That the case was complicated by malaria, and a hypodermic injection of quinine was given soon after the original infection, but apparently had no ill effect. No conclusion can, however, be drawn from this, as the incubation period may be prolonged in man.

Camus,[2] in a paper on the treatment of tetanus in animals, finds that advanced tetanus in dogs can be more easily cured by anti-tetanic serum than tetanus in smaller animals. He finds, moreover, that intravenous injections do not in his experiments supersede in value subcutaneous injections of anti-tetanic serum.

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[1] Fink, L. G. (June 1, 1911), "A Case of Tetanus: Two severe Relapses, due to Development of 'Latent or Dormant' Spores." *Journal Tropical Medicine and Hygiene.*

[2] Camus, J. (May 5, 1911), "Contribution à l'étude de Traitment du Tétanos Expérimental." *C. R. Soc. Biol.*, Vol. LXX., No. 15.

Ticks. A useful illustrated work on South African ticks is that by Howard,[1] and it is of special interest to practical South African workers, especially as regards the differentiation of species and of the various forms of the same species. It contains a good table of "Animals which act as hosts for South African ticks," and the following table showing the relation of South African ticks to disease:—

RELATION OF SOUTH AFRICAN TICKS TO DISEASE

Disease	Host	Organism causing Disease	Transmitted by
Redwater ... ... Texas Fever ... ... Bovine Piroplasmosis ...	Cattle	*Piroplasma bigeminum*	*Margaropus annulatus* *decoloratus* *M. annulatus australis*
East Coast Fever ... ... Rhodesian Redwater ...	Cattle	*Piroplasma parvum*	*Rhipicephalus appendiculatus* ,, *capensis* ,, *evertsi* ,, *simus* ,, *nitens*
Distemper ... ... Malignant Jaundice ... ... Biliary Fever of Dog ... Canine Piroplasmosis ...	Dog	*Piroplasma canis*	*Hæmaphysalis leachi*
Biliary Fever	Horse	*Piroplasma equi*	*Rhipicephalus evertsi*
Equine Piroplasmosis	Mule Donkey		
Heartwater	Sheep Goats Cattle	Unknown	*Amblyomma hebræum*
Spirillosis	Cattle	*Spirochæta theileri*	*M. annulatus decoloratus*
Human Tick Fever	Man	*Spirochæta duttoni*	*Ornithodoros savignyi caecus*

To these may be added spirochætosis of fowls transmitted by *Argas persicus*, the tampan tick.

Those interested in the anatomy of ticks will find that the first fasciculus of Professor Blanchard's[2] work deals with the subject thoroughly, and when it is remembered that the glandular apparatus, consisting of salivary glands proper and the poison gland, play such a large part in the transmission of both piroplasmata and spirochætæ, it is evident that the subject is well worth close study. Amongst an extensive collection of Indian ticks infecting domesticated animals in India, six common species have been found. The occurrence of other types is so rare as to be economically unimportant, and only three of the six have any interest as disease carriers; they are:—

(1) *Argas persicus*, transmitting fowl spirochætosis.

(2) *Boophilus australis*, transmitting bovine piroplasmosis or Redwater fever.

(3) *Rhipicephalus sanguineus*, transmitting canine piroplasmosis or malignant biliary fever.

A new Indian tick has been found in the Punjab which has been described by Newman,[3] and has been called by him *Ornithodoros lahoriensis*. It gives rise to a more or less acute disease of sheep characterised by rapid pernicious anæmia and death.

An excellent publication on the nine species of ticks found in Jamaica, together with much interesting matter concerning them, is to be found in the *Reports of the 21st Expedition of the Liverpool School of Tropical Medicine*. The observations are of interest, and will be referred to again. Under the heading of enemies of ticks it is found that the two species

[1] Howard, C. W. (1908), "A List of the Ticks of South Africa, with Descriptions and Keys." *Transvaal Department of Agriculture, Farmers' Bulletin*, No. 30.

[2] Blanchard, R. (September, 1909), "L'Insecte et l'Infection." *Hist. Nat. et Méd. des Arth. Path.* Quoted in *British Medical Journal*, September 25, 1909.

[3] Newman, L. G. (1908), "A New Indian Tick, *Ornithodoros lahoriensis*." *Journ. Trop. Vet. Sc.*, Vol. III.

of local blackbirds, besides ordinary fowls, are the friends of the farmers in the work of tick destruction. Just as small fry have been used to destroy mosquito larvæ, these birds may be employed in tick destruction. Ticks—*continued*

Theiler [1] has shown that spirochætes and piroplasms can be carried by different species of ticks; the following is a quotation from his work:—

By experiments at Pretoria and Alfort it was demonstrated that *Sp. theileri* (Laveran) was carried by the *Boophilus decoloratus*, and it was proved that the infection passed through the eggs and was transmitted by the larvæ.

He found that the larvæ of *Rhipicephalus evertsi* and the adult tick itself acted in the same way.

Further, it was proved that *Piroplasma bigeminum* was transmitted by *Boophilus decoloratus*, and that the adult and larvæ of *Rhipicephalus appendiculatus* were also vectors.

Theiler also showed that the adult *Rhipicephalus appendiculatus* and *Rhipicephalus evertsi* transmitted the *Piroplasma mutans*.

Tick Prevention, and tick disease prevention.

Tick prevention has of recent years been the subject of many articles and experiments, and much good work has been done. It deserves our attention, and is of interest, not alone from a scientific point of view with regard to human disease prevention, but as it is of great financial importance in stock-rearing countries.

The question may be usefully considered under the following headings:—

I. Cattle Washes and Dips.
II. Rotation of Crops.
III. Burning of Pastures.
IV. Immunisation, or the use of Salted Herds.
V. Quarantine and control of the movements of stock.

These will be considered here shortly, more attention being paid to the most successful methods.

I. *Cattle Washes and Dips.*

Until recently the active agent in these methods has been arsenic in different forms, usually arsenious oxide or arsenite of soda, and the difficulties met with in the use of this drug have been the toxic effect it is liable to produce on the animals and workers, and its irritant action on the skin. Many preparations, proprietary and otherwise, have been put on the market, and amongst all these Cooper's Dip Powder is probably one of the best.

Among other agents which have been advocated as being useful for tick prevention is Beaumont oil. Its disadvantages are its high price and the difficulty of obtaining it. However, it is said that any crude petroleum will answer as well, the only difficulty being the emulsification. A satisfactory emulsification of Beaumont oil is—

Crude Petroleum	2 gallons
Water	½ gallon
Hard Soap	½ pound

Other crude petroleums may be emulsified as follows: Dissolve one half-pound of soap in one half-gallon of hot water. To one measure of this soap solution add four measures of the crude petroleum which is to be tested, and shake well in a stoppered bottle or flask for several minutes. If the proper proportions of oil, soap and water have been used, a perfectly uniform mixture should result when one part of this emulsion is shaken with seven parts of water. If, however, after this dilution there is a separation of a layer of pure oil within half-an-hour, the emulsion is imperfect, and a modification of this formula will be required. To accomplish this the proportion of oil should be varied till a good result is obtained.

Among other agents picric acid, pyridine, commercial methylene blue, mercury and lead salts have been put forward, but none of these have been experimented with sufficiently for any opinion on their value to be given.

The question has also been much debated of how often to dip. Fortnightly dipping was the usual procedure, but recently Watkins Pitchford advocated "Five-day spraying"; the following is the gist of Cooper's [2] paper on the subject.

[1] Theiler, A. (June 6, 1909), "Transmission des Spirilles et des Piroplasmes par différentes espèces de tiques." *Bull. Soc. Path. Exot.*

[2] Cooper, W. F. (September, 1910), "Five-Day Spraying; The Brown Tick and the East Coast Fever." *Journal of Agricultural Science*, Vol. III.

Ticks— *continued*

He is dissatisfied with regard to "Five-day spraying," as advocated by Watkins Pitchford, for though he found it had no injurious effect on beasts so treated and kept them tick-free, he states that the experiments were not conducted under natural conditions, and gives experiments under natural conditions where it did not prevent animals from contracting East Coast fever.

He further states that fortnightly dipping, as advocated by the Cape Government, though of use in the case of the Blue tick, or *Margaropus annulatus*, which remains attached to its host for three weeks, is of little use against the Bont tick, *Amblyomma hebræum* (Koch), or the Brown tick, *Rhipicephalus appendiculatus* (Newman), as these last two only remain attached for 7 and 4 days respectively.

II. *Rotation of Crops.*

This has been found useful in certain parts of the United States, but is a system which cannot be practised in many countries.

III. *Burning of Pastures.*

Rather a drastic measure, while, after burning, the ticks return immediately. Moreover, some may lie hidden where the fire cannot reach them, and this plan is inapplicable in many places.

IV. *Immunisation, and the use of Salted Herds.*

Something is to be said for immunisation. It has been employed against Texas fever by inoculation, but commonly has failed against East Coast fever.

The employment of salted herds is certainly of some use, but it is the case that the salted cattle are from the native herds and are not of such monetary value as imported cattle. Progress may possibly be effected on these lines by cross breeding.

V. *Quarantine* and the control of movements of stock have been used for some time with good results.

Newstead's[1] article contains many important practical hints with regard to appliances for washing and spraying, and the following points as regards the use of Cooper's Dip and Paranaphtha * are well worth mentioning. They are :—

(1) The application of this mixture, which contains poison, must not under any condition be repeated at a less interval than fourteen days, and in our experience every five to eight weeks during the winter months is sufficient to keep cattle practically free of ticks.

(2) All spraying or washing should take place in the early morning, and the cattle should be allowed to dry in the shade before turning out to graze.

(3) If cattle have to be driven for any distance they should be allowed to cool before spraying. Driving both before and after should be quiet.

(4) Cattle of all ages, also cows in calf, may be sprayed. Cows in milk should have the lower portions of their udders sponged before milking on the first day of spraying.

(5) The spray should be so finely distributed that practically none of the liquid drips off the animals treated. To avoid danger the operation should be conducted on a site devoid of grass.

(6) All waste products and washings from the apparatus used should be thrown into the drains, or, safer still, into a hole in the ground and covered with a layer of soil.

(7) All these instructions are applicable both for dipping as well as for spraying. But in-calf animals should not be dipped a month or so before calving.

A few works for special reference may here be mentioned.

(*a*) A good illustrated paper on ticks, dealing with anatomy and classification, is one by Bonnet.

(*b*) *Über das Zecken, genus Amblyomma*, by W. Donitz, illustrated.

(*c*) "The Structure and Biology of *Hæmaphysalis punctata*," by Nuttall, Cooper and Robinson. *Parasitology*, Vol. I., No. 2, June, 1908.

(*d*) "On the presence of an anticoagulin in the salivary glands and intestines of *Argas persicus*," Nuttall and Strickland. *Parasitology*, Vol. I., No. 4, December, 1908.

(*e*) *Ticks, a monograph of the Ixodidæ*, by Nuttall, Warburton, Cooper and Robinson. So far only Part I. on the *Argasidæ*, has been issued.

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[1] Newstead, R. (November 17, 1909), *Reports of the Twenty-First Expedition of the Liverpool School of Tropical Medicine.*

* The formula for this preparation is :—

1.	Soft Soap (Chiswick Imperial)	55·6 per cent.
2.	Water	21·7 ,,
3.	Naphthaline	5·2 ,,
4.	Paraffin	17·5 ,,

Formula of Wash—

Paranaphtha, 1 part—water 6 parts.
Cooper's Dip, 1 pkt.—20 gallons of water.

Ticks—*continued*

Additional Notes

Maver [1] has proved by experiment that different species of ticks collected from various regions are able to transmit the virus of spotted fever, and thereby has shown that the disease may find favourable conditions for its existence in localities other than those to which it is now limited.

With *Dermacentor marginatus* (Utah), and *Amblyomma americanus linnæus* (Missouri), transfer was made with nymphs. In the case of *Dermacentor variabilis* (Mass.) transmission was effected by nymphs and adult ticks.

Interesting experiments by Moore [2] tend to show (1) the minimum duration of feeding by infected ticks necessary to infect the guinea-pig; (2) the minimum duration required for the infection of the tick from the infected guinea-pig; and (3) the length of the incubation period in the tick—that is, the period of time required for the etiological factor to establish itself in the tick and render it infective. His summary is interesting. The minimum duration of feeding necessary to infect a guinea-pig was found to be one hour and forty-five minutes. The average time necessary seems to be about ten hours, while twenty hours were almost constantly infective. The duration of feeding necessary to infect a tick is approximately twenty-five hours, while the minimum incubation period in the tick was not definitely determined.

In the case of ticks under natural conditions it is possible that the duration of feeding necessary to infect the tick and the incubation period in the tick will be found to be much less than is here indicated.

An excellent paper by Nuttall [3] is well worthy of study by those interested in ticks, and especially by those who require a general knowledge of the life of ticks; their methods of feeding; their relations to their hosts and their geographical distribution, without dipping too deeply into subjects which are generally only interesting to special workers.

An article by Nuttall and Merriman [4] is a welcome addition to a subject which has up to the present been neglected by other writers. It deals with the process of copulation in *Ornithodoros moubata.*

Sant Anna [5] and Nuttall [6] in two separate papers discuss a disease quite distinct from spirochætosis but due to tick-bite. It would seem that the bites of *Amblyomma hebræum* and of *Boophilus annulatus decoloratus* may, under certain conditions, induce a febrile illness with glandular enlargement, severe headache and other symptoms. Sant Anna mentions the occurrence of a slight papular eruption. This is a matter which requires further investigation. Nothing of the kind has hitherto been reported from the Sudan. The fever, which has a cyclical character, is apt to be confused with so-called Tick Fever, a term which Nuttall thinks should be abolished.

Tropical Medicine. Under this heading it is not of course intended to consider the subject as a whole, but to treat of certain subjects of tropical interest which cannot be dealt with under any of the separate sections, and yet are of sufficient importance to merit attention in a review of this kind.

Following on Castellani's [7] description of an *endemic funiculitis* occurring in Ceylon, mentioned in our first Review, a good deal of attention has been paid to this condition.

Coutts [8] describes acute and chronic cases of the same affection from Egypt. He has been able to isolate a diplococcus as Castellani did, but he thinks that the suppurative condition of the spermatic cord is due to the extension of an infective process from the urethra by way

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[1] Maver, M. B. (April 12, 1911), "Transmission of Spotted Fever by the Tick in Nature." *Journal Infectious Diseases.*

[2] Moore, T. T. (April 12, 1911), "Time Relationship of the Wood-Tick in the Transmission of Rocky Mountain Spotted Fever." *Ibid.*

[3] Nuttall, G. H. F. (March, 1911), "On the Adaptation of Ticks to the Habits of their Hosts." *Parasitology.*

[4] Nuttall, G. H. F., and Merriman, G. (March, 1911), "The Process of Copulation in *Ornithodoros moubata.*" *Ibid.*

[5] Sant Anna, J. F. (June, 1911), "On a Disease in Man following Tick-Bites, and occurring in Lourenço Marques." *Ibid.*

[6] Nuttall, G. H. F. (June, 1911), "On Symptoms following Tick-Bites in Man." *Ibid.*

[7] Castellani, A. (July 4, 1908), "Endemic Funiculitis." *Lancet.*

[8] Coutts, D. K. (January 23, 1909), "Endemic Funiculitis." *Ibid.*

Tropical Medicine —*continued*

of the *vas deferens*. He finds this diplococcus to be one of the common flora of the urethra in chronic gleet, and he further considers that chronic gleet has some bearing on the disease.

Castellani [1] found the organism present in the urethra of two cases of chronic gleet, but failed to do so in six others. He has, however, isolated a diplococcus from the heart's blood in two cases post-mortem, and from the general circulation during life in septicæmic cases.

A peculiarity of the germ is, that it decolorises by Gram's method in sections of tissues and in smears from the pus, while preparations made from cultures decolorise incompletely, and some cultures may even be Gram positive. This peculiarity is, however, shared by other diplococci.

With regard to treatment Coutts recommends free incision and drainage preferably to orchidectomy.

Jones,[2] however, is in favour of orchidectomy, and does not consider the disease to be limited to young adults.

An interesting verrucotic condition affecting the skin of the upper and lower limbs, which has been named "Mossy Foot," has been described as occurring among the natives of the Amazon region.

The condition is of slow growth, and the primary lesion seems to be a moist vesicular eruption. This gives place to a dry warty growth which spreads slowly, the disease appearing to be auto-infective.

The appearance resulting is as if the part affected (usually the foot) was covered with old dried moss. The slightest injury causes pain and bleeding. Portions of the diseased limb may be swollen and pit on pressure. In places the hypertrophied patches of papillæ may form elevated plaques with a thick and horny or swollen epidermis. Ulceration may occur. The disease has been reproduced by Thomas and Stephens [3] in a rabbit by subcutaneous inclusion of a portion of the growth.

The prevalent opinion is that the causal organism is a staphylococcus. The disease is not the same as the warty conditions that are found associated with elephantiasis. It is best treated by the actual cautery and the knife, but cure is rare.

O'Zoux [4] has described a tropical dyspnœa occurring at Réunion Island. The condition is one of interest and of importance, as it is a distressing malady, and even causes death. All races, sexes and ages may be attacked; the half-breed is, however, more likely to be so than the pure white or black; the disease is also more frequently seen in adult life, and it is common in the female. It occurs during both seasons, but with recurrences during the hot season. The greatest case incidence is during the months of December, January, and February; the disease has been seen chiefly along the coast-line, but cases sent to the hills do not become free.

The dyspnœa may come on rapidly or insidiously, and the advent may be heralded by fever. Once it has occurred it may disappear never to recur, or it may reappear after some days. The termination of the attack like the onset may be rapid or slow. The liver is enlarged in about 25 per cent. of cases, and renal congestion is seen in about 10 per cent. of cases. About 13 per cent. of cases terminate fatally.

The condition is not asthma, which is an expiratory trouble; tropical dyspnœa being an inspiratory one; the sputum is in nummular masses, not in threads. Charcot-Leyden crystals and Curschmann's spirals are never found. An eosinophilia is, however, present.

No cause has as yet been found for the condition, and the question of its being a definite entity is still *sub judice*. Castellani [5] in a paper on tropical bronchomycosis in Ceylon describes the condition discovered by him, and quotes cases of bronchitis, both mild and severe, due to a special fungus. The paper is well illustrated, and his conclusions, which we give here, are of great interest:—

(1) A type of bronchomycosis in which oïdium-like and saccharomyces-like fungi are found is not rare in Ceylon. The condition might be called bronchooïdiomycosis. or more briefly bronchooïdiosis.

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[1] Castellani, A. (September 18, 1909), "Etiology and Pathology of 'Endemic Funiculitis.'" *British Medical Journal.*

[2] Jones, A. W. (February 20, 1908), "Endemic Funiculitis." *Lancet.*

[3] Thomas, H. W. (June 1, 1910), "'Mossy Foot' of the Amazon Region, an Infective Verrucotic Condition affecting the Skin of the Upper and Lower Limbs." *Annals Tropical Medicine and Parasitology*, Vol. IV., No. 1. *Vide* also Thomas, H. W. (December, 1909), *Transactions Society of Tropical Medicine and Hygiene.*

[4] O'Zoux, L. L. (July 21, 1909), "La Dyspnée tropicale." *Bull. Soc. Path. Exot.*

[5] Castellani, A. (July, 1910), "Tropical Bronchomycosis: Observations on a New Species of Epidermophyton found in *Tinea cruris*, also a new Intestinal Spirillum." *Philippine Journal of Science*, B.

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(2) Two types of the condition may be clinically distinguished, a mild and a severe one; the latter closely resembles phthisis. The mild type is apparently amenable to treatment with potassium iodide.

(3) The strains of oïdia found in my cases are different from the ordinary *Oïdium albicans* and *Oïdium lactis*, as they do not affect milk.

(4) All the strains found by me are identical in all respects, except that some produce gas in galactose and others do not. For the oïdium which produces gas in galactose I propose the name *Oïdium tropicale;* for the saccharomyces I suggest the name *Saccharomyces krusei.*

(5) The diagnosis of bronchooïdiosis can be made only by bacteriological methods. It is differentiated from phthisis by the absence of tubercle bacilli and the negative animal inoculations; from bronchial spirochætosis by the absence of spirochætæ; and from endemic hæmoptysis by the absence of the ova of the trematode.

(6) Care should be taken before making the diagnosis of bronchomycosis that the sputum is collected in sterile vessels and examined as soon as possible, because sputa left exposed to the air frequently become contaminated in the Tropics with various species of non-pathogenic saccharomyces and oïdia. Primary bronchomycosis should be also differentiated from those cases of chronic debilitating disease in which *Oïdium albicans* spreads from the mouth to the bronchi.

A paper by Osler [1] on splenic enlargements other than leukæmic will be of interest to those in the Tropics. Although the tropical enlargements of the liver are not specially dealt with, much information may be gleaned which is not to be found in the text-books, and a perusal of the paper may check the tendency to overlook in tropical practice some of the enlargements of the liver which occur in temperate climates.

A form of splenomegaly with hepatic cirrhosis, endemic in Egypt, has been described by Day and Ferguson.[2] The condition is extremely like Banti's disease. The chief characteristics of both being (*a*) an extraordinary chronicity, (*b*) the large size of the liver, (*c*) the blood changes, (*d*) involvement of the liver, (*e*) jaundice and ascites, and (*f*) the tendency to hæmorrhages, especially hæmatemesis. No cause for the condition has as yet been discovered.

Faichnie and Bond [3] have described a case of enlargement of the spleen cured by the use of senega. The tincture of senega was given in half-drachm doses three times a day. They are inclined to regard the case as one of kala-azar. Owing to want of more extended trial nothing definite can be stated as to the usefulness of the drug in splenomegaly, but it is worth bearing in mind, for Ensor, who introduced it, has recorded a similar result.

For those interested in the different forms of splenomegaly some very useful reviews of papers are to be found in the *Folia Hœmatologica.*[4] A paper on cirrhosis of the liver in India by Rogers [5] is well worthy of study. Unfortunately it is too lengthy to be dealt with fully here. The conclusions, however, embody most of the important points, and are as follows :—

(1) Cirrhosis of the liver is several times as frequent in Calcutta among natives of India as it is in a temperate climate, but is not especially common among European residents there.

(2) Although Mahommedans are forbidden the use of alcohol by their religion, the cirrhosis is only slightly less frequent among them than in Hindus in proportion to their relative numbers; not more so in fact than in the case of abscess of the liver, in which alcohol is only a predisposing and not an exciting cause. For this and other reasons the increased frequency of cirrhosis in India cannot be explained on any theory which makes alcohol the most important exciting cause of cirrhosis.

(3) One-fifth of the cases in Calcutta are secondary to kala-azar, being partly of the typical intralobular form described by me, but also commonly of the ordinary portal or multilobular type, or both combined.

(4) There is no evidence that malaria ever produces a clinically evident cirrhosis of the liver in Calcutta.

(5) Hanot's hypertrophic or biliary cirrhosis is rare in Calcutta, but a form of infantile biliary cirrhosis described by Gibbons of unknown origin is met with.

(6) In Calcutta, cirrhosis of the liver is so frequently associated with chronic dysentery, usually of the amœbic type, as to suggest that the fibrosis of the liver is secondary to the bowel ulceration.

(7) Chronic inflammatory changes due to bacterial infection or toxic absorption through ulcers of the gastro-intestinal tract is also a likely cause of cirrhosis of the liver.

(8) Leucocytosis is common in the ordinary type of cirrhosis of the liver, a high degree being of very bad prognostic significance. On the other hand a leucopenia points to a cirrhosis being secondary to kala-azar.

A good deal of attention has recently been paid to the biliary cirrhosis of children met with in Bengal. The disease is by no means new to science, and it appears to be of a parasitic nature, though whether of microbic origin or not it is hard to say. Absorption of toxic

[1] Osler, W. (October 17, 1908), "Discussion on Splenic Enlargements other than Leukæmic." *British Medical Journal.*

[2] Day, H. B., and Ferguson, A. R. (November 1, 1911), "An Account of a Form of Splenomegaly with Hepatic Cirrhosis, Endemic in Egypt." *Annals Tropical Medicine and Parasitology.*

[3] Faichnie, N., and Bond, J. H. R. (September, 1910), "Long-continued Fever with Marked Enlargement of the Spleen cured by the use of Senega." *Journal Royal Army Medical Corps.*

[4] *Folia Hœmatologica* (October, 1910), Bd. X., Heft 3.

[5] Rogers, L. (February, 1911), "Gleanings from the Calcutta Post-Mortem Records: IV. Cirrhosis of the Liver." *Indian Medical Gazette.*

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material from the intestinal tract does not seem to play any part in its occurrence. A paper by Pearce [1] will be found useful to those desirous of studying this condition.

An extremely interesting general paper on hospital work in Egypt is one by Day,[2] and though some of the points in it have been already dealt with, such as "Endemic Funiculitis," and "Splenomegaly" associated with hepatic cirrhosis, it contains much other useful matter.

Marchoux [3] has described a tropical condition which is characterised by digestive disturbances, known as Gubler's atonic dyspepsia or tropical *hypochlorhydria*. It is especially liable to occur in moist, hot climates, and arises owing to the lack of gastric acidity, which in turn is caused by the abstraction of large quantities of sodium chloride from the blood, the salt taken with the food not being able sufficiently to compensate for this leakage. The chief symptoms are briefly: acid regurgitation, somnolescence, diarrhœa or constipation, with rheumatic troubles, and neuralgia. The condition ultimately gives rise to varicose dilatation, varicocele and hæmorrhoids. Eczema or furunculosis are fairly common results. The subject is at the mercy of the slightest intestinal infection, and may run a continued fever resembling that caused by the paratyphoid group of organisms.

The lactic bacilli treatment has been strongly recommended.

Four cases of peripheral neuritis, which, though resembling beri-beri, were probably not that condition, have been reported by Nattan-Larrier [4] from the French Congo.

They differed from beri-beri in having disorders of sensation associated with the nerve roots and in presenting meningeal symptoms.

A condition which has been termed Buba is described by Teira in Brazil.[5] The disease resembles both yaws and syphilis, but is distinct from both. The etiology has not yet been determined.

Castellani, in a paper to the *Philippine Journal of Science* (*loc. cit.*), describes a new spirillum which he considers to be a new species, and names *Spirillum zeylanicum*. The spirillum was isolated from two cases of fatal entero-colitis showing symptoms intermediate between dysentery and cholera. Pinroy,[6] in a paper on methods of preserving and sending away moulds in tropical countries, recommends the following technique :—

For Aspergillus and Penicillium ; they ought to be collected and sent away in tubes stopped with cotton wool. The medium should be perfectly dry, desiccation being secured under a bell jar with a receptacle holding sulphuric acid. In this way these moulds keep well, and may be re-germinated at a later date.

The spores of the *mucorines* are, however, less resistant. The best method of keeping these is in a liquid medium (bouillon with 1 per cent. of sugar added), and under a layer of vaseline. For a tube containing 10 c.c. of bouillon, 3 c.c. of liquid vaseline is added. By this method, after two and a half years, a culture of *Rhizomucor parasiticus* or *Rhizomucor equinus* may be obtained in twenty-four hours. From *Phycomyces nitens* by this method after a year and a half, a culture may be obtained in less than three days at a temperature of 22°. He also gives methods of fixing cultures at different stages of development, and details of a mounting medium for microscopical specimens.

The effect of sunlight on the eyes is always of interest to the tropical practitioner. An extract from the conclusions of a paper by Sisson [7] on the effect of intense sunlight on the eyes will not be out of place here.

(1) There is ample proof that light does injure the eye, and it is possible that some of the eye diseases whose etiology is obscure may find their explanation in that way.

(2) That in view of the fact that glass stops the ultra-violet light, while quartz allows it to pass through, we have in the wearing of glasses a protection from the harmful rays.

An interesting discussion on the feeding and treatment of children in the Tropics is found

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[1] Pearce, F. T. (January 16, 1909), "The Biliary Cirrhosis of Children, otherwise known as 'Infantile Liver.'" *Lancet.*

[2] Day, H. B. (January 23, 1909), "Hospital Work in Egypt." *Ibid.*

[3] Marchoux, E. (December 16, 1908), "L'hypochlorhidrie tropicale." *Presse Médicale.*

[4] Nattan-Larrier, L. (April 13, 1910), "Sur quelques cas de néurite périphérique observés chez des sujets ayant résidé au Congo français." *Bull. Soc. Path. Exot.*

[5] Teira, F. (1909), "Über Buba." *Brazil, Medico*, 42, quoted in *Arch. für Schiffs-u. Tropen-Hyg.*, Vol. XIV., No. 8, 1910.

[6] Pinroy, E. (January 13, 1911), "Conservation et envoi des cultures de champignons inférieurs." *Bull. Soc. Path. Exot.*

[7] Sisson, E. O. (January, 1909), "The Effects of Intense Sunlight." *Ophthalmology*, quoted in *Indian Medical Gazette*, May, 1909.

Tropical Medicine—*continued*

following a paper by Carnegie Brown.[1] The subject is becoming of greater interest yearly, owing to the increasing tendency for families to settle down in tropical countries.

A paper [2] on the climatic treatment of tropical convalescents is a very welcome addition to our general information. The question is one often put to the tropical and the home physician by the tropical patient as to where he is to reside at home to gain the full benefit of the climate for his health's sake. A few extracts will be of interest :—

The patient generally arrives in England in spring, generally about the month of May. After a week or a fortnight's rest at his native place another resort has perhaps to be recommended. As a general rule the seaside should be avoided.

An altitude of 400 feet should be chosen; this may be obtained along the East coast or even in Surrey or Hertfordshire.

The Eastern Highlands of Scotland are also suitable. The object to be aimed at is an attempt to combine ocean and mountain air.

Ill-ventilated places such as theatres are to be avoided, and also exposure to the sun, which often causes a recurrence of fever in malarial cases.

In a paper by Cantlie [3] on tropical life as it affects assurance, several important points are brought out which are of interest to us as regards tropical medicine. Under the heading of "Effects of a Warm Climate upon British Born Folk" he mentions that the first effect of such a climate is stimulating, with the result that increased activity, appetite, digestion, work and recreation, throw a great strain on the system. This initial stimulus wanes after about two years' residence, and the critical period of the tropical resident's life begins. It now depends upon his soundness of mind and limb, and the strength of character of the individual as to what his future is to be.

Among the most deterrent influences to health he mentions want of sleep at night, and chills.

The old resident studies his condition, but this is not so with the young arrival, and the matter rests greatly with age and stability. The younger the age at which a man proceeds to the Tropics the greater the risk of his contracting disease.

The chances of a youth of eighteen to a man of twenty-five of contracting diseases are about two to one.

The chances of a young man of thirty to a man of forty of contracting diseases are about ten to one.

The second portion of an article on technique by Langeron [4] may be of interest; his earlier work was mentioned in the First Review.

For hints on the preservation of instruments and drugs in the Tropics the reader is referred to an article in the *Lancet*.[5]

The second edition of Harford's book,[6] named *Hints on Outfit*, will be found useful to all persons who intend to travel in tropical countries.

Additional Notes

An article by Wellman,[7] being an extract of lectures given by him on "Diseases in the Tropics," is of interest.

He deals with the subject under four headings :—

I. Insects and human disease in the Tropics.

II. The diseases of Portuguese West Africa.

III. Why the physician in temperate climates should study tropical diseases.

IV. The health problems for Caucasians in tropical colonisation.

The articles are important and form very interesting reading. The paper is too lengthy, however, to be further considered here.

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[1] Brown, W. C. (September 18, 1909), "Discussion on the Feeding and Treatment of Children in the Tropics." *British Medical Journal.*

[2] Cantlie, J. (July 15, 1910), "The Tropical Invalid in Britain." *Journal Tropical Medicine and Hygiene.*

[3] *Idem* (February 1, 1911), "Tropical Life as it Affects Life Assurance." *Ibid.*

[4] Langeron, M. (October 10, 1908), "Technique des manipulations complémentaires de Parasitologie." *Arch. de Paras.*

[5] *Lancet* (December 11, 1909), "The Preservation of Drugs and Instruments in the Tropics."

[6] Mentioned in *Lancet*, April 22, 1911.

[7] Wellman, C. (1910), "Diseases in the Tropics." *American Society of Tropical Medicine.* Collected Papers.

Tropical Medicine —*continued*

Another article by the same author,[1] entitled "A List of the Tropical Diseases observed in the Region of San Francisco Bay, California," which contains notes on some of these affections, may be of use to those who are interested in tropical medicine.

Two communications on arrows and arrow-wounds, dealing with the poisons generally used, and the treatment of cases, are of interest.

Parsons[2] considers the Nigerian varieties, and Anderson,[3] the Indian. The subject is too large to allow of its being dealt with here, but some points are worthy of notice. Anderson mentions a method of removing barbed arrows through the entrance wound by inserting grooved directors over the barb points.

Parsons mentions that tannic acid rubbed into the wound is supposed to have a beneficial effect either by contracting the blood-vessels or by neutralising the poison. He employs it in every case and its use is highly spoken of by French surgeons.

Anderson also mentions it in his paper, but has not used it. Its mode of action might be arrived at by following the lines of the investigation of the action of potassium permanganate in snake-bite, and this would form an interesting research.

Trypanosomiasis. The literature bearing on trypanosomiasis and sleeping sickness is of such an extensive nature that an adequate review of it can only be obtained from such a source as the *Bulletins of the Sleeping Sickness Bureau,* to which we would refer all those to whom these subjects are of importance. The questions here considered are those likely to be of interest to the more general reader.

Chagas's work[4] on the human trypanosomiasis of Brazil is of such clinical and scientific interest that one is inclined to enter into the subject somewhat fully.

His attention was drawn to a complex of symptoms, affecting children chiefly, which he observed while organising measures against malaria for the railway under construction in the north of the Minas Geraes State in Brazil.

The chief symptoms in children were :—

Extreme anæmia with marked degeneration of the organs and delayed development with infantalism ; œdema, sometimes general, sometimes limited to certain areas ; enlargement of all the peripheral glands, cervical, axillary, femoral, and inguinal ; constant enlargement of the spleen, less frequently of the liver ; and lastly functional disturbances, especially of the nervous system, with frequent occurrence of actual imbecility. Elsewhere, fever is mentioned. The mortality amongst children was great, and was attributed chiefly to convulsions. The children died either with nervous symptoms or with dropsy comparable with that of ankylostoma infection. The names given to the disease, *Opilacao* and *Canguary,* are those given in other regions to ankylostomiasis. To exclude this disease the fæces of many cases were examined, with a negative result. In the blood of one of the cases Chagas found a trypanosome identical with that seen in the laboratory in animals infected by *Conorrhinus.* From the blood of this child, two guinea-pigs and one *Callithrix* were inoculated. The guinea-pigs died on the sixth day, and in the lungs of each were found forms of parasites corresponding to those already studied in the developmental stages of the parasite. The monkey after eight days had trypanosomes in its blood, of the form of the parasite already studied.

The transmitting agent was found to be a biting insect known as *Barbeiro.*

It lives in human habitations, comes out when the lights are extinguished and attacks the inmates ; in the day it remains hidden in cracks in the walls or ceiling. It is most common in the houses of the poor, which are not whitewashed and roofed with grass ; it may occur in enormous numbers. People are bitten chiefly on the face. If a light is struck the insects quickly escape to their hiding-places. A deserted house they very soon leave. The insect belongs to the *Hemiptera heteroptera,* to the family *Reduviidae,* and to the genus Conorrhinus ; the species is probably *megistus,* Burm. It is more than an inch long, the female somewhat larger than the male. In the hind gut of these bugs, collected in houses, Chagas found numerous flagellates with the morphological characters of *Crithidia.* Some of the bugs were sent to Dr. Oswaldo Cruz, who caused them to bite a small monkey, *Callithrix penicillata ;* twenty to thirty days afterwards numerous trypanosomes were found in the animal's blood, differing obviously from other members of the genus. Chagas succeeded in transmitting the parasite to guinea-pigs, rabbits, dogs, and other monkeys, for all which animals it was pathogenic, least to adult dogs ; *Callithrix* and the guinea-pig are the most susceptible.

Chagas has created a new genus for these parasites, *Schizotrypanum,* and supports the nomenclature on grounds of protozoological analogy.

Morphology and development of *Schizotrypanum cruzi* in vertebrates :—

Two phases of development are seen, one intraglobular, the other free in the plasma. At the beginning of the infection the intraglobular forms are the more numerous, and are in some cases the only ones to be found in the peripheral blood. Sometimes they are completely, sometimes one half, enclosed and very frequently they are united with the red cells by the blepharoplasts only. Later in the infection these forms are seldom seen. From

[1] Wellman, C. (1910), "A List of the Tropical Diseases observed in the Region of San Francisco Bay, California." *American Society of Tropical Medicine.* Collected Papers.

[2] Parsons, A. C. (January 23, 1909), "Arrows and Arrow-wounds in Northern Nigeria." *British Medical Journal.*

[3] Anderson, S. (January, 1911), "Arrows and Arrow-wounds in Manbhum." *Indian Medical Gazette.*

[4] Chagas, C. (1909), "Über eine neue Trypanosomiasis des Menschen. Studien über Morphologie und Entwicklungszyklus des Schizotrypanum cruzi, n. gen. n. sp. Erryer einer neuen Krankheit des Menschen." *Mem. Inst. Oswaldo Cruz.* Translation in *Bulletin Sleeping Sickness Bureau* (1910), Vol. II., No. 16, *et seq.,* Vol. I., No. 2.

Trypanosomiasis—*continued*

the intraglobular stages onwards there is a morphological dualism, shown especially in differences in shape and size of nucleus and blepharoplast.

Schizotrypanum cruzi in the peripheral blood of a man.—Two forms are described. In one form there is a large, egg-shaped blepharoplast very near to or quite at the hinder end of the parasite, with its largest diameter transverse. It has a chromatin appendage. The nucleus is usually oval, or appears as a long chromatin band lying in the longitudinal direction. It contains a more strongly-coloured chromatin corpuscle, corresponding to the centrosome. The flagellum, which starts from the blepharoplast or its appendage, has a free portion of variable length. The anterior end of the parasite is pointed. In the other form the blepharoplast is more or less round, and considerably smaller than in the first form. There is as a rule no chromatin appendage. The nucleus is round, and the chromatin less condensed. The body is decidedly broader than that of the other. Another form was seen in which the blepharoplast was far from the posterior end. Forms are often seen also within the blood corpuscles.

Around the phases of the life history of this parasite, which occurs in the lung, centres, perhaps, the greatest interest of this discovery.

Schizogony of *Schizotrypanum cruzi in the lungs of vertebrates.*—No sign of longitudinal division was ever seen in the peripheral blood or internal organs, which shows, the author says, that there must exist some other process of multiplication; this consists in schizogony in the lungs. It was not easy to demonstrate, as its existence depended on variations in the virulence of the infection. The best method was to inoculate under the peritoneum 1 to 2 c.c. of blood from a guinea-pig infected by a *Conorrhinus*, and to kill the animal on the fifth or sixth day; the schizogonous forms would then be numerous. Chagas believes that the increase of the parasites is periodical; there are fluctuations in the numbers of flagellates in the peripheral blood. The schizogony takes place in the capillaries. The flagellum and undulating membrane are lost and the nucleus comes forward; the anterior end of the creature approaches the posterior and merges with it; the blepharoplast in some cases disappears with the flagellum, in others blends with the nucleus. The nucleus or nucleus-blepharoplast then divides (the process has not yet been studied in fresh preparations nor even after wet fixation), eight club-shaped products being formed. The membrane (periplast) in which they lie irregularly, might incorrectly be described as a cyst. There are two forms of merozoites which differ in several respects: one has, the other has not, a blepharoplast; these, the smaller, are considered to be female, those male. The merozoites seem to slip out of the membrane one by one. They penetrate into the red corpuscles and become flagellates. The young endoglobular forms show the same morphology as the merozoites in the lungs.

From a large number of systematic experiments the observer came to the following conclusions with regard to the part played by the carrier :—

(1) An undetermined percentage of *Conorrhinus* coming from houses in the infected region is infective to vertebrates.

(2) *Conorrhinus* larvæ reared in the laboratory and fed on infected animals with numerous parasites in the peripheral blood are not always infective, although they harbour flagellates in the mid-gut.

(3) The larvæ which prove infective in such conditions become so first on the eighth to the tenth day after the infective feed, but retain this property for a long period, the limits of which are not yet known.

(4) Two to three days after the infective feed the bites of the larvæ are not infective to vertebrates.

Cultivation. The parasites in artificial culture. Schizotrypanum cruzi is easily cultivated on the Novy-MacNeal medium. Chagas obtains the blood from the heart of a rabbit and mixes it with an equal volume of agar; he inoculates into the water of condensation. The first changes begin after six hours; these and the subsequent changes correspond closely to those described as occurring in the bug,—round forms, pear-shaped forms dividing rapidly, and crithidial forms; in other cultures these may be of large dimensions. All may be seen in the cultures for two months. The first two sub-inoculations almost always succeed. Neither the forms with the thickened membrane nor the schizogonous forms were ever seen, but in two cultures from the blood of *Callithrix*, flagellates appeared which correspond with those from the peripheral blood and from the salivary glands. Other forms, seen twice, resembled, in Giemsa-stained preparations, the ookinets of *Hæmoproteus;* they require more investigation.

Trypanosoma americanum. Crawley,[1] in following up the work of Miyajima (1907), cultivated from the blood of cattle in America a trypanosome, to which he gave the name *T. americanum.* It will be remembered that Miyajima concluded that the trypanosome cultivated by him was a developmental change from the hæmocytozoon, *Piroplasma parvum.*

Crawley's notes are as follows :—

Bovine blood, cultured in common beef bouillon, develops trypanosomes in from two to four days, dependent upon temperature. They also appeared in cultures of cow's blood in mutton bouillon, either acid or alkaline, and, furthermore, they developed in the case of every cow tested.

The methods were as follows: Blood was drawn from the jugular vein of the cow by means of a syringe, and transferred to flasks of 100 c.c. capacity. About 30 to 50 c.c. of blood was taken in each case. In each flask were placed six to eight facetted beads of rough glass, such as those found in shops, strung together, for sale as very cheap necklaces. A few minutes shaking of the flask serves to collect the fibrin into a solid clot, embedded in which will be the beads. In these operations suitable precautions were taken to prevent contamination.

To take the blood from the flasks, pieces of glass tubing were used, one-fourth inch in diameter and eight to ten inches long. Over one end of each of these a piece of rubber tubing was pulled to serve as a mouthpiece. The quantity of blood desired may then be drawn up into the glass tube by suction. The tubes with the rubber tubing attached were sterilised by boiling for five to ten minutes and then used at once. Owing to the poor conductivity

[1] Crawley, Harold (October, 1909), "*T. americanum,* n. sp." *Bureau of Animal Industry,* Department of Agriculture, U.S.A., *Bulletin* 119.

Trypanosomiasis—*continued*

of glass they do not cool readily, and it was considered possible that they might heat the blood sufficiently to kill any animal life present. Accordingly, the precaution was usually taken of allowing the first filling of the glass tube to drop back into the flask and of using only the second.

As soon as the glass tube was filled with the blood to be used, the rubber tube was closed by pinching and the contents transferred at once to a culture tube. This operation was always performed by two persons, one to handle the blood, the other the culture tubes. In this way the latter were not exposed to the possibility of contamination for more than a second or two.

This procedure gave entirely satisfactory results. Bacterial contamination, when it occurs, appears to be the result either of getting the blood contaminated during the process of drawing it or in the later handling of the tubes. Moreover, it is not quite so destructive to the growth of the trypanosomes as some authors maintain. While the contaminating of cultures is a reflection on the operator's technique, the trypanosomes seem able to endure a certain amount of plant life, and may even be found alive in very foul cultures. It was also at times noted that bacteria would start in a tube and later die out.

The trypanosomes appeared on the third day, and Crawley found that he could cultivate the trypanosome from the blood both of cattle that had suffered from *P. bigeminum* and from normal cattle, thus throwing some doubt on Miyajima's conclusion.

The trypanosome is large, and may measure as much as 60 μ in length; he observed the development through crithidia-like stages. No trypanosomes were observed in the fresh blood.

In connection with this work, Stockman [1] has made a most interesting observation on the blood of cattle in England. On April 23, 1910, ten pedigree cattle which were going to South Africa were inoculated with the object of giving them immunity against piroplasmosis. The strain employed was one which had been obtained from a case of naturally acquired redwater in England. None of them showed piroplasms, and while there was no acute attack of piroplasmosis, the animals fell off in condition. Trypanosomes were found in very small numbers after the ninth day, and were only found for a few days. Attempts to cultivate the trypanosome were unsuccessful.

Edmond and Etienne Sergent,[2] in Algiers, carrying out the same methods as Crawley, obtained a growth of trypanosomes in 10·9 per cent. of cattle brought to the abattoir of Algiers —82 different bloods were experimented with. Their trypanosomes in the first cultures were 24 μ in length, without counting a long flagellum.[3]

Differentiation of Trypanosomes. Levaditi and Mutermilch [4] have made use of the phenomenon known as "attachment" as an aid to the differentiation of trypanosomes; the determining factors in the process are of considerable interest, and the following résumé of the work, as given in the *Bulletin of the Sleeping Sickness Bureau*, is here quoted :—

(1) If one brings together in the test-tube guinea-pig leucocytes (peritoneal exudate), a drop of blood of a mouse infected with Nagana, and the serum of a healthy guinea-pig inactivated at 56°, one finds that the trypanosomes come in contact with the leucocytes and displace them, but do not become incorporated with them. If, however, one replaces this serum by the serum of an infected guinea-pig bled at the crisis and inactivated (specific trypanocidal serum), one finds that as soon as the very motile trypanosomes meet with the leucocytes they fix themselves by their aflagellar extremity on the leucocytic protoplasm. This phenomenon of "attachment," which was first described by Laveran and Mesnil (*Trypanosoma lewisi*), and then by Mesnil and Brimont for pathogenic trypanosomes, is constant in experiments done in the test-tube, and appears at laboratory temperature. After a short time the leucocyte puts out pseudopodia which blend with the extremity of the trypanosome. The parasite remains motile as long as the blending stops short of the nuclear region; it then moves less and less, and at last becomes immobilised and transparent, and finally is altogether phagocyted.

There are therefore two phases in phagocytosis: (1) that of attachment of the organism to be phagocyted to the leucocyte, and (2) that of the actual incorporation (englobement).

For the attachment of sensitised trypanosomes it is not necessary for the white cells to be alive; the process goes on just as well when they have been previously killed by a prolonged stay on ice (three days), by heating to 45°, 55°, or 60°, by successive freezing and thawing, or by mechanical action. Phagocytes heated beyond 60° lose to some extent the faculty. Attachment occurs also if the mixture is kept at zero; the trypanosomes, still very motile, then attach themselves to the cells, but are not incorporated with them. The authors infer that the attachment of the phagocytible organism to the leucocytes is a physico-chemical phenomenon analogous to agglutination; for it takes place in conditions which exclude any active intervention on the part of the phagocyte. The phenomenon is specific, because (1) only sensitised trypanosomes (in the presence of the antibody or after fixing this antibody) attach themselves to the white cells; (2) they stick to the leucocytes, and not to any other cells. In the first phase of phagocytosis, the authors write, the initial act of attachment results from the chance meeting of the phagocyte and the trypanosome, which proves the existence of a specific affinity between the sensitised antigen and the leucocytic protoplasm. They add that the vitality of the trypanosomes facilitates attachment.

The second phase is a vital phenomenon. If the vitality of the phagocyte is interfered with, one prevents the incorporation of the parasites as well as trypanolysis. Trypanosomes resistant to antibodies do not attach themselves to the leucocytes, and are not phagocyted.

In actual experimental proof of the use of a method dependent on these factors the

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[1] Stockman, S. (June, 1910), "Preliminary Note on a Trypanosome of British Cattle." *Journal Comparative Pathology and Therapeutics.*

[2] Sergent, Ed. and Et. (January 11, 1911), "Présence des trypanosomes chez les bovidés en Alger." *Bull. Soc. Path. Exot.*

[3] Cryptic trypanosomiasis in cattle has also been found to exist in France, Germany, Tunis and Brazil.—A. B.

[4] Levaditi, C., and Mutermilch, S. (June, 1910), "Mécanisme de la Phagocytose." *C. R. Soc. Biol.*

authors [1] experimented with three species of trypanosomes—*T. dimorphon*, *T. nagana*, and *T. nagana* of Togoland (Schilling), the latter two types being very nearly allied. **Trypanosomiasis—** *continued*

Their results certainly point to the value of this method, as in each case the "attachment" phenomena were found to be specific. The method has considerable practical advantages for laboratory use.

A method of facilitating the search for trypanosomes and filaria in the blood has been introduced by Levaditi and Stanesco,[2] who make use of ricin for this purpose.

Thea uthors found that ricin, although strongly agglutinating the corpuscles, has no action on the trypanosomes. They have used this peculiarity in their researches into trypanosomes and spirilla. If Merck's ricin be used, a solution of 1 per cent. in isotonic saline solution is prepared and placed in centrifuge tubes, 4 c.cm. in each tube; the tubes are sealed and are then kept at 60° for an hour. When required for use a circular cut is made round the tube and 20 to 30 drops of blood allowed to fall into this fluid. Agglutination commences immediately, and is complete in some minutes. When all the cells have fallen to the bottom of the tube, the supernatant fluid is placed in another tube and centrifuged. The supernatant liquid is again decanted, leaving one or two drops at the bottom of the tube which serves to dilute the clot. The deposit thus formed is aspirated and examined fresh, or stained with diluted Giemsa.

The animal trypanosomiases of Uganda. The Uganda Sleeping Sickness Commission of the Royal Society have published a number of interesting papers on the animal trypanosomiases of Uganda, and a brief reference is here made to some of them.

1. *Trypanosoma ingens* [3]—an immense trypanosome was found in a reed buck, measuring from 70 to 80 mm. in length, and with a breadth of from 7 to 10 mm.

2. Work was done on *T. vivax*,[4] which appears to be widely distributed in that country, and of considerable economic importance.

(i.) *Trypanosoma vivax*, an easily recognisable species, gives rise to a fatal disease of cattle in Uganda.
(ii.) The carrier of *Trypanosoma vivax* is probably *Glossina palpalis*, which is found naturally infected on the Lake shore.
(iii.) The reservoir of the virus is possibly the antelope which frequent the *Glossina palpalis* area.

3. They found what they consider to be *T. brucei* [5] in oxen.

4. They have proposed a new name, *T. pecorum*,[6] for a trypanosomiasis of domestic animals in Uganda. They state that:—

(i.) *Trypanosoma pecorum* is an important trypanosome disease of domestic animals in Uganda.
(ii.) It is similar in morphology, action on animals, and cultural characters, to the *Trypanosoma dimorphon* described by Laveran and Mesnil, and to Dr. Edington's trypanosome from Zanzibar, except that *Trypanosoma pecorum* is not pathogenic to guinea-pigs.
(iii.) The carrier is unknown, but is probably a Tabanus, and not Stomoxys.

5. They found *T. nanum* [7] twice in cattle, but on account of its apparent rarity are unwilling to class it a Uganda species. They consider—

(i.) *T. nanum* is indistinguishable from *T. pecorum*, either in the living condition or when fixed and stained.
(ii.) It differs from *T. pecorum* in not being pathogenic to the smaller laboratory animals.
(iii.) The carrier of *T. nanum* is probably the same as that of *T. pecorum*, as both diseases occur under the same conditions, but there is no evidence available as to what the carrier is.

6. A trypanosome found by them resembling *T. vivax* in many ways has been named *T. uniforme*;[8] the amount of evidence concerning this trypanosome is limited. Their conclusions are—

(i.) *Trypanosoma uniforme* resembles *T. vivax* in shape and general appearance, but differs markedly in size.
(ii.) It also resembles *T. vivax* in not being pathogenic to the smaller laboratory animals.
(iii.) There is no evidence available, as in the case of *T. vivax*, as to what the carrier of *T. uniforme* is.

They also found a trypanosome in the African elephant.

Fry [9] gives a résumé of our knowledge regarding the animal trypanosomes of the Sudan, some of which appear to be identical with certain of the Uganda species.

Trypanosomiasis treatment. Holmes [10] in India has perhaps done the most striking work with the treatment of trypanosomiasis in equinæ. He has treated considerable numbers of transport ponies with arsenious acid, and the results which he obtained were striking. The arsenic was given, as a rule, in balls. The original article is well illustrated with photographs

[1] Levaditi, C., and Mutermilch, S. (December, 1910), "Diagnostic des Trypanosomiases par le Phénomène de 'l'Attachement.'" *C. R. Soc. Biol.*

[2] Levaditi, C., and Stanesco, V. (1910), "Résumé sur un procédé facilitant la recherche des trypanosomes et des filaires dans le sang." *Journal Tropical Veterinary Science*, Vol. V., No. 3.

[3] Bruce, D., and others (May, 1910), "*Trypanosoma ingens*, nov. sp." *Proceedings of the Royal Society*, B, Vol. LXXXI., 1909.

[4] *Idem* (July, 1910), "*Trypanosoma vivax*." *Ibid*, Vol. LXXXIII., 1910.

[5] *Idem* (July, 1910), "*Trypanosoma brucei*." *Ibid*, Vol. LXXXIII., 1910.

[6] *Idem* (June, 1910), "*Trypanosoma pecorum*." *Ibid*, Vol. LXXXII., 1910.

[7] *Idem* (December, 1910), "*Trypanosoma nanum*." *Ibid*, Vol. LXXXIII., 1911.

[8] *Idem* (December, 1910), "*Trypanosoma uniforme*, nov. sp." *Ibid*, Vol. LXXXIII., 1911.

[9] Fry, W. B. (1911), "Animal Trypanosomiases in the Anglo-Egyptian Sudan." *Fourth Report, Wellcome Tropical Research Laboratories*, Vol. A.

[10] Holmes, J. D. E. (1910), "The Cure of Surra in Horses by the Administration of Arsenic." *Parasitology*, Vol. III.

Trypanosomiasis— *continued*

of animals before and after treatment. It should be consulted by any one interested in this subject.

The conclusions Holmes arrives at are as follows :—

1. The results herein recorded are further evidence that arsenic is a specific for Surra in horses; that a permanent cure is effected, and not merely a temporary tolerance of the disease; that the treatment is simple, and that by careful dosage 70 per cent. and upwards of Surra cases, even when contracted spontaneously and in the last stage, can be cured.

2. Arsenic is best administered in form of arsenious acid, in bolus, or in solution. Atoxyl is a convenient form of giving arsenic hypodermically.

The methods of dosage which have been found successful are :—

(i.) Arsenious acid alone. This is given in bolus, in gradually increased doses, with one day's interval between each dose. Eight to ten doses are sufficient.

(ii.) Atoxyl and arsenious acid, given alternately in gradually increased doses, with one day's interval between each dose. Five doses of atoxyl and five doses of arsenious acid are sufficient.

(iii.) Arsenious acid in solution, atoxyl and arsenious acid in bolus. The dose of arsenious acid solution is followed by atoxyl, and arsenious acid in bolus, on successive days. The doses are repeated once or twice after an interval of four days between each series, and finally after an interval of eight days.

The solution of arsenic was made up according to the method of Lœffler and Ruehs' as follows :—

Take 1 gramme arsenious acid, 10 c.c. normal soda solution. Dissolve by boiling. Add 10 c.c. normal hydrochloric acid and make up to 1000 c.c.

The doses vary from 4000 c.c. to 1000 c.c. of the arsenious acid solution.

Heavy artillery horses appear to tolerate doses up to 2·5 and 3 grammes.

An instructive table is given in the comment on this paper in the *Sleeping Sickness Bureau Bulletin*, No. 15, Vol. II., in which the known methods of transmission of trypanosomiasis are compared.

METHODS OF TRYPANOSOME TRANSMISSION SO FAR ASCERTAINED

Species of Trypanosome	Insect	Duration of Non-infective Period	Place of Development	Duration of Infectivity	Observer
T. brucei (?) ...	*G. palpalis* ...	20 days	—	at least 83 days	Kleine.
T. gambiense and a trypanosome of *dimorphon* type	*G. palpalis* ...	16, 19, and 22 days	Intestine ...	at least 75 days	Bruce, Hamerton, Bateman and Mackie.
T. gambiense ...	*G. palpalis* ...	18 days	Intestine ...	—	Kleine.
T. cazalboui ...	*G. palpalis* ...	7 days	Proboscis ...	at least 2½ months	Bouffard.
T. lewisi	*Ceratophyllus fasciatus*	6 days	Begins in rectum	at least 6 weeks	Minchin and Thomson.

Transmission of trypanosomiasis. Minchin and Thomson [1] have gone far to clearing up the problem of the transmission of *T. lewisi* in nature. The results of a series of experiments on the rat-flea as a transmitting agent are given; the following are conclusions which the authors arrived at :—

(1) The rat flea, *Ceratophyllus fasciatus*, can transmit *Trypanosoma lewisi* from infected to non-infected rats.

(2) The transmission takes place by the cyclical method.

(3) Transmission by the direct method has not been proved to occur.

(4) The incubation-period in the flea—that is to say the period occupied by the developmental cycle of the trypanosome—has a minimum length of six or seven days, but may be longer.

(5) The multiplication-period of the trypanosome in the rat has a length of about twelve days.

(6) In the developmental cycle the establishment of the trypanosome in the flea begins with multiplication of crithidia-like forms in the rectum.

Additional Notes (A.B.)

At the International Hygiene Exhibition, Dresden, there was an excellent exhibit of specimens and photographs illustrating the trypanosome disease of Chagas. Especially noticeable were those dealing with its more chronic forms which are exemplified chiefly by changes in the colour of the skin, loss of hair, a pseudo-myxœdema and thyroiditis. There is

[1] Minchin, E. A., and Thomson, J. D. (March, 1910), "The Transmission of *T. lewisi* by the Rat Flea." *Proceedings Royal Society*, B, Vol. LXXXII.

also glandular hypertrophy, tachycardia and convulsions. A description of this protean form and also of the acute disease is given by Chagas.[1] With the exception of newcomers the acute disease occurs almost exclusively in small children, there being continued fever with slight morning remissions, increase in the size of the thyroid gland, crepitation of the skin of the face such as occurs in gelatine discs, hypertrophy of the liver and spleen, and often symptoms of meningitis. Another paper by Chagas [2] enters more fully into the schizogony of the parasite in the lungs, and declares that it has a predilection for the cardiac muscle, the central nervous system and the striated muscles. A translation of this important article will be found in the *Sleeping Sickness Bureau*, *Bulletin* No. 29, 1911.

Trypanosomiasis—*continued*

A paper by Darling [3] may be mentioned, as it is rarely one reads an account of prophylactic measures in animal trypanosomiasis on a large scale. In Panama it was found that the disease was being transmitted mechanically by flies through the medium of superficial lesions, and measures adopted to cope with this source of infection proved eminently successful. Amongst other points one notes the use of dressing containing such substances as creolin, kresol, etc., distasteful to flies.

For recent work on the transmission of trypanosomes, and especially of *T. gambiense* and *T. lewisi*, *Bulletin* No. 27 *of the Sleeping Sickness Bureau* may be consulted with advantage, and indeed these bulletins are now indispensable to the tropical worker and obviate the necessity for further consideration here of a subject which is as vast as it is important.

Tsetse Flies. Since the issue of the last Review the most important observation from a tropical disease standpoint is probably the discovery of the cycle of development of *T. gambiense*, which has been found to occur in *G. palpalis*, first observed by Kleine, and afterwards confirmed by the Sleeping Sickness Commission in Uganda, and other workers.

It was for so long taken as an axiom that the transmission of sleeping sickness was a mechanical one, that the conclusions arrived at by the Uganda Commission are here given :—

(1) The mechanical transmission of sleeping sickness by means of *G. palpalis* can take place if the transference of the flies from the infected to the healthy animal is instantaneous—that is, by interrupted feeding.

(2) The mechanical transmission does not take place if any interval of time comes between the feedings.

(3) Mechanical transmission plays a much smaller part, if any, in the spread of sleeping sickness than has been supposed.

The last conclusion is indeed remarkable, when it is remembered what was thought a year or two ago.[4]

In a previous report they gave the results of their experiments on the actual time required for the fly to become infective, and the proportion of flies which acquired power of infection given opportunity.

Their results are the outcome of a large series of experiments, and are very interesting.

They conclude :—

(1) That *T. gambiense* multiplies in the gut of about one in every twenty *G. palpalis* which have fed on an infected animal.

(2) That the flies become infective, on an average, thirty-four days after their first feed.

(3) That a fly may remain infective for seventy-five days.

Their experiments on other trypanosomes led to further conclusions :—

(4) That *T. dimorphon*, *T. vivax*, and *T. nanum* may also multiply in *G. palpalis*, which must therefore be looked upon as a possible carrier in these diseases.

(5) That multiplication in the tube of the proboscis is characteristic of *T. vivax*.[5]

Observers are agreed that *G. palpalis* differs little in its habits and requirements from *G. fusca*, so that both of them differ in these respects from *G. morsitans*.

With regard to the natural food of *G. palpalis* the following are the conclusions arrived at by the Sleeping Sickness Commission of the Royal Society, Uganda, 1908–10, after a series of experiments to ascertain the natural food of the tsetse fly.

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[1] Chagas, C. (1910), "Schysotripanose Cruzi ou 'Dœnça de Carlos Chagas.' Nova entidade morbida do homem." *Revist. med. S. Paulo*, Nos. 22 and 23.

[2] *Idem* (July, 1911), "Le Cycle de *Schizotrypanum cruzi* chez l'Homme et les Animaux de laboratoire." *Bull. Soc. Path. Exot.*

[3] Darling, S. T. (June, 1911), "The Probable Mode of Infection and the Methods used in Controlling an Outbreak of Equine Trypanosomiasis (*Murrina*) in the Panama Canal Zone." *Parasitology.*

[4] Bruce, D., and others (1910), "Mechanical Transmission of Sleeping Sickness by the Tsetse Fly." *Proceedings Royal Society*, B, Vol. LXXXII.

[5] *Idem* (1910), "The Development of Trypanosomes in Tsetse Flies." *Ibid*, Vol. LXXXII.

Tsetse Flies— *continued*

220 *G. palpalis* were caught on various parts of the Lake shore and at intervals extending over several months; they were examined about twenty-four hours after capture. The examination of their intestinal contents revealed the fact that about 27 per cent. contained the remains of blood, the majority of which was of mammalian origin.

In the second experiment, 183 *G. palpalis* were caught at one spot where the food supply was abundant, birds and crocodiles—and the flies were examined at once. A much higher percentage (nearly 60 per cent.) contained the remains of a blood meal. The blood in the majority of the flies had been obtained from birds or reptiles, and of these the reptilian blood was twice as frequent as the blood of birds.[1]

In this connection it is interesting to read what is said by the Portuguese Sleeping Sickness Commission in the Island of Principe, which lies near the Island of S. Thoma, which is free from trypanosomiasis, human and animal.

After speaking of the habits of the fly, which do not appear to differ from descriptions given of them in other parts of the world, and saying that the favourite biting time with them on this island is from 8 to 11 in the morning and 3 to 5 in the afternoon, they write :—

There are no crocodiles in the island. The glossina feed on the blood of man and other mammals. Contrary to what has been generally observed, these flies depend especially on the blood of pigs, which they prefer to that of any other animal. In the north and in the centre, where the plantations hold great numbers of pigs at large, the glossina is sure to be found wherever this animal exists.

They are of the opinion that the absence of the fly from the southern extremity of the island is related to the fact that any pigs in this region are protected by being confined to sties.[2]

The habits of G. fusca have been investigated by Davey,[3] and it would appear that these flies occur under two conditions, (1) in considerable numbers over a limited area, and not extended over wide tracks of country as *G. morsitans*. (2) In very small numbers on the shores of lakes.

In nearly all cases they seem to prefer places where there is abundant shade, and where there is a considerable growth of creepers and young forest trees, though they seem to be most numerous under the larger trees. In every case water is close at hand.

Time of activity. As a rule, *G. fusca* feeds chiefly in the evening, but it does not set to work as rapidly and voraciously as *G. morsitans*. It appears to lie in wait at 4 p.m. on dry sticks and leaves near paths, apparently watching for prey.

Both *G. morsitans* and *G. fusca* seem more inclined to settle on khaki coloured stuffs than on the bare skin, except when hungry. In the early morning *G. fusca* flies about, apparently taking its departure for its day haunts. During the daytime it is found on tree trunks surrounded by creepers and undergrowth, hidden away in crevices of the bark about 2 or 3 feet from the ground, and when disturbed it does not fly far and shows no tendency to feed. The search for larvæ and pupæ was unsuccessful. Found at low levels.

Relation to game. Found generally where game is abundant; the best time to catch them is in the evening.

Further notes on the habits of *G. fusca* are given by Sanderson,[4] who illustrates the habitat of the fly.

Habits of G. morsitans. Never found in open country or in the bush, nor are dense forests or shady trees necessary; it prefers low ground. Discussion is in progress as to whether tsetse flies are dependent for their existence on the blood of wild animals. Sir Alfred Sharpe[5] states he has never caught one with blood in the abdomen except those in the act of feeding; he also thinks that the existence of wild game has very little to do with the occurrence of this species of tsetse fly.

Enemies of tsetse flies. Bouffard has found that a species of wasp violently attacks glossina and kills it. Picard[6] describes the insect as a fossorial wasp, *Oxybelus*, twenty African species of which are known, some from the Cape, others from Egypt and Abyssinia. He thinks Bouffard's specimen from Bamako is a new species belonging to the section,

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[1] Bruce, D. (1910), "The Natural Food of *Glossina palpalis*." *Proceedings Royal Society*, B, Vol. LXXXII.

[2] Mendes, A. C., and others (November, 1909), "La maladie du Sommeil à l'île du Prince." *Arch. de Hyg. et Path. Exot.*

[3] Davey, J. B. (July, 1910), "Notes on the Habits of *Glossina fusca*." *Bulletin of Entomological Research.*

[4] Sanderson, M. (January, 1911), "Notes on *Glossina fusca* (Walk.) in North Nyasa." *Ibid.*

[5] Sharpe, A. (October, 1910), "Notes on the Habits of *Glossina morsitans* in Nyasaland and the adjoining Territories." *Ibid.*

[6] Picard, F. (August 6, 1909), "Sur un Hyménoptère fouisseur du genre Oxybelus, chasseur de glossines au Soudan Français." *C. R. Soc. Biol.*

Notoglossa, and near *O. pinnatus* (de Saussure). These wasps live on the nectar of flowers, do not kill or eat the insects which they hunt, but paralyse them by puncturing their nerve centres and bury them in their nests, where they serve as food for their larvæ. **Tsetse Flies—** *continued*

A summary of our knowledge of *G. palpalis* is given in the *Bulletin of the Sleeping Sickness Bureau*,[1] and a complete and well worked out scheme of investigation for workers on the bionomics of this fly is given later in the same publication for 1910, *pages* 189 *to* 191. This is somewhat lengthy, so a reference is only made to it here as most tropical workers will be in possession of the above bulletin.[2]

To breed flies. A good method is to keep pupæ in a box in a cool place with a little of the earth in which they were found, and await the emergence of the imago.

To keep flies. They should be kept singly, or they foul one another with excreta and die; and in glasses with wide mouths, covered with mosquito netting. They are fed every four or five days.

The recognition of the tsetse fly and its identification are so generally useful that a concise classification will probably be of great use to tropical observers. Eight species of tsetse fly are generally recognised, and a good classification is that of Austen which Castellani [3] quotes in his recent manual of tropical medicine; it is here given in full, as it is invaluable to those to whom this subject presents some difficulties.

A. Hind tarsi entirely dark (female of *Glossina tachinoides*;—basal and half of first and extreme bases of succeeding joints pale).

I. Ground colour of abdomen ochraceous buff, with interrupted dark brown deep transverse bands and sharply defined pale hind borders to segments. A very conspicuous square or oblong pale area in the centre of the second segment. Small species: body-length 7 millimetres—(1) *G. tachinoides.* Westwood, 1850.

II. Abdomen very dark; pale area in second segment usually triangular. Large species.

1. Third joint of the antenna dusky brown to cinereous black: body-length 8 to 9 millimetres—(2) *G. palpalis.* Robineau-Desvoidy, 1830.

2. Third joint of antenna pale: body-length 8 to 9 millimetres—(3) *G. pallicera.* Bigot, 1891.

A. Hind tarsi not entirely dark.

I. Small species: body-length 8 to 10 millimetres. Length rarely 11 millimetres. Wing expanse not more than 25 millimetres.

(*a*) Last two joints of front and middle legs with sharply defined dark brown or black tips.

1. Large species: Wide head, darker anteriorly; abdominal bands deep—(4) *G. longipalpis.* Wiedemann, 1830.

2. Smaller species: Narrower head—(5) *G. morsitans.* Westwood, 1850.

(*b*) Last two joints of fore and middle tarsi pale: body-length 8 to 10 millimetres—(6) *G. pallipides.* Austen, 1903.

II. Large species: body-length 11 to 13 millimetres. Wing expanse 25 millimetres at least.

(*a*) Dorsum of thorax with four sharply-defined small black spots—(7) *G. longipennis.* Corti, 1895.

(*b*) Dorsum without spots—(8) *G. fusca.* Walker, 1849

A species, *G. maculata*, is described by Newstead, but it may only be a variety of *G. palpalis.* It was described from only one damaged specimen, and Newstead says that it looks very like a dark specimen of *G. palpalis.**

Tsetse fly transmission. Bouet and Roubaud,[4] working in Dahomey, have confirmed Bouffard's results on the transmission of *T. cazalboui* by *G. palpalis* with regard both to the time necessary to attain infectivity—six days after the infective feed—and to the fact that the development of the parasite takes place extensively in the proboscis.

They could not ascertain that the infectivity could be recognised by any morphological stage in the developmental changes in the trypanosomes.

With regard to experiments on the transmissibility by *G. tachinoides* and *longipalpis*, experiments under this heading were positive. They say :—

These experiments show that the enzootic rôle of *G. palpalis* towards *T. cazalboui* is not specific, and the species *tachinoides* and *longipalpis* behave in exactly the same way with respect to this virus.

Here, too, the non-infective interval was six days, and the development was limited to the canal of the proboscis.

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[1] (January, 1909), "*Glossina palpalis*, A Summary of Our Knowledge of the Species." *Sleeping Sickness Bureau, Bulletin* No. 3.

[2] (1910), *Bulletin Sleeping Sickness Bureau*, Vol. II., No. 17.

[3] Castellani, A., and Chalmers, A. J. (1910), *Manual of Tropical Medicine.*

* This classification, though useful, is superseded by that given in Austen's new *Handbook of the Tsetse Flies*, 1911.

[4] Bouet, G., and Roubaud, E. (August, 1910), "Expériences diverses de transmission des trypanosomes par les glossines." *Ann. de l'Inst. Past.*

Tsetse Flies—*continued*

Methods. Hamerton [1] has written a concise and very practical paper on the methods of studying the morbid histology of disease-carrying insects. Any one contemplating taking up this field of research will be well repaid by studying the article in the original. It is too detailed for reproduction here.

Additional Notes (A.B.)

Newstead [2] has carried into effect a new scheme for the classification of tsetse flies which, as he says, is contrary to nearly every precedent, inasmuch as it begins with the lower and rises to the higher or more complex forms. It is entirely based upon the taxonomic characters of the armature of the males, and, so classed, the species fall into three very striking and distinct groups, *i.e.* the *fusca* group, the *palpalis* group, and the *morsitans* group. Considerations of space forbid a more extensive excursion into Newstead's paper, which is well illustrated and which bids fair to revolutionise the classification of these flies. It may be said, however, that he recognises *G. submorsitans* as a distinct species. This he described in a previous paper [3] together with *G. brevipalpis* and *G. fuscipes*, other new species. He also described what he then believed to be the unknown male of Bigot's *G. grossa*, but more recently [4] he has found that this was an error, and that the fly in question is really another new species, which he has named *G. nigrofusca*.

A writer in *Deutsches Colonialblatt*, who deals with clearing questions and *G. morsitans*, is quoted in the *Bulletin of the Sleeping Sickness Bureau*, Vol. III., No. 23, for January 20, 1911, where the results are summed up as follows :—

> In parts where the flies were numerous and the cleared area was 100 metres wide the fly certainly diminished, but not to any great extent, and even the cleared area of 200 and 300 metres width was not sufficient to keep the flies entirely from the road.

The writer of the note thinks, therefore, that we must give up the hope of freeing trade routes from *Glossina morsitans* by clearing ; for the cost of this operation over strips more than 300 metres wide would be so great as to make the measure impracticable.

The work of Roubaud on the bionomics of *G. palpalis*, *tachinoides* and *longipalpis* is reviewed in the above Bulletin for March 14, 1911. Of the three species *G. longipalpis* is the most circumscribed in habitat, and mixes least with the others.

Tuberculosis. So much has been written on this subject within recent years, that, in a review such as this, it would be impossible to deal with all the papers relating to tuberculosis, and only those will be referred to that have a practical interest to the practitioner, sanitary officer, and laboratory worker in the Tropics. Whitla,[5] in an instructive and interesting paper entitled "The Etiology of Pulmonary Tuberculosis," discusses all the recent work on human and bovine tuberculosis,and has confirmed the results obtained by Calmette.[6] Among other points he notes that the tubercle bacillus can pass through the intestinal mucous membrane without causing any local lesion. Calmette comes to the conclusion that under natural conditions dry dust containing the tubercle bacillus does not play any rôle in infection, and that in the immense majority of cases pulmonary tuberculosis is not contracted by inhalation, but that the site of entrance of the tubercle bacillus is *viâ* the intestinal epithelium rather than through the pulmonary alveoli.

On the other hand, Reichenbach and Bock [7] favour the inhalation theory in the production of pulmonary tuberculosis. Experiments were carried out on guinea-pigs and goats to find out the relative importance of inhalation or swallowing in the production of tubercular infection. In guinea-pigs they found that it took 3,500 times as many organisms to cause infection by feeding than it did by inhalation. In goats, too, it took a 500 times greater dose to produce infection by feeding than by inhalation. These observers concluded that infection by inhalation is quicker and more certain, and takes place with smaller doses than by feeding.

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[1] Hamerton, A. G. (September, 1908), "An Introduction to Methods of Studying the Morbid Histology of Disease-carrying Insects." *Journal Royal Army Medical Corps.*

[2] Newstead, R. (May, 1911), "A Revision of the Tsetse Flies (*Glossina*) based on a Study of the Male Genital Armature." *Bulletin of Entomological Research.*

[3] *Idem* (December 20, 1910), "On Three New Species of the Genus *Glossina*, together with a Description of the Hitherto Unknown Male of *Glossina grossa* (Bigot)." *Annals Tropical Medicine and Parasitology*, Vol. IV., No. 3.

[4] *Idem* (April 20, 1911), "Some Further Observations on the Tsetse Fly described in these Annals as *Glossina grossa*." *Ibid*, Vol. V., No. 1.

[5] Whitla, W. (July 18, 1908), "The Etiology of Pulmonary Tuberculosis." *Lancet.*

[6] Calmette, A. (September, 1907), "Les voies normales de pénétration du virus tuberculeux dans l'organisme." *Bull. de l'Inst. Past.*

[7] Reichenbach, H., and Bock, S. (1908), "Versuche über die Durchgängigkeit des Darms für Tuberkelbazillen." *Zeit. f. Hyg. u. Infekts.*, Vol. IX., No. 3.

Alexander [1] carried out a similar set of experiments to the last, but used rabbits instead, and also different types of tubercle bacilli. He found that infection was more easily produced by inhalation than by feeding and that the bovine type of bacilli were more virulent to rabbits in the inhalation than in the feeding experiments. **Tuberculosis—** *continued*

Ballin [2] carried out a series of interesting experiments with the inhalation of spores of fungi in order to ascertain by analogy the fate of the tubercle bacilli when inhaled, whether they were arrested in the bronchi or reached the alveoli. He found that the spores, whether inhaled in the form of dust, or in a spray, went direct into the alveoli and in a short time penetrated the wall of the alveoli and developed there. He concluded from these experiments that tubercle bacilli could penetrate direct into the alveoli.

Bruno Heymann [3] carried out some experiments to discover the fate of inhaled tubercle bacilli in the lungs of guinea-pigs.

Three series were conducted: in the first the inhalation lasted ten minutes, 10,000 bacilli being inhaled; in the second the inhalation lasted five minutes, 100,000 bacilli being inhaled; and in the third the inhalation lasted fifty minutes, during which time 1,000,000 bacilli were inhaled. The animals were then killed at varying intervals, from 1 to 24 hours, and the lungs carefully examined biologically and microscopically. In the first series the lungs contained tubercle bacilli after inhalation of one hour, while the bronchial glands only showed them after three days, and they disappeared from the latter after six days; series two gave similar results, as also series three, except that the bronchial glands contained bacilli one hour after inhalation and did not get rid of them. Microscopical examination also showed that tubercle bacilli could penetrate to the finest bronchi and alveoli.

Köhlisch [4] carried out some important experiments in connection with dried sputum dust. As a result of these he concluded that dust infection had been considerably over-estimated, for certain conditions require to be fulfilled before dust can act as an agent in the spread of tuberculosis, viz.: (1) It must be very finely pulverised. (2) It must be completely dried. (3) Tubercle bacilli must be present in great numbers. (4) As it soon settles, infection can only take place during its actual disturbance. Köhlisch considers that the fine infected spray ejected into the atmosphere during the act of coughing by phthisical patients is more dangerous than infected dust.

Harris [5] has an interesting paper on tuberculous diseases in India. In his experience the commonest variety met with is the fibro-caseating type, and the disease begins more often as an insidious broncho-pneumonia affecting the upper and back part of the right lung. He considers that many of the cases of ascites which are thought to be due to cirrhosis of the liver are in reality insidious cases of peritoneal tubercle. With regard to climatic treatment Harris recommends that patients should live for months at Almora in the Garhwal hills, a place also strongly recommended by Pilgrim,[6] who deals with the subject of tuberculosis in Calcutta, and considers that the most frequent path of infection is by way of the upper respiratory tract. He urges the importance of early surgical measures being employed in connection with all cases of enlarged tonsils and adenoid growths, as their existence apparently predisposes to tuberculosis.

Griffin [7] has a paper dealing with the use of tuberculin in general practice, and considers that its use is beneficial, particularly in long standing tuberculous lesions of bone. It is also valuable in tuberculous peritonitis, and in diseases of the joints, where it should be given in careful and graduated doses. It appears to be of little use for cases of tuberculous adenitis, and is contra-indicated in all acute or recently acute tuberculous lesions, and in tuberculous eye lesions. Tuberculin in conjunction with light treatment is of great value in cases of lupus. In such cases the tuberculin should be given in small doses. The following points should be borne in mind:—

(1) The idiosyncrasy of the individual, though not marked as a rule, may, however, be so; and unless graduated dosage be employed, excessive reaction may occur. Children as a rule take tuberculin well.

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[1] Alexander, J. (1908), "Das Verhalten des Kaninchens gegenüber den verschiedenen Infektionswegen bei Tuberkulose und gegenüber den verschiedenen Typen des Tuberkelbazillus." *Zeit. f. Hyg. u. Infekts.*, Vol. LX., No. 3.

[2] Ballin (1908), "Das Schicksal inhalierten Schimmelpilzsporen." *Ibid.*

[3] Bruno Heymann (1908), "Versuche an Meerschweinchen über die Aufnahme inhalierter Tuberkelbazillen in die Lunge." *Ibid.*

[4] Köhlisch (1908), "Untersuchungen über die Infektion mit Tuberkelbazillen durch Inhalation von trockenem Sputumstaub." *Ibid.*

[5] Harris, G. A. (February, 1909), "Tuberculous Disease in India." *Indian Medical Gazette.*

[6] Pilgrim, H. W. (April, 1909), "Tuberculosis amongst Europeans in Calcutta." *Ibid.*

[7] Wandby Griffin, J. W. (June, 1909), "Tuberculin in General Practice." *Ibid.*

Tuberculosis—*continued*

(2) The temperature is a valuable indication of the condition of the patient; a rise of two or three degrees within a day or two usually indicates that the dose has been excessive, although, however, not necessarily unbeneficial nor injurious. In some cases this evidence of reaction is delayed for a week or ten days.

(3) The actual lesion also may exhibit evidences of reaction if the dose has been large; there is then redness and swelling round the opening of the sinus with some skin infiltration which persists usually for some days, after which the wound frequently looks more healthy, and healing continues more rapidly and effectively. Tuberculous joints occasionally react sharply to tuberculin, and considerable damage may be caused. Graduated dosage is therefore essential in such until clinical evidences have established the optimum dose.

Tuberculin may be administered by hypodermic injection or by the mouth. An average hypodermic dose for sinuses of long standing is 1/2000 mg. (old style); this is a very convenient dose to stock, since from it lesser quantities can be easily measured. Tuberculin must be quite freshly prepared, unless the concentrated fluid retailed in 1 c.c. phials is used, which is said to keep well if stored in a cool and dark place; the process of dilution is, however, rather tedious. In many cases it is advisable to begin with a dose of 1/10,000 or 1/8000 of a milligramme (old style) repeated at fortnightly intervals, the dose being gradually increased until a definite improvement appears, this dose being then taken as the standard for the individual. Rarely there may result some local infiltration of the tissues at the site of injection; this may persist for a few days and be a little painful, but soon subsides without other adverse signs. Oral administration has some advantages over hypodermic; it is less alarming to the patient, and there is less danger of overdose and excessive reaction. Larger doses are necessary than in hypodermic treatment; 1/5000 milligramme (old style) is a fair initial dose. The best time for taking tuberculin thus is probably one hour before breakfast; the tabloid should be crushed to powder, and the dose repeated on the two following mornings, and then discontinued for a fortnight. Given thus, reaction occurs later than in hypodermic dosing, and is less marked, so that this method is safer for cases in which serous surfaces are involved. The opsonic index is affected by oral administration of tuberculin precisely as by hypodermic administration.

Row,[1] in his observations on tubercle in Bombay, has noted characteristic changes occurring in the tubercle bacilli present in the sputum of phthisical patients who are showing some clinical improvement. These are :—

(1) Characteristic grouping of the tubercle bacillus—instead of being diffuse and scattered, or at best in twos and threes, they group in masses of eight, ten, or twelve or more bacilli, scattered here and there in the specimen, coming under focus as the search is proceeded with—in addition to the singles, twos or threes, which appear to be fewer.

(2) A gradual diminution of the number of the bacilli found in the sputum.

(3) A morphological change of the individual bacilli—the individual rods, which were at first solid, show more beading, erosion of edges, and thinning—an appearance of distinct degenerative change in the bacilli.

(4) A very great diminution of even these degenerate bacilli, so that one observes a few granules here and there indicative of some bacilli or their products.

(5) Loss of their virulence, as no result is obtained by inoculation experiments.

From these results he concluded that the grouping of the bacilli was due to the presence of agglutinins. This led him to isolate a material from tubercular foci which, when acted upon by the serum of undoubtedly tuberculous patients, would in all probability demonstrate the presence of agglutinins. With this in view he prepared an extract from the caseating spleens of tuberculous guinea-pigs which was desiccated and mixed with normal saline solution, and finally centrifuged, leaving an opalescent fluid which kept its physical characters for several days. The precipitative reaction was tested by adding an equal quantity of the suspected serum. The results obtained were not uniform, as a few of the serums which came undoubtedly from tuberculous cases failed to give a positive reaction. Positive results were obtained from cases of sprue, while negative ones occurred in cases of malaria, enteric, dysentery, meningitis and bronchitis, and a few other septic conditions, so that there appears to be a certain amount of specificity in the test.

McNeill[2] has studied the tuberculin reaction in the skin and eye in a hundred and fifty-three cases. In carrying out the skin reaction he used a modification of von Pirquet's[3] original method by applying the tuberculin to the exposed *cutis vera*, the epidermis having been previously chafed off by means of a straight surgical needle, avoiding bleeding or oozing. On this vascular surface the tuberculin was rubbed in by rotation of the head of the needle. A positive reaction showed the presence of a red papule which persisted for seven days. The colour of the papule must be of a deep livid hue, which must persist for not less than a week after its appearance. McNeill found the test of great value in obscure joint conditions where the clinical diagnosis was doubtful. Enlarged or suppurating neck glands generally gave a positive reaction. In comparing the skin reaction with Calmette's eye reaction McNeill found that the former was the more useful and reliable of the two. It was not reliable in advanced tuberculous cases, but was so in early and chronic conditions. Even when the skin reaction was repeated it was always confirmed, provided the general condition of the patient remained the same. Throughout his tests McNeill always used a control surface test on the

[1] Row, R. (November 6, 1909), "Some Observations on Tubercle in Bombay." *British Medical Journal.*

[2] McNeill, C. (November 6, 1909), "A study of the Tuberculin Reactions in Skin and Eye." *Ibid.*

[3] v. Pirquet, C. (May 23, 1907), "Über Tuberculinimpfung." *Deut. Med. Woch.*

exposed *cutis vera*, to which 50 per cent. of glycerine in water was applied. Sometimes there appeared in 24 hours, both in the control and in the tuberculin inoculated area, a narrow red ring around the puncture. This, however, always disappeared within 48 hours, and was never regarded as a positive reaction. Tuberculosis—*continued*

Krantz [1] points out the value of the thermometer in the early diagnosis of tuberculosis. In the sanatorium at Hendaye he has made a careful study of the variations of temperature in several children, some of whom were tuberculous, while others were not, and found that the following conditions point to tuberculosis :—

(1) A subfebrile condition, with normal morning temperature, evening slightly over 100° F. during sleep.

(2) Fever with morning remissions.

(3) Sudden and marked rise of temperature, either at unusual hours, or, instead of the moderate rises, constant slight increase of temperature in the absence of cold or gastric disturbance.

(4) Persistence of pyrexia or continued rise of temperature in a child previously resting quietly without fever with a morning temperature of over 100° F.

(5) A temperature of 99° F. and over on waking.

(6) Irregularities in the variations after walking, being sometimes slight, sometimes considerable, with the same amount of exertion.

Krantz found that rises in temperature after exercise were very variable with negative as well as positive ocular reactions ; but that pyrexia continued much longer after rest in tuberculous children. Even those that had no tubercular taint often had a temperature of 100° F. The really valuable test is the average temperature of ten or more days.

In a paper read before the British Medical Association, Roberts [2] has directed attention to certain early manifestations present in tuberculosis met with in India. These are (1) an acute febrile form occurring in young adults ; acute tuberculous fever, resembling atypical typhoid, and simple continued fever ; (2) an irregular fever with enlargement of glands in children ; (3) a debility resembling tropical debility, with a daily rise of temperature to about 100° F.

Dealing with acute tuberculous fever, he pointed out its long duration, the remittent or intermittent pyrexia associated often with some liver enlargement, but no splenic increase, constipation and some meteorism, vomiting and nausea, and as the most characteristic symptoms, epigastric pain and tenderness, making the diagnosis from liver abscess difficult. The pyrexia produces less prostration than that of malaria or enteric ; the tongue is not like the typhoid tongue, and there are none of the malarial sweats. This fever, he adds, has often been confounded with enteric or so-called simple continued fever. It is not the acute generalised tuberculosis or typhoidal type seen in Europe, with their high mortality, for in India the majority recover. This acute tuberculous fever is the beginning of a tuberculous career—a tuberculous cachexia with periods of comparative health. Consultants in England should remember this form of Indian tuberculosis in difficult and obscure cases when a history of fever is given. Especially among Indians subsequent obvious localised tubercle follows an attack, whether of the lungs, glands, bones, etc. The question is mooted, because of the abdominal symptoms, whether this is not a form of bovine tubercle. As in Indian practice it has become the routine in continued pyrexia to examine blood slides for malaria, perform Widal's tests for typhoid or paratyphoid, make blood counts against liver abscess, the differential diagnosis is rendered easier, especially when a case responds to the cutaneous or ophthalmic tests, with tuberculin. In tuberculous fever the opsonic index is high, falling later on, and then the value of tuberculin treatment is a point for consideration. T.R. injections are of great use in warding off the subsequent tuberculous cachexia.

The second form of early tuberculosis seen in children is characterised by enlarged lymphatic glands and irregular fever. It is this latter fever that contrasts the condition in India with that in Europe. The condition is very widespread.

The third form is one of ill-health, neurasthenia, with dyspepsia, and affords a puzzling class of cases until tested by the thermometer, when a daily rise to about 100° F. is noted, and the tuberculin reactions aid in definitely making the diagnosis.

Turner,[3] in a report entitled " How tuberculosis is spread in India," has shown that the mortality from tuberculosis is higher in India than in England, due doubtless to the methods of life led by the natives, which specially tend to disseminate the tubercle bacillus. He found that the cattle in India only suffer to a slight extent from tuberculosis, but that the filthy customs and habits of the gowlis, who scour the milking vessels with cow dung and dirt, and who employ water used for their own toilet for cleansing all milk receptacles, etc., will go far to propagate tuberculosis. Considering that the results of the Royal Commission prove clearly that the fæces of the tuberculous cow are loaded with tubercle bacilli, the danger of infecting milk is considerable.

Further, another possible source of danger exists in the fact that cow dung mixed with urine and mud is used for plastering the walls, floors and roofs of houses. The nature of the

[1] Krantz (April 3, 1909), " Des résultats fournis par l'étude de la temperature pour le diagnostic précoce de la tuberculose." *Progrès. Méd.* Quoted in Epitome, *British Medical Journal*, November 20, 1909.

[2] Roberts, J. R. (August 1, 1910), " Some Features of Tuberculosis in India." *Journal Tropical Medicine and Hygiene.*

[3] Turner, J. A. (March 25, 1911), " Tuberculosis in India." *Lancet.*

Tuberculosis— *continued*

climate in India tends to counteract in some measure the danger by inhalation, and if the risk of infection by food and milk could be lessened the mortality now caused by the disease would be considerably lessened.

Cobbett,[1] after discussing at length the theories promulgated by Behring, and by Calmette and Guérin, as to the frequency and importance of intestinal infection in the causation of chronic pulmonary tuberculosis, describes in a paper the results of his experiments on the production of pigmentation of the lungs by feeding with Indian ink.

Under exceptional circumstances, when the minute carbon particles were mixed with dry powdery food this feeding caused pigmentation of the lungs and bronchial glands. In this case there was the obvious possibility of the entrance of the carbon particles directly through the air passage into the lungs. Otherwise in all his feeding experiments he failed to get pigmentary changes in the lungs or bronchial glands. Indian ink mixed with cream was not absorbed from the intestines. As the result of his experiments Cobbett is opposed to the theory that the intestine provides a common port of entry for the tubercle bacilli which cause phthisis.

Geilinger [2] has carried out a number of experiments in order to ascertain the best chemical disinfectant for sputum containing tubercle bacilli. As the result, phenol in a 3 per cent. to 5 per cent. solution was found to act efficiently and quite satisfactorily. Lysol in a 5 per cent. solution and cresol soap were less active in their bactericidal properties.

Rosenberger [3] has been successful in isolating the tubercle bacillus from the blood in various forms of tuberculosis. Out of 125 cases he obtained positive results in them all, and from his results concluded that in all forms of tuberculosis there is a bacteræmia. His technique was as follows :—

He took five cubic centimetres of blood from a vein in the arm, and immediately placed it in an equal quantity of normal saline solution containing 2 per cent. of sodium citrate. He shook the mixture well and placed it in a refrigerator for 24 hours. At the end of this time there were an abundant sediment and a slightly turbid solution. He removed some of the sediment with a pipette and placed it upon a slide which he dried with moderate heat, and then placed in distilled water until the blood was completely laked. Then only a delicate film remained. This was dried and fixed in a Bunsen flame, and stained for tubercle bacilli. As a rule, bacilli with the morphological and tinctorial characters of the tubercle bacillus could be found in the first slide so prepared, though in several cases three slides had to be searched before they were found. A negative result should not be concluded until at least 30 minutes are spent in the search. By cleaning with pure nitric acid and solution of caustic soda, every precaution was taken against contamination of the pipettes. The syringe was boiled and placed in caustic potash. Intimate mixture of the blood with the saline solution is essential lest any clotting occurs, for then the greatest difficulty is experienced in demonstrating the bacilli. He also examined the blood from the umbilical cord of children of tuberculous mothers and always found the bacilli. Sometimes only a few were seen, but usually there were large numbers, clumps of 30 or 40 bacilli being not unusual, especially in acute miliary tuberculosis. Most of the organisms were of normal size but some were short and even clubbed ; a few very long forms were also encountered. In several cases clumps of the bacilliwere observed in the leucocytes, indicating phagocytosis.

Anderson [4] and other observers have not confirmed the results obtained by Rosenberger. Rosenberger [5] also examined the fæces of 672 cases, and found tubercle bacilli in 19·6 per cent. The cases represented all varieties of tuberculosis, tubercle bacilli being found in cases of glandular enlargement, meningitis, hip-joint disease and in Potts' disease of the spine. He employed the following technique :—

If the fæces to be examined were fluid or semi-solid, a small quantity from any part of the stool was taken and spread on a slide, dried, and stained. When the fæces were solid, a small amount of sterile distilled water was put upon the slide and a small mass of fæcal matter added, mixed thoroughly, spread, dried, and stained. Not one of the specimens was centrifugalised.

In staining the preparation, carbol-fuchsin was applied for fifteen minutes in the cold, the excess drained off, and Pappenheim's solution poured on the preparation. This was allowed to act for two or three minutes, washed with water, and if the specimen was of a uniform blue colour it was dried and examined in cedar oil. If the preparation was not uniformly blue, Pappenheim's solution was applied and reapplied until the smear was blue. By observing this technique carefully, no mistake can happen regarding the diagnosis of the tubercle bacillus, as this organism and spores of other bacilli are the only bodies retaining the carbol-fuchsin stain. All other bacteria and cellular elements are stained blue. Great care must be taken lest some artifact be mistaken

[1] Cobbett, L. (1910), "The Portals of Entry of the Tubercle Bacilli which cause Phthisis." *Journal Pathology and Bacteriology*, Vol. XIV.

[2] Geilinger, H. (1909), "Experimenteller Beitrag zur chemischen Desinfektion des tuberkelbazillenhaltigen Sputums." *Arch. f. Hyg.* Quoted in *Journal Royal Institute of Public Health*, July, 1910.

[3] Rosenberger, R. C. (March 6, 1909), "The Constant Presence of Tubercle Bacilli in the Blood in Tuberculosis." *Lancet.*

[4] Anderson, J. F. (September, 1909), "The presence of Tubercle Bacilli in the circulating blood in clinical and experimental Tuberculosis." *Bulletin* No. 57. *Treasury Department, Public Health and Marine Hospital Service of the United States.*

[5] Rosenberger, R. C. (December, 1907), "The significance of Tubercle Bacilli in the Fæces." *American Journal Medical Sciences.*

Tuberculosis—*continued*

for the tubercle bacillus, such as a minute scratch in the glass, a small crystal, or the periphery of a cell. The organisms, as a rule, are comparatively few, in cases not plainly diagnosticated as tuberculous, but in well-marked cases of pulmonary or intestinal tuberculosis they are comparatively abundant. The finding of the tubercle bacillus in a spread is not always easy of accomplishment.

As a result of his investigations the following conclusions were arrived at :—

(1) No acid-fast bacillus other than the tubercle bacillus was found in the fæces.

(2) The presence of the tubercle bacillus in the fæces means that active tuberculosis exists somewhere in the body.

(3) In acute miliary tuberculosis the bacillus is always present in the fæces.

(4) In all cases of chronic diarrhœa and in cases of general glandular involvement, the fæces should be examined for tubercle bacilli.

(5) Finding tubercle bacilli in the fæces does not mean intestinal ulceration in all cases.

(6) In arrested or healed pulmonary tuberculosis no tubercle bacilli are found in the sputum or the fæces.

(7) The fæces should be studied for tubercle bacilli as a part of the routine examination, especially in suggestive cases, and when no expectoration can be obtained.

Dold [1] describes a rapid method for the detection of the tubercle bacillus in guinea-pigs inoculated with suspected tuberculous material. Before the operation of inoculation the inguinal lymphatic glands of the guinea-pig are taken between the thumb and the forefinger and squeezed by exerting pressure on the glands. The suspected material is then injected subcutaneously into each inguinal region. At the end of nine to twelve days the glands will enlarge to the size of a pea or a hazel nut, and if tubercle bacilli are present they are usually found in large numbers in the gland.

Lange and Nitsche [2] describe a method of demonstrating tubercle bacilli, by means of which even small numbers can be separated from other micro-organisms. The method is dependent on the fact that the surface tension of tubercle bacilli corresponds to that of some of the hydrocarbons. The procedure is as follows :—

A homogeneous emulsion of the sputum or other material containing tubercle bacilli is made with normal sodium hydrate solution, and this is shaken up with ligroin. On separating, the tubercle bacilli are carried up by means of the rising droplets of ligroin, and collect at the junction of the two liquids. Uhlenhuth previously described a method of separating tubercle bacilli by means of a liquid containing an alkaline hypochlorite and an alkaline hydrate. When ordinary micro-organisms are treated with solutions containing up to 20 per cent. of this liquid, which is known under the name of "antiformin," solution takes place; tubercle bacilli, however, are not attacked by the alkaline hypochlorite solution. G. Bernhardt (*Deut. Med. Woch.*, August 19, 1909) has combined these two methods and finds that excellent results can be obtained in this way. The sputum is rendered homogeneous by shaking up with four times its volume of a 20 per cent. solution of antiformin (for example, 3 c.cm. of sputum in a 20 per cent. solution of antiformin), and allowing it to stand until a completely homogeneous emulsion results. This takes from half-an-hour to several hours, according to the nature of the sputum. The process can be carried out in an ordinary graduated measure cylinder having a capacity of from 50 to 200 c.cm. A special stoppered cylinder graduated in c.cm. is still better. When the emulsion is homogeneous, from 1 to 3 c.cm. of ligroin is added. Previous to this, 25 c.cm. of tap-water may be added, but this is not necessary. The ligroin will form a layer above the fluid of from 3 to 5 mm. in depth. The whole is then shaken, a white emulsion resulting. On allowing the emulsion to stand, the ligroin rises in droplets to the surface. This can be accelerated by warming the cylinder in a water-bath at 60° C. When the ligroin has separated from the fluid sharply, the tubercle bacilli will be found in the layer between the two fluids, and may be gathered by means of a platinum loop. The loopful is spread on to a warmed slide, from which the ligroin rapidly evaporates, leaving the bacilli, often in surprisingly large numbers. The bacilli must then be fixed and stained as usual. The author points out that while the antiformin does not kill tubercle bacilli, they cannot withstand the action of the ligroin, which obviously dissolves the waxy coat. Tubercle bacilli treated with ligroin in the manner described above are no longer capable of infecting guinea-pigs.

Russ [3] has carried out an interesting piece of research work upon microbic electric reactions, and has made use of the application of this property of bacteria in separating the tubercle bacillus from urine. He found that certain bacteria tend to aggregate at one or other electrode when a suitable current is passed through a fluid in which they are suspended, and that when the current is reversed they move in an opposite direction. After repeated trials with a number of electrolytes, Russ obtained the best results with a mixture of ethylamine, lactic and bromic acids in certain proportions. By using a special form of electrode arranged so as to trap the bacilli when aggregated in its vicinity, he was able to recover tubercle bacilli from urines to which they had been added in such small numbers that previous attempts to prove their presence by centrifugalisation had failed. He considers that this method may be utilised for purposes of discriminating specific bacteria according to their differences of behaviour when exposed to these electric currents.

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[1] Dold, H. (September, 1908), "A Rapid Method for the Detection of the Tubercle Bacillus." *Journal Royal Institute of Public Health.*

[2] Lange, L., and Nitsche, P. (1909), "Eine neue Methode des Tuberkelbazillennachweises." *Deut. Med. Woch.*, quoted in Epitome, *British Medical Journal*, January 8, 1910.

[3] Russ, C. (July 3, 1909), "The Electrical Reactions of Bacteria applied to the Detection of Tubercle Bacilli in Urine by means of a Current." *Lancet.*

Tuberculosis— *continued*

Gasis [1] has detected a new quality of the tubercle bacilli, viz., that they are not only acid alcohol but also alkali-fast. He claims that they are the only bacilli that are alkali-fast. Based on these facts he has employed a new method of differential staining for the tubercle bacillus, which is as follows :—

(1) Preparation of the dye : To 5 c.c. of a 1 per cent. solution of eosin (1 gr. crystallised eosin, 5 c.c. absolute alcohol, 95 c.c. distilled water), a piece of corrosive sublimate of the size of a lentil is added, and the solution is gently boiled with constant agitation till the corrosive sublimate is entirely dissolved. The dye then assumes a brighter shade and a flocculent deposit is formed.

(2) The film preparation is now fixed and covered with the warm dye for one to two minutes.

(3) It is then washed in water and the decolorising solution (0·5 sodium hydrate, 1·0 potash iodide, 100 c.c. of 50 per cent. alcohol) poured on till the red colour is gone and a whitish-green colour appears.

(4) The decolorising solution is then removed by absolute alcohol.

(5) The preparation is then counterstained with a solution of methylene blue (1·0 crystallised methylene blue, 10 c.c. absolute alcohol, 0·5 c.c. hydrochloric acid, 9·0 c.c. distilled water) two to three seconds, and—

(6) Thoroughly washed in water, dried over a small flame, and mounted.

If after the washing in water the preparation appears yet red, the decolorising operation has to be repeated till it is quite decolorised. The tubercle bacilli appear, if successfully stained, bright red, all other elements (bacteria and cells) blue.

Kœgel [2] has a paper describing a method which he claims will show fifteen to thirty times more bacilli than any other process, and will give positive results where other methods fail. The procedure recommended is as follows :—

From 10 to 15 c.c. of sputum are mixed in a stoppered cylinder with half their volume of 0·6 per cent. sodium carbonate solution, and kept at 37° C. for twenty-four hours. The greater part of the liquid is then decanted and centrifugalised. The deposit thus obtained is treated with four times its volume of 0·25 per cent. sodium chloride solution and heated to boiling. When cold it is again centrifugalised, and the deposit is examined in the usual manner.

Merkel [3] has a paper on the use of antiformin for the histological diagnosis of tuberculosis, and the detection of the tubercle bacillus. Used in a solution of 15 to 20 per cent. it destroys all the other bacteria present in sputum or pus, leaving the tubercle bacilli morphologically intact. It is especially useful in dealing with tissues in which there are few tubercle bacilli, such as in the lymphatic glands in children, and also the tissues in lupus. In dealing with tissues Merkel and Heuner recommend that the tissues be cut up in a freezing microtome, as a temperature below zero has no effect on the tubercle bacillus, and then that a 15 to 20 per cent. solution of antiformin slightly warmed be added. The pieces of tissue dissolve at once. After centrifuging once or twice with distilled water the sediment is ready for microscopical examination. In order to make a good film, proteid glycerine mixture is added to the sediment. Sections previously fixed in alcohol, embedded in paraffin, can be cut and treated by this antiformin method.

Krueger [4] has found antiformin useful in detecting the causal organism of lupus, when it exists as *Much's* form, in which the tubercle bacilli are present in the shape of granules, which do not stain by Ziehl's method.

Alexander [5] carried out an extensive investigation on the acid-fast bacteria met with in human fæces, and came to the same conclusion as Rosenberger, who, as already mentioned, found that all acid-fast bacilli in the fæces are tubercle bacilli. Alexander found there was an intermittency in the appearance of tubercle bacilli in the fæces which, he considered, may be connected with the flow of bile ; an explanation which is supported by the action of the cholagogue, calomel.

Levy [6] tested Gasis' method with tuberculous sputum, and with pure cultures of the tubercle bacillus, and found that the bacilli appeared as light red-coloured rods on a greenish-blue background. There was no evidence of the existence of spores when this method of staining was employed. Smegma bacilli are stained from a blue or violet to a red colour ;

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[1] Gasis, D. (1909), " Über eine neue Reaktion der Tuberkelbazillen und eine darauf begründete differential-diagnostische Färbungsmethode derselben." *Cent. f. Bakt.*, I. Orig., Vol. L., pp. 111–128.

[2] Kœgel, H. (1909), " Über den Nachweis von Tuberkelbazillen im Sputum nach der Doppelmethode von Ellermann-Erlandsen." *Deut. Med. Woch.*

[3] Merkel, H. (March 29, 1910), " Der Tuberkelbazillennachweis mittelst Antiformin und seine Verwendung für die histologische Diagnose der Tuberkulose." *Münch. Med. Woch.*

[4] Krueger (May 31, 1910), " Über den Nachweis des Tuberkulosevirus in Lupus vulgaris durch die Antiforminmethode." *Ibid.*

[5] Alexander, D. M. (April, 1910), " An Investigation into the Acid-Fast Bacteria found in Human Fæces, with special reference to their Presence in Cases of Tuberculosis." *Journal of Hygiene.*

[6] Levy, M. (1910). *Cent. f. Bakt.*, 1, *Ref.*, Vol. LV.

timothy grass bacilli and some acid-fast bacilli of urine were stained partly red and partly blue, and certain grass bacilli and bovine pseudo tubercle bacilli were stained red.

Tuberculosis—*continued*

Goodman [1] describes a useful technique for making the examination of sputum for tubercle more certain. The object of his method is to convert the sputum into a homogeneous mass of a thin liquid consistency from which the organism can be thrown down in a compact mass ; in other words to enrich the sputum with tubercle bacilli. The enriching solution used by him is prepared as follows :—

One hundred and fifty grammes of chlorinated lime are thoroughly triturated with 200 c.cm. of water, added gradually until a uniform mixture results. This mixture is allowed to stand for a short time, and until all the heavier particles have subsided. The supernatant fluid is then filtered off. The residue on the filter is treated with 200 c.cm. of water, and the mixture is poured on to a filter. The residue now on the filter is washed with 100 c.cm. of water, and the filtrate added to the others. The filtrates being mixed, 150 grammes of sodium carbonate, dissolved in a small quantity of warm water, are added. The mixture is stirred thoroughly, and if it should become gelatinous, is warmed until it liquefies. It is then filtered, and the residue on the filter is washed with sufficient water to make the filtrate-product up to one litre. Thirty grammes of sodium hydroxide are then added. The mixture is stored in brown glass bottles, and kept away from sunlight. Goodman's solution yields 6·57 of available chlorine per cent., and contains 3 per cent. of sodium hydroxide.

For diagnostic purposes equal volumes of the sputum and solutions are mixed and kept over a water bath. When the sputum has become homogeneous after from twenty to fifty minutes' heating, a small quantity of water is added to the emulsion, and then this is thoroughly centrifuged. The sediment is then smeared on slides in the usual manner and stained in the ordinary way.

Philip and Porter [2] have applied Uhlenhuth and Xylander's [3] antiformin method for the examination of tubercle bacilli in fæces. Their procedure is as follows :—

A small piece of fæces, about a cubic ½ in. in size, is placed in a conical glass, and to this some 20 c.cm. of antiformin, which has been diluted with water to 15 per cent. is added. The fæcal matter is well broken up and mixed with the fluid, and thereafter as much again of the dilute antiformin solution is added. This is further mixed, and allowed to stand for about an hour. A white curdy precipitate appears on mixing, and in the course of an hour settles into a white layer which varies in breadth. Beneath the white layer some unchanged fæcal matter remains, and above the white layer the fluid is of a clear yellow or brownish colour. A residue, including tubercle bacilli, which have been set free by the destruction of the other constituents of the fæces, appears to be gathered into the white layer by a process of sedimentation. During the precipitation and sedimentation of the organic matter the bacteria are carried down, perhaps in some degree agglutinated. This concentration of the organisms makes up for the disadvantage caused by the initial dilution of the material. For microscopic examination a drop is then taken from the white curdy layer by means of a pipette and placed at the end of a slide, along with a drop of albuminous water from a mixture containing 1 part of egg albumin to 10 of distilled water and 1 per cent. of formalin, and 90 per cent. of distilled water is added. A film is made in the usual way by drawing out the fluid with a second slide along the surface of the first.

The action of the antiformin seems to be chiefly exerted during the first hour, so that according to Philip and Porter there seems to be no reason to continue the process for more than that time. The prepared slides are fixed by heat and stained in the usual way with carbol-fuchsin and methylene-blue, and then decolorised with both acid and alcohol.

Jacobson [4] has carried out a series of experiments on the diagnosis of tuberculosis by deviation of the complement by Marmorek's [5] method. Jacobson's results show that when very small quantities of complement are used Marmorek's method is rendered more sensitive and is therefore useful in the diagnosis of latent or localised tuberculosis, even when the degree of intoxication is not sufficient to cause general symptoms, as there may be sufficient antigen circulating in the blood and excreted with the urine to enable a diagnosis to be made.

The question of tuberculosis in monkeys has been carefully studied by Rabinowitsch,[6] who found that monkeys in captivity could be infected with any of the types of tubercle bacilli according to the circumstances attending their environments.

Mention may be made of some feeding experiments carried out by Trotter [7] on nine

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[1] Goodman, E. (July 2, 1910), "A Method of Examining Sputum for Tubercle Bacilli." *New York Medical Record.*

[2] Philip, R. W., and Porter, A. E. (July 23, 1910), "Tubercle Bacilli in the Fæces in Tuberculosis." *British Medical Journal.*

[3] Uhlenhuth, P., and Xylander, R. C. (July 20, 1908), "Antiformin, ein bakterienawflösendes Desinfektionsmittel." *Berl. Klin. Woch.*

[4] Jacobson, D. (1910), "On the Diagnosis of Tuberculosis by Deviation of the Complement." *C. R. Soc. Biol.*, Vol. LXVIII.

[5] Marmorek, A. (1909), "Diagnostic de la tuberculose par la méthode de la déviation du complément." *Presse Méd.*

[6] Rabinowitsch, L. (1907), "Über spontane Affentuberkulose, Ein Beitrag zur Tuberkulosefrage." *Virchow's Arch. f. Path. Anat.* Quoted in Epitome, *British Medical Journal*, October 10, 1908.

[7] Trotter, A. M. (September 30, 1910), "Feeding experiments with the fæces of tuberculous cows." *Journal Comparative Pathology and Therapeutics.*

Tuberculosis—*continued*

guinea-pigs. These animals were fed with cows' fæces heavily infected with tubercle bacilli. The guinea-pigs were killed at varying intervals, and only in one case did the test animals contract the disease. Milter considers that the administration of fæces to guinea-pigs *per os* is not a reliable method of determining whether a cow is affected with open tuberculosis and passing fæces contaminated with tubercle bacilli.

Whitmore [1] has recently published the results of treatment of a hundred cases of pulmonary tuberculosis with various "specifics," such as tuberculin—given by the mouth and hypodermically—succinimide of mercury, atoxyl, and cinnamate of mercury. These specifics, however, proved to be of no value in the treatment of pulmonary tuberculosis in natives of the Philippines.

In conclusion, mention may be made of an excellent English translation of a monograph by Bandelier and Rœpke,[2] entitled *Tuberculin in Diagnosis and Treatment.* The book will be found to be an indispensable *vade mecum* to all concerned with the diagnosis and treatment of tubercular disease. It summarises all the results of importance in a field, the literature of which is so enormous and so scattered as to be difficult of access.

Additional Notes

Magill [3] in a very interesting paper discusses all the latest methods employed in diagnosing tubercular infection. Among them he mentions (1) Use of tuberculin. (2) The Pfeiffer serum agglutinating reaction. (3) The appearance of lecithin substances in the blood of tubercular patients.

Mangeri [4] has examined sputa for tubercle bacilli by different methods, and concludes that the antiformin method gives the best results.

The author's method is as follows:—Into a test tube of about 50 c.cm. capacity he pours 5 c.cm. of sputum and adds 25 c.cm. of antiformin solution diluted from 10 to 20 c.cm. according to the density of the sputum, shakes well until the whole is homogeneous (about a quarter of an hour), then centrifuges, washes three times with physiological solution, centrifuging after each washing, dries the sediment on a slide, and stains with Ziehl's solution.

Pekanovitch [5] describes a new method of demonstrating tubercle bacilli in sputum:—

The method is a modification devised by the author of the antiformin treatment of sputum recommended by Uhlenhuth and Xylander in 1908. Shaking up sputum with antiformin renders sputum homogeneous, and provided that the contact is not too protracted the virulence and staining peculiarities of the bacilli are not affected. Uhlenhuth recommended centrifugalisation of the mixture to obtain the deposit, but this is not always convenient, because to be effective centrifugalisation must be carried out at a rate of at least 4000 revolutions per minute, and a hand centrifugaliser is therefore not available. The author has made considerable use of Bernhard's and Haserodt's modification of the antiformin method. In this the sputum, after being rendered homogeneous by preliminary treatment with four times its volume of 20 per cent. antiformin, is shaken up with ligroin, and the mixture allowed to stand for from half to one hour. The ligroin separates out from the sputum, and appears above it in two layers, the upper one clear, the lower greyish and turbid. The bacilli are found in the lower layer, and the author employs a very fine pipette for removing the material on to cover-glasses for examination. The results obtained compare very favourably with those of the usual method of examination of loopfuls of sputum. Thus in a series of a hundred cases, positive results were obtained in eight cases which had given negative ones by the other method. The bacilli appear to be present in greatest numbers in the layer just above the antiformin. Careful fixing is necessary and the author carries out Lagreze's recommendation of treating the preparation for one to one and a half minutes with 3 per 1000 sublimate solution, and decolorising with 3 per cent. hydrochloric acid alcohol. The disadvantages of the antiformin and ligroin method are that it is tedious and needs care and expertness in carrying out, and that both antiformin and ligroin have an effect upon the staining capacity of the bacilli. The author has devised a further modification of the method, based upon the fact that antiformin oxidises organic matter by the virtue of the sodium hypochloride which it contains, and that the process of oxidisation, if carried too far, injures the vitality and staining capacity of the bacilli. To check oxidisation, as soon as solution of the sputum has been obtained lead acetate is added, and forms a precipitate of lead sesquioxide if an excess of sodium hypochloride is present, and otherwise leads to the formation of sodium acetate, which acts as an indifferent body, and does not aid oxidisation. The method is as follows:—20 per cent. antiformin is added as before, and the mixture is shaken up with sputum until solution occurs, the process being hastened, if necessary, by slightly heating the flask over a flame. After cooling, 30 per cent. lead acetate is added until the characteristic white flocculent precipitate is brought down. An excess of lead acetate is desirable. Centrifugalisation is the readiest method of obtaining the deposit, which is transferred to cover-slips, stained, and examined. The results obtained by this method were always positive, except in one instance in which a suspicion only of tuberculosis existed, and in which repeated examinations by ordinary methods gave negative results. The whole examination on these lines can be carried out easily and rapidly, and the fixing of the specimen presents no difficulty.

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[1] Whitmore, E. R. (December, 1910), "Tuberculosis in the Philippines: Final result of one year's specific treatment of eighty cases of Pulmonary Tuberculosis." *Philippine Journal of Science*, B.

[2] Bandelier and Rœpke (1909), *Tuberculin in Diagnosis and Treatment.* Translated from the second German edition by E. C. Morland.

[3] Magill, W. S. (April 22, 1911), "New Methods in Diagnosis and Treatment of Infectious Diseases." *Medical Officer.*

[4] Mangeri (February 27, 1911), "Antiformin Methods in Examination of Tuberculous Sputum." *Rif. Med.* Quoted in Epitome, *British Medical Journal*, April 29, 1911.

[5] Pekanovitch, S. (1910), "Demonstration of Tubercle Bacilli in Sputum." *Pest. Med.-Chir. Presse.* Quoted in Epitome, *British Medical Journal*, May 20, 1911.

Lloyd[1] has an interesting paper entitled "Suggestions for Controlling Tuberculosis among Food Animals." He recommends that the following measures should be carried out :— Tuberculosis—*continued*

(1) An order by the Board of Agriculture compelling compulsory notification, investigation and slaughter of dangerously infective tuberculous animals—that is, animals affected with "open" tuberculosis, with compensation according to carcase value, and prosecution for failure to notify.

(2) Pecuniary assistance by the State to owners of stock who are willing to attempt the production of tubercle-free herds, and agree to carry out requirements considered necessary to obtain success, special consideration being given to the production of tuberculin, free testing, segregation, sanitary buildings, disinfection, etc.

(3) Experiments in vaccinating young animals against tubercular infection to be carried out by, and at the expense of, the State.

Typhus Fever. A considerable amount of important work has been recently carried out on this disease, and many new and interesting facts have been established.

An outbreak of typhus fever in a certain district of Tunis afforded Nicolle[2] an opportunity of prosecuting some interesting pathological researches. He was successful in inoculating a chimpanzee with 1 cubic centimetre of blood removed from a case of typhus fever on the third day of the disease. After an incubation period of twenty-four days the ape developed a typical attack of typhus fever, with a febrile period lasting seven days. From the blood of this animal Nicolle successfully produced the disease in a bonnet monkey after an incubation period of thirteen days.

In collaboration with Conor he carried out further investigations. Another bonnet monkey was infected fourteen days after inoculation with blood taken from the first one on the second day of the disease, and a third monkey of the same species after a similar inoculation developed the disease without showing any incubation period.

Dogs and white rats proved to be immune as well as some *macacques* such as the *Macacus cynomolgus, M. rhesus* and *M. inuus*. The serum of a bonnet monkey convalescent from the disease produced a definite toxic action when injected into healthy monkeys. In conjunction with Comte and Conseil, Nicolle made some interesting observations which tend to prove that the human body louse is a possible agent in the dissemination of the disease. Body lice collected from healthy men and allowed to feed on monkeys infected on the third day of the disease were subsequently allowed to feed on two other monkeys of the same species, and the latter contracted the disease.

Nicolle also made some interesting observations in collaboration with Jaeggy on the blood of experimentally infected monkeys. The blood showed an increase in the total number of leucocytes towards the end of the incubation period, a diminution during the disease with a relative increase in the lymphocytes associated with the presence of myelocytes. The polymorphonuclear neutrophiles exhibited a necrosis. This necrosis possibly accounted for the liberation of non-specific agglutinins which are present in typhus fever cases. As illustrative of this, Nicolle and Comte found that the serum of typhus fever patients frequently agglutinated the *Micrococcus melitensis* and the *B. typhosus*.

Wilson,[3] in a long and interesting paper on the etiology of typhus fever, arrived at the following conclusions :—

(1) A relative increase in the large mononuclear leucocytes, especially towards convalescence, was very characteristic of the blood in typhus fever.

(2) During the febrile period the eosinophile cells were absent, or very scanty in numbers. In two cases an eosinophilia was observed during convalescence.

(3) The blood of 33 different cases was examined by cultural methods. In 18, no growth of micro-organisms occurred, whilst in 15, characteristic diplococci were cultivated. These diplococci were agglutinated by the blood serum, and the agglutinins could be removed from the serum by saturating it with the cocci.

(4) From the fæces of one case a variant form of *B. coli communis* was cultivated, on which the blood serum of 17 typhus fever cases was found to have 3 to 10 times the agglutinative effect of normal serum.

(5) From the urine of two cases a bacillus resembling *B. coli communis*, but having no action on lactose, was cultivated. This bacillus was agglutinated in dilutions of 1·50 and 1·100 by the serum of the cases, but not by normal serum.

(6) The facts established by Anderson and Goldberger, which showed that the virus of typhus fever was present in blood which afforded no growth on ordinary media, suggest that the above micro-organisms are secondary invaders.

(7) Of 35 cases examined the blood serum of 19 gave a positive Widal reaction with the *B. typhosus*. Hence this reaction was of little or no value in differentiating typhus from typhoid fever.

[1] Lloyd, J. S. (June, 1911), "Suggestions for Controlling Tuberculosis among Food Animals." *Journal Royal Institute of Public Health.*

[2] Nicolle, C. (April 25, 1910), "Recherches expérimentales sur le Typhus Exanthématique." *Ann. de l'Inst. Past.*

[3] Wilson, W. J. (August, 1910), "The Etiology of Typhus Fever." *Journal of Hygiene.*

Typhus Fever—*continued*

Pignet [1] carried out a number of experiments on guinea-pigs and rabbits. Lice that were previously fed on a typhus case were subsequently fed on guinea-pigs. The latter died after varyingi ntervals ; the only pathological lesion present being congestion of the lungs. A similar experiment on a rabbit caused the death of that animal in 30 days with intense congestion of the lungs and liver, hyperæmia of the intestines and the presence of blood-stained fluid in the peritoneal cavity. Further experiments were conducted by this observer, and in almost all cases the constant lesion present was a congestion of the lungs. Symptoms of paraplegia were produced in rabbits as the result of subcutaneous inoculation with infected blood. A point of interest in these animal experiments was the fact that frequently effusions of blood occurred in the psoas muscle, a complication sometimes present in typhus fever.

Conseil,[2] in an interesting paper, has described the epidemic of typhus fever in Tunis in the year 1909. His observations tend to confirm the rôle played by biting insects in transmitting this disease, which was almost exclusively confined to the poorer and vagrant classes of Tunis.

Anderson and Goldberger [3] experimented with two species of monkeys, *Macacus rhesus* and *Cebus capuchinus*, and found that the blood from cases of typhus fever met with in Mexico was capable of producing a characteristic fever in these animals after an incubation period of five to eleven days. Passage experiments gave further support to their view that they were dealing with a virus which was capable of further multiplication. As a result of their investigations in Mexico city these observers were inclined to consider that lice were the transmitting agents of this disease. They endeavoured to infect monkeys by means of lice but their experiments in this direction failed.

Nicolle,[4] in a further series of investigations on typhus, obtained some interesting and very important results. He found that the serum of convalescent typhus cases was endowed with prophylactic and curative properties when used either for prophylaxis or for the treatment of typhus, thus confirming the observations previously made by Legrain [5] and Raynaud.[6] The serum should be given in doses of twenty cubic centimetres, and repeated if necessary. In grave cases of typhus it may be given with advantage by the intravenous method. Nicolle arrived at his conclusion by experiments on infected monkeys and on cases of typhus fever. He found that the serum showed these curative properties for ten to twelve days after the temperature had fallen. Animals that had recovered from the disease also contained these specific properties in their sera.

Nicolle,[7] continuing his investigations, compared the virulence of unfiltered serum obtained by centrifuging defibrinated blood with the virulence of serum obtained after the blood had coagulated. He found that the former serum was invariably virulent, while it was somewhat rare to find the latter showing any virulence. In Nicolle's paper a very full résumé of the result of his researches is given. He examined the blood of infected monkeys at all stages of the disease and was never able to find any micro-organism that could be considered pathogenic. In one of his experiments the serum obtained by coagulation was passed through a Berkefeld filter, and showed both virulent and immunising properties for the bonnet monkey. From this result Nicolle considers that the specific agent of typhus is an organism capable of passing through a filter, and in all probability is intra-cellular. Some experiments carried out to test the action of heat on the virus of typhus showed that a temperature varying from 50° to 55° was sufficient to destroy the virus. Blood serum showed no bactericidal action on the virus in nine hours at a temperature of plus 12 degrees. As the result of the various lice-feeding experiments that were instigated, Nicolle concluded that the bite of the louse was effective in transmitting the disease from the fifth to the seventh day after it had fed on infected blood.

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[1] Pignet, M. (December 8, 1909), "Essais d'inoculation du typhus exanthématique aux petits animaux de laboratoire." *Bull. Soc. Path. Exot.*

[2] Conseil, E. (1910), "Le Typhus exanthématique en Tunisie." *Arch. de l'Inst. Past. de Tunis.*

[3] Anderson, J. F., and Goldberger, J. (February 18, 1910), "On the infectivity of Tabardillo or Mexican Typhus for Monkeys, and studies on its mode of transmission." *Public Health Reports*, Vol. XXV., *Public Health and Marine Hospital Service, U.S.A.*

[4] Nicolle, C. (January 25, 1911), "Recherches expérimentales sur le typhus." *Ann. de l'Inst. Past.*

[5] Legrain, E. (January 19, 1895), "Sur les propriétés biologiques du sérum des convalescents de typhus exanthématique." *C. R. Soc. Biol.*

[6] Raynaud, L. (1896), "Essais de sérothérapie contre le typhus exanthématique." *Travail Couronné par l'Academie des Sciences* (prix Barbier, 1896).

[7] Nicolle, C. (February 25, 1911), "Recherches expérimentales sur le typhus exanthématique." *Ann. de l'Inst. Past.*

Typhus Fever—*continued*

Gobert [1] has a short paper on the prophylactic measures to be employed amongst natives during a typhus epidemic, especially where disinfection by sulphur is not practicable. The infected localities should be closed for a month and the lice removed from the inhabitants. All the huts should be closed and burnt, and the natives be given an indemnity.

Morsby [2] appears to have had excellent results in the treatment of typhus fever by giving injections of the essence of turpentine into the thigh or buttock of the patient. This procedure was followed by the formation of an abscess which was opened after pus had formed. With this method of treatment eighty-eight per cent. of recoveries occurred.

The diagnosis of typhus fever has in some cases been rendered difficult by the fact that the blood serum has shown agglutinative reactions for the *B. typhosus* and for the *M. melitensis*. Wilson,[3] Nicolle and Comte [4] and other observers have noted this.

Ricketts and Wilder [5] in a recent paper consider the relation of typhus fever to Rocky Mountain spotted fever. These two diseases differ in point of view of transmission, for the former is in all probability conveyed by the louse, while the latter is transmitted by means of a tick; further, the guinea-pig is susceptible to spotted fever, but not to the virus of typhus. Agglutination tests carried out against the bacillus isolated by Ricketts in cases of spotted fever might help to differentiate these two diseases.

As regards the etiology of typhus fever, various observers have isolated different organisms. Ricketts and Wilder [6] obtained from the blood of typhus cases in Mexico, bacilli resembling those found in hæmorrhagic septicæmia. As already noted, Wilson [7] has isolated Gram-positive diplococci from the blood of typhus cases in Belfast. Similar diplococci were also obtained by Stanichevskaja.[8] Predtjetschevsky [9] has recently isolated from the blood of typhus cases on the sixth to the ninth day of the disease a short Gram-negative and non-motile bacillus. This bacillus was also present in large numbers in the sputum. In various culture media, involution forms of this bacillus appeared. On sloped agar the cultures resembled diplococci. The serum of typhus cases showed agglutinin reactions with pure cultures of this short bacillus. The highest agglutination reaction was obtained in a dilution of 1·40 in four hours.

Additional Notes

Mention may be made of a paper by Dreyer [10] dealing with typhus in Egypt, and to one by Conseil [11] referring to the typhus epidemic in Tunis during the year 1910. The epidemic in Tunis was less severe than in former years owing to the rigorous measures adopted in dealing with the foci of infection. The establishment of isolation camps and observation posts on caravan routes where measures were adopted for destroying the ecto-parasites infesting the bodies and garments of the travellers, went far to assist in arresting the spread of infection.

Vaccination. The effect of temperature on calf vaccine is a matter of economic and scientific importance, as it is well known that the potency of a vaccine is very liable to deteriorate in the Tropics.

Green [12] has carried out some experiments to test the influence of temperature and other

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[1] Gobert, E. (December 14, 1910), "Note sur la prophylaxie du typhus en milieu indigène." *Bull. Soc. Path. Exot.*

[2] Morsby, T. (October 13, 1909), "Nouveau traitement du typhus exanthématique par les abcès de fixation." *Bull. Soc. Path. Exot. Ibid.* (March 9, 1910). *Ibid.* (July 13, 1910).

[3] Wilson, W. J. (August, 1910), "The Etiology of Typhus Fever." *Journal of Hygiene.*

[4] Nicolle, C., and Comte, C. (April 13, 1910), "Sur la présence fréquente d'un pouvoir agglutinant vis à vis du '*Micrococcus melitensis*' dans le sang des malades atteints de typhus exanthématique." *Bull. Soc. Path. Exot.*

[5] Ricketts, H. T., and Wilder, R. (April, 1910), "The relation of Typhus Fever to Rocky Mountain Spotted Fever." *Archives of Internal Medicine.*

[6] *Idem* (April 23, 1910), "The Etiology of Typhus Fever." *Journal American Medical Association.*

[7] Wilson, W. J. (August, 1910), "The Etiology of Typhus Fever." *Journal of Hygiene.*

[8] Stanichevskaja, M. (1905), "Recherches bactériologiques du sang au cours du typhus exanthématique." *Russk. Vrach.*, Vol. IV., quoted in *Journ. de Physiol. et de Pathol. Générale*, 1906, VIII., p. 365.

[9] Predtjetschevsky, W. (July 9, 1910), "Zur Frage über den Flecktyphuserreger." *Cent. f. Bakt.*, I. Orig., Vol. LV., No. 3.

[10] Dreyer, W. (May, 1910), "Untersuchungen über den Typhus exanthematicus in Ägypten." *Arch. f. Schiffs-u. Tropen-Hygiene*, Vol. XV., No. 10.

[11] Conseil, E. (1911), "Le Typhus exanthématique en Tunisie pendant l'année 1910." *Arch. de l'Inst. Past. de Tunis.*

[12] Green, A. B. (September, 1908), "The influence of Temperature and some other Physical Conditions on Calf Vaccine." *Journal of Hygiene.*

Vaccination—*continued*

physical conditions on calf vaccine. As a result of these this observer found that dried powdered calf vaccine in sealed glass capillary tubes still retained its potency after exposure to a temperature of 100° C. for from five to ten minutes. Expressed calf lymph and lanolinated calf lymph lost their potency after exposure for one minute to a temperature of 99° C. to 100° C.

Hutchinson [1] has a useful paper on the preparation and use of calf vaccine in India. This observer is in favour of glycerinated calf lymph as opposed to lanolinated; although the latter is kept in a better state of preservation the bactericidal power of the lanoline is practically negative, for bacteria usually developed and multiplied in the lymph made up with lanoline. The vaccine is sterilised by the passage of chloroform vapour through the glycerinated vaccine emulsion for a period of two hours during the monsoon weather, and two and a half to three hours during the dry weather. If any bacteria remain they are usually killed by the action of the glycerine during storage for 7–14 days at a temperature of 15° C.

Voigt [2] has compared the efficacy of the lanolinated and glycerinated vaccine, and notes that the former retains its potency for a longer period than the latter, although its bactericidal powers are considerably less. He found that a vaccine made up with vaseline was unsatisfactory, as the number of micro-organisms increased from week to week.

Achalme and Phisalix [3] show that a vaccine dried "en masse" is the most suitable for use in tropical climates, as it retains its potency and is in a suitable form for transport. The method of desiccation recommended is as follows:—A thirtieth of a gramme of the raw vaccine, obtained by scraping the pustules on heifers, is rapidly dried on porous plates in a vacuum in the presence of sulphuric acid. After twelve hours the desiccation is completed and the material now consists of horny, brittle, irregular masses which are put into sealed tubes containing a partial vacuum. These observers have noted that this dried vaccine retains its qualities longer when kept in masses than when in powder, and also when in a vacuum than when in contact with the air.

When required the vaccine is made up into a pulpy mass, either with normal saline, sterile water, or with water containing glycerine, and forms a ready emulsion with these liquids very suitable for inoculation.

Voigt [4] has recently carried out a series of investigations on the production and efficacy of cow-pox lymph derived by transmission through the dromedary. He made a series of comparisons of the results obtained by vaccination with ordinary calf lymph and with lymph obtained from the vesicles on a dromedary, and found the results practically identical; in some cases he obtained better results by using the strain from the latter animal. The dromedary is in no way affected during the process, and the lymph obtained was efficacious both for primary vaccination and re-vaccination. This being so, the dromedary would be a most useful animal as a provider of vaccine lymph in the Tropics, especially in those parts where calves are difficult to obtain, or where they are liable to disease.

Walton [5] and Spong [6] have published practical papers on the procedure and technique of vaccination of recruits in the army. The former observer favours a point two inches below the elbow on the outer side of the forearm as the inoculation site. This site, however, is certainly open to a few objections.

Mention may be made of a new vaccinating instrument devised by Isambert.[7] It consists of a piece of steel, at the end of which are two sharp prolongations which can only penetrate the skin to a limited extent when slight pressure is applied.

Répin [8] has discovered a method of preserving lymph vaccine which will be of use in tropical climates. This observer, after trying various reducing agents, found that apomorphine and tyrosinase gave the best result. The best form of tyrosinase is obtained from mushrooms of the family *Ruosules*, notably *R. delica*, *R. emetica*, and *R. queleti*. A glycerinated emulsion of these mushrooms is prepared. To three cubic centimetres of vaccine pulp a cubic

[1] Hutchinson, F. H. G. (1909), "Preparation, Distribution and use of Calf Vaccine in the Tropics." *Transactions Bombay Medical Congress.*

[2] Voigt, L. (1909), "Expériences sur la conservation du vaccin." *Réunion des Directeurs des Instituts de Vaccine Allemands.* Quoted in *Bull. de l'Inst. Past.*, August 15, 1909.

[3] Achalme, P., and Phisalix, M. (July 21, 1909), "Contribution à l'étude de la conservation du vaccin dans les pays chauds." *Bull. Soc. Path. Exot.*

[4] Voigt, L. (1910), "Der Transport wirksamen Kuhpockenimpfstoffes in das Innere der Afrikanischen Kolonien auf lebenden Tieren, z. B. den Dromedaren." *Cent. f. Bakt.*, I. Orig., Vol. LIII., No. 2.

[5] Walton, H. B. G. (April, 1909), "Vaccination." *Journal Royal Army Medical Corps.*

[6] Spong, W. A. (September, 1909), "On Vaccination." *Journal Royal Army Medical Corps.*

[7] Isambert (January 13, 1909), "Nouveau Vaccinateur." *Bull. Soc. Path. Exot.*

[8] Répin (March 9, 1910), "Un procédé de conservation du vaccin." *Ibid.*

centimetre of the glycerinated emulsion is added, and also a cubic centimetre of a concentrated solution of tyrosinase. It is advisable previously to take up the proteid material present in the pulp by first adding normal salt solution. Vaccination—*continued*

Répin has found that a vaccine so prepared retains its virulence for 12 to 16 days at a temperature of 38°, while the ordinary glycerinated vaccine retains its virulence at that temperature for 4–5 days.

Neveux,[1] as a result of animal experiments, ascertained that the monkey was a suitable animal to use as a vaccine purifier, and suggests the use of this animal when it is impossible to obtain rabbits. He found that the higher apes gave better results than the lower ones.

Proca [2] has carried out some work with the micro-organism of vaccinia (*Cladothrix vaccinæ*). He found that this cladothrix could pass through filters, was very polymorphic, and bore a striking resemblance to the bodies of Guarineri; some forms were almost of a bacillary type. Cultures inoculated under the skin produced lesions and intravenous inoculation in rabbits produced petechiæ in the ears. When the bacillary forms were injected into the anterior chamber of the eye an ulcerative keratitis occurred.

Wasserman [3] describes a new method of vaccination by means of a special instrument shaped like a chisel with a sharp point. After the arm is cleaned the lymph is applied to the surface and the chisel is then pointed perpendicularly to the skin and pressed against it by a few rotatory movements. An abrasion is produced, and a minimum amount of vaccine virus is implanted. Within a minute a typical reddish urticarial papule is formed. Only the superficial layers of the epidermis are removed, and no blood oozes from the scarified skin surface when this method is employed.

As the method of keeping vaccine by cold storage is employed in various parts of the Tropics, the results obtained by this procedure, as recorded in the report [4] of the medical officer to the Local Government Board, London, will be of interest:—

The Medical Officer of the Local Government Board reports that during the past twelve months 400,820 charges of glycerinated calf lymph were issued from the Board's laboratory. In primary vaccination the "case-success" was 99·4 per cent., and the "insertion-success" 95·9 per cent., so that the high quality of the lymph was maintained. Some time ago a preliminary report by Dr. Blaxall and Mr. Fremlin was published on the results of sustained subjection of glycerinated calf lymph to temperatures below freezing-point, and the present report contains further information dealing with lymph kept in cold storage for periods of two years, and six months respectively. The two-year-old lymph when withdrawn from cold storage was found to be free from extraneous organisms, and when used by public vaccinators in the vaccination of 8,559 cases gave "case" and "insertion" percentage successes of 97·8 and 91·4 respectively. The lymph from six calves in all was used, and in only one of these instances, explicable apart from the cold storage, did the lymph in any degree lose its activity. Since July 1908 the lymphs collected weekly from two calves have been divided into equal portions, one portion being placed in cold store for six months, and then issued to public vaccinators, the other portion being issued to public vaccinators without having been previously subjected to a temperature below freezing-point. The communication by Dr. Blaxall and Mr. Fremlin contains a comparison of the results of the use of lymph from 54 calves, which were each thus divided into two portions. The samples which had been exposed to a temperature below freezing-point for six months were used for 40,931 vaccinations, and gave a case success of 99·6 per cent., and an insertion success of 96·7 per cent. The portions issued without cold storage at the end of six to eight weeks were used for 44,962 vaccinations, and gave a case success of 99·5 per cent., and an insertion success of 96·5 per cent. Thus the results obtained in both cases are identical. These results have considerable importance, since cold storage will enable a supply of lymph to be prepared and stored to meet any sudden expansion in the demand for lymph that may arise by reason of an outbreak of small-pox.

Additional Notes

Two papers referring to this subject have recently been published, one by Schilling,[5] who carried out some researches on vaccination in the sheep, and the other by Ross,[6] advocating the use of dried vaccine in tropical countries. Ross prepared this vaccine according to the methods recommended by Achalme and Phisalix (*loc. cit.*), viz., by drying it over sulphuric acid in a partial vacuum, and distributing it in tubes which were also sealed in a partial vacuum. Prepared in this manner the vaccine could be kept at room temperature for several months without seriously deteriorating, and the results obtained by its use in East Africa, where it was supplied to distant and hot out-stations were so excellent that Ross strongly advocates its use in all tropical countries.

[1] Neveux (October 12, 1910), "Emploi du singe comme animal de passage pour purifier le vaccin." *Bull. Soc. Path. Exot.*

[2] Proca, G. (May 30, 1910), "Essais de culture du micro-organisme de la vaccine." *Bull. de l'Inst. Past.*

[3] Wasserman, S. (September 17, 1910), "New method of Vaccination." *Journal American Medical Association.*

[4] (June, 1910), "The Effects of Cold Storage on Vaccine." *Indian Medical Gazette.*

[5] Schilling, C. (March, 1911), "Übertragungsversuche von Vakzine auf das Schaf." *Arch. f. Schiffs-u. Tropen-Hygiene,* Vol. XV., No. 9.

[6] Ross, P. H. (May 10, 1911), "Some Experiments with Vaccine prepared According to the Method of Achalme and Marie Phisalix." *Bull. Soc. Path. Exot.*

Vermin. Since the publication of the last Review, the subject of vermin has received so much attention that it has been considered worthy of a separate heading. The study of recent work may, however, be here somewhat curtailed, as many important points have been dealt with under the headings of Insects and Plague.

A prominent place in the group of "vermin"—*i.e.* of animal and vegetable parasites harmful to man [1]—is occupied by the rat. Investigations during the last few decades have conclusively demonstrated the rôle of the rat in disease dissemination. Besides its rôle in the spread of plague and possible rôle in the spread of trichiniasis, the destruction it causes in agricultural countries is not to be overlooked. In Great Britain alone, according to recent estimates, the damage caused by rats amounts to as much as £10,000,000 per annum.

The work of rat destruction is therefore worthy of notice here.

The old means, namely the use of traps, dogs, cats and poisons, have in a great measure given way to newer and possibly more effective methods. These are the employment of the *Salmonella* or *Bacillus enteritidis* group of microbes. The idea of rat extermination by turning against them their own bacteria originated with the well-known fact, that there exist diseases which affect only animals of certain species, such as hog cholera and swine fever in pigs, and specific diarrhœa in calves.

A great many of these viruses are at present in use, but three commercial products are worthy of mention; namely:—

(1) The Liverpool virus.

(2) The Danysz virus; and

(3) Ratin.

The two former were originally isolated from the intestinal contents of rats, the latter from the urine of a child.

Conclusions drawn from reports of areas treated with these viruses, from an article by M'Lauchlan Young,[2] are of interest, and an extract of his paper is given here:—

(1) Is any one or all of these successful in killing rats?

Yes, each is successful in killing rats.

(2) Are they harmless to man, animals, birds, etc., other than rats?

There was no suggestion of their being hurtful to other animals except in the case mentioned in the report.*

(3) Do the diseased rats spread a fatal disease amongst their fellows?

In the case of the first, the report says, yes. In the case of the second the farmers are of the opinion that it does not. In the case of the third, the users cannot say definitely whether it does or not.

(4) Can they be readily used by unskilled labour?

Yes. The virus put up in tins ready for use is most convenient, but if it has to be prepared it is more troublesome. If put out in tubes for preparation with bread it requires some technical knowledge.

(5) At what cost can they be applied?

Over extended areas, as in this test, the cost was: Liverpool virus for 100 acres, £1; Danysz for 100 acres, £1, 10*s.*; Ratin virus No. 1 and No. 2 for 100 acres, £2, 5*s.* These prices are based on the advertised cost of each virus.

As to the possible danger of disease production in other animals or man an extract from Danysz's [3] paper is here given.

It should be noted that in 1903 and 1904 nearly 600,000 litres of cultures of Danysz's bacillus were distributed in France in different departments, for the purpose of destroying field mice. That for more than ten years some hundreds of litres of virus have been distributed every week for the destruction of rats, and that consequently more than a million

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[1] Prausnitz, C. (July–October, 1910), "The Destruction of Rats on Ships." *Journal Incorporated Society for the Destruction of Vermin.*

[2] M'Lauchlan Young, J. (July–October, 1909), "Report on the use of Virus for extermination of Rats." *Journal Incorporated Society for the Destruction of Vermin.*

* Some farmers thought that hens were affected in the case of the second, but there is no direct proof for this statement.

[3] Danysz, J. (July 23, 1910). "Some reflections regarding the free use of bacteriological cultures for the destruction of rats and mice." *British Medical Journal.*

persons have handled this virus without taking any special precautions, and in spite of that, no appreciable case of illness has resulted either in man or other domestic animals. Vermin—*continued*

The possibility, however, of virus bacteria causing human disease cannot be overlooked, and though in spite of the very extensive use of virus, cases of disease production in man have been few, still, until the virus microbes have been definitely and conclusively proved to be harmless to man, their employment must not be considered absolutely free from danger.

In a communication by Baker [1] interesting figures are given showing the prevalence of trichinosis among rats in European countries. As Hogberg's investigations proved experimentally that trichinosis in pigs is carried from the infected to the healthy by the fæces, the infected rat may possibly, therefore, be also regarded as an important source of infection.

Hydrocyanic acid gas has recently been put forward as a means of ridding houses of rats. It has been largely used of late years in America, Australia, and South Africa for the destruction of insect pests on plants and fruit-trees, and also for the "disinfection" of houses, jails, and railway carriages to rid them of vermin. The use of this gas is not attended with any injury to the most delicate plants; dry grain acquires no poisonous properties when exposed to its fumes, nor is germination affected.

It has no deleterious action on metals or textile fabrics, but moist foods absorb the poison and it does not kill bacteria. It is cheap and an efficient pulicide. The only drawback is found in its very poisonous properties and the risk to human life connected with its employment would seem to be too great to permit of its general adoption.

The subject of rat destruction on ships is an interesting one, and a good article on the subject is that by Prausnitz,[2] whose conclusions are given here :—

(1) Rats may be successfully combated on board ship by the use of well-trained animals, *e.g.* dogs, cats, etc.

(2) This is better done by suitable traps.* The simplest traps, attended to with reasonable care and properly baited, will give the best results. Rat-catching by the crew should be encouraged by the payment of premiums for each animal captured.

(3) The use of poisons requires great care, owing to the danger of accidental poisoning of foodstuffs intended for human consumption. Arsenic and strychnine should not be employed for this reason. Phosphorus, especially in fatty foods, gives good results, but must be used fresh.

(4) Complete extermination of rats can only be effected by fumigation.

(5) Fumigation of empty holds may be carried out at a reasonable cost by the old method of burning sulphur with charcoal in braziers.

(6) Fumigation of a full cargo can only be satisfactorily carried out by carbon monoxide or sulphur dioxide The advantages of the carbon monoxide method of Nocht and Giemsa are the high degree of penetration, its harmlessness to every cargo, and its cheapness ; the disadvantages are that it is neither an insecticide nor a disinfectant, and that although highly dangerous to man, the gas has very little smell. On the other hand, sulphur dioxide does not penetrate nearly so well, but kills insects and bacteria. A fair degree of penetration can, however, be effected with sulphur dioxide by using dilute gas containing about 3 per cent. of sulphur dioxide for an extended period—*e.g.* eight hours in the case of a 500-ton hold—and keeping the hold closed overnight. Certain articles are damaged, thus necessitating special precautions. Sulphur dioxide may be applied either by means of the Clayton apparatus or the "Auto-injector" method. The latter has the advantage of cheapness, if worked not more than once a year, and the apparatus required is simpler. If more frequent fumigation is required, the Clayton apparatus is the most suitable.

(7) The use of virus on ships, although they may give fairly good results, is not advisable until it has been definitely proved that they are harmless to man.

It has been noted recently that petroleum has some action in preventing rats, and it has been found that in ships which use petroleum to prevent mosquitoes, rats disappear ; also that ships engaged in carrying petroleum never harbour rats.

A very useful circular on rat extermination, plague prevention, and bacteriological diagnosis, with directions for obtaining and forwarding material for examination, is one by the Local Government Board, which will be found of value to sanitary officers whose districts are threatened with plague. It is therefore especially applicable to our workers in the Sudan. A copy may be found in the *British Medical Journal* under the heading of "Rat-Extermination." [3]

A very complete paper on the races of Indian rats is one by Lloyd.[4]

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[1] Baker, L. (January, 1909), "Rats and Trichinosis." *Journal Incorporated Society for the Destruction of Vermin.*

[2] Prausnitz, C. (July–October, 1910), "The Destruction of Rats on Ships." *Journal Incorporated Society for the Destruction of Vermin.*

* In Khartoum the Henri Marty trap has rendered good service.

[3] "Rat Extermination" (November 19, 1910). *British Medical Journal.*

[4] Lloyd, R. E. (May, 1909), "The Races of Indian Rats." *Records of the Indian Museum,* Vol. III., Part I. *Vide also* Vol. V., Part II. (June, 1910).

Vermin—*continued*

An experiment dealing with the destruction of cockroaches by hydrocyanic acid gas forms the subject of a report by Barrett, (*see page* "Insects"), but the general use of the gas for this purpose is undesirable, as it is not free from danger.

Warburton [1] has investigated the life history of lice. It may be detailed as follows: Incubation period eight days to five weeks; period from larva to imago eleven days; non-functional, mature condition, four days; adult life of male three weeks; female four weeks. He further points out that flock has to be regarded with suspicion as a possible distributer of vermin and that ova may pass through the flock-making machine without being crushed. The ova may, therefore, hatch out in bedding five weeks after manufacture. It has been estimated that an extra cost of two shillings per bed for disinfection would obviate this danger.

A useful book for general reference is one by Boelter,[2] which has been published under the name of *Household Pests and Household Remedies*, and may be of use to those who live in the Tropics, where vermin are numerous and, apart from the rôle they play in disease transmission, are often the cause of serious nuisance.

Additional Notes

Barium carbonate has been advocated as one of the cheapest and most effective poisons for rats and mice.[3] It is without taste or smell, has a corrosive action on the mucous lining of the stomach and, causing thirst, induces the vermin to seek water in the open, where they die. In small doses it is said to be harmless to domestic animals. It may be spread on fish or moist toasted bread, or it may be employed in the proportion of one part to four parts of meal, mixed to a dough with water.

Leaflets issued by the Board of Agriculture dealing with the destruction of rats, containing notes on some rat poisons with instructions how to prepare and lay them and with a note on the Poisoned Grain Prohibition Act and the Poisoned Flesh Prohibition Act may be useful as reference papers.

Verruga. Basset Smith [4] has studied the pathological changes seen in blood films taken from two acute cases of verruga. There is apparently an intense anæmia, as shown by the marked variations in size and shape of the red cells, the presence of normo, micro and megaloblasts in large numbers and of polychromatophilia with abundant basophilic stippling of the red cells. The nuclei of the nucleated red cells showed great variation in size and shape, and frequently exhibited mitotic changes. There was an undoubted relative leucocytosis with a slight increase of large mononuclears and eosinophiles. A few myelocytes were present, about 0·5 per cent.

In films stained deeply by Giemsa there were present in the cytoplasm of the red cells minute rod-like bodies showing either as diplococci from the intense staining of the ends, or as beaded forms, from two or more of them lying end on. Ring-shaped and pyriform bodies were also present in the cytoplasm of the red blood corpuscles. Chromatin was not observed. From the symptoms, limited distribution, specific nature and profound blood changes, Basset Smith is inclined to consider that the cause of verruga is a minute intra-corpuscular organism which is difficult to stain.

Biffi [5] has isolated in two cases of Carrion's fever the organism discovered by Barton in 1902. The cultural characters, agglutinative reaction and virulence in animals were the same as those given by paratyphoid B. and the bacillus of Gærtner. Biffi considers that Carrion's fever is a septicæmia following on an attack of verruga.

Jadassohn and Seiffert [6] were able to transmit the disease to apes from a case which came under their observation.

Galli-Valerio [7] has recently found the presence of red-staining, circular, intra-corpuscular

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[1] Warburton, C. (April 24, 1909), "Flock as a possible distributor of Vermin." *Lancet.*

[2] Boelter, W. R. (1910), *Household Pests and Household Remedies.* London.

[3] "The Destruction of Rats" (March 25, 1911). Quoted in *The Medical Officer.*

[3] Glen, R. A. (April, 1911), "Destruction of Rats." *Journal Royal Institute of Public Health.*

[4] Basset Smith, P. W. (September 18, 1909), "The Pathology of the Blood in Verruga." *British Medical Journal.*

[5] Biffi, U. (1908), "Verruga Peruviana und 'Schwere Fieber Carrions.'" *Arch. f. Schiffs-u. Tropen-Hygiene,* Vol. XII.

[6] Jadassohn, J., and Seiffert, G. (1910), "Ein Fall von Verruga peruviana; gelungene Übertragung auf Affen." *Zeit. f. Hyg. u. Infekt.*, Vol. LXV.

[7] Galli-Valerio, B. (April 4, 1911), "Observations microscopiques sur la 'Verruga peruana' ou Maladie de Carrion." *Cent. f. Bakt.*, I. Orig., Vol. LVIII., No. 3.

bodies in the blood of cases of verruga. These bodies were similar to those described by Basset Smith and others. Some of these intra-corpuscular bodies had a clear halo round them, and resembled in appearance those met with in *Anaplasma marginale* of oxen. Pigment was never present. Verruga—*continued*

In sections taken from the warty growths this observer has also found the presence of acid-fast bacilli occurring singly or in clumps. They were extra-cellular, slightly curved, and sometimes showed a slight enlargement at the extremity. In shape and dimensions they resembled the tubercle bacillus, but stained uniformly and showed no beading.

Veterinary Diseases

Rinderpest. Workers in veterinary science have recently achieved great results in the prophylactic and therapeutic measures adopted in combating rinderpest or cattle plague.

In India, Holmes [1] has employed the "serum alone" method in dealing with this disease. A number of experiments was carried out by this observer, and as a result of them the conclusions arrived at were as follows :—

(1) A single dose of anti-rinderpest serum confers immunity against the inoculated virus for about two weeks only.

A double dose protects for about three weeks, a treble dose for five weeks, and four times the single dose for about six weeks.

(2) The serum protects against natural infection for the same period as against the inoculated disease.

(3) The immunity following a simultaneous injection of serum and virus, even when no reaction occurs, is of an active nature and lasts for several months, and to produce this result it is not necessary to determine a balance between serum and virus, nor to give rise to any clinical symptoms of the disease.

(4) When animals are injected with serum and immediately exposed to infection, they acquire an active immunity of several months' duration, without evincing any clinical symptoms of the disease.

The dose of the serum employed by Holmes was fixed at 72 c.c. for cattle of hill breed, and 4 c.c. for plains cattle per 600 lbs. body weight. In field operations the chief facts to be observed are that the dose is protective and that the animal is exposed to infection before the protective effect of the serum has worn off.

Holmes considers that the infection gets immediately into the system after the serum injection and that it produces its reaction at the time when the immunity is decreasing. Also that under the conditions present in India, where sick and healthy cattle are invariably brought in contact, natural infection takes the place of virus inoculation. Consequently he considers that the "serum alone" method produces the same results as the "serum simultaneous" process where serum and virulent blood are injected at the same time, but that it is safer.

Ruediger [2] carried out some filtration experiments with the virus of cattle plague. He found that the virus present in the bile and blood of an animal infected with rinderpest did not pass through the pores of Berkefeld filters. A further interesting observation was made by him, namely, that if physiological salt solution be injected into the peritoneal cavity of an animal suffering from cattle plague, and that fluid be collected after an interval of an hour or two it is infectious, even after being passed through the Berkefeld filters used in his previously mentioned experiment. This peritoneal fluid was as virulent as the blood of the infected animal. In a further series of experiments Ruediger [3] found that this peritoneal fluid retained its virulence when passed through Berkefeld filters of a coarse, medium and fine-grained consistence, but was harmless after traversing a Chamberland filter.

Ruediger's experiments with the infectivity of the peritoneal fluid confirmed the previous work carried out on these lines by Nicolle and Adil Bey,[4] and later by Yersin.[5]

In a further series of experiments Ruediger [6] found that the serum of animals injected subcutaneously with infected peritoneal fluid has a higher potency than the serum of animals

[1] Holmes, J. D. (1900–1909), "The 'Serum Alone' Method as a Means of Combating Rinderpest in India." *Indian Civil Veterinary Department Memoirs*, Part IV., No. 1.

[2] Ruediger, E. H. (April, 1908), "Filtration Experiments with Cattle Plague." *Philippine Journal of Science*, B.

[3] *Idem* (September, 1908), "Further Filtration Experiments with Virus of Cattle Plague." *Philippine Journal of Science*, B.

[4] Nicolle, M., and Adil Bey (1902), "Études sur la Peste Bovine." *Ann. de l'Inst. Past.*, Vol. XVI.

[5] Yersin (July, 1904), "Études sur quelques épizooities de l'Indo-Chine." *Ibid.*, Vol. XVIII.

[6] Ruediger, E. H. (November, 1908), "A Reduction in the Cost of Anti-cattle Plague Serum." *Philippine Journal of Science*, B.

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injected subcutaneously with virulent blood. As a result of these experiments he was able to obtain at a cheaper cost anti-cattle plague serum, as by injecting the infected peritoneal fluid into a bullock weighing between 200 and 250 kilos, five litres of peritoneal fluid and five litres of blood were obtained from the animal, after it was bled to death. His method of obtaining artificial peritoneal fluid was to inject 50 c.c. of a 1 per cent. solution of potassium citrate into the peritoneal cavity of the virulent blood animal, and to collect this fluid after the animal had been bled to death.

Baldrey [1] conducted some experiments to test the power of the serum produced from the injection of peritoneal fluid as compared with that produced from the inoculation of virulent blood only. The tests were carried out on plains and hill cattle. Cattle were selected for providing inoculable material, and were injected intraperitoneally with ·5 per cent. sterile citrate of potash solution, the amount injected varying between 1000–2000 c.c. As a result of his experiments he drew the following conclusions :—

(1) That the method of employing peritoneal washings to augment the amount of inoculable virulent material was a good one.

(2) It produced an anti-rinderpest serum of a high value, but less potent than that produced by blood inoculation.

(3) In comparison with serum from blood inoculations it was of greater value in the less susceptible plains animals than in the highly susceptible hill cattle.

(4) That its reaction was produced principally by a toxin which was rapidly formed under the vital influence of the peritoneal cavity.

(5) The inoculation of very large doses was not advisable in Indian cattle on account of the danger of death from toxæmia, the inability of the animals to absorb it subcutaneously, and the extreme caustic action it has upon the tissues.

Gibson [2] describes a method of dealing with rinderpest in the field without the aid of a laboratory. In the event of an outbreak of rinderpest, blood is taken from the jugular vein of an immune animal, citrated, and inoculated subcutaneously in doses of 120–240 c.c. in affected and in contact animals. The blood is used preferably when warm, as absorption is more rapid. The immune animal is then inoculated with 60–120 c.c. of virulent blood. A reaction occurs lasting 3–5 days, and when this has subsided more blood may be withdrawn. Gibson has found that the blood remains potent for many months without further fortification. If temporary immunity be required he recommends that serum only be given. If permanent immunity, 180 c.c. of serum should be injected, to be followed four days afterwards by a further injection of 180 c.c. and 5 c.c. virulent blood.

The animal goes through a mild attack of rinderpest and recovers.

An officer stationed in an outlying district can be supplied with a few immune bullocks which represent the serum supply. If the outbreak of rinderpest is an extensive one, the stock of immune cattle increases, and at the same time the stock of serum.

The Ehrlich-Hata preparation, " 606 " was tried by Dschunkowsky [3] in the treatment of rinderpest. A cow artificially inoculated with this disease was given 2 grammes of the drug intravenously in 1 litre of salt solution on the fourth day after inoculation. The disease, however, ran its usual course and the animal died.

Horse Sickness. In a large number of immunisation experiments carried out in mules with the virus of horse sickness, Theiler [4] found that the mortality of immunised mules when exposed to natural infection amounted to 0·6 per cent. This, he explained, was due to the presence of virus of varying virulency in different districts. As this question of immunity was of importance, he undertook a further series of experiments with various kinds of virus, noting the results obtained by testing animals with (*a*) the same and (*b*) a different strain of virus to that with which they were immunised. As a result of these experiments Theiler [5] found that when a horse or a mule was inoculated with a certain strain of virus, the animal, as a rule, was immune against that particular strain, but when tested or hyper-immunised at a later date with virus of a different strain, reactions and deaths occurred, showing that the immunity conferred by the first inoculations was not a complete one. Theiler then carried out

[1] Baldrey, F. S. (1911), " The Preparation of Anti-Rinderpest Serum by means other than the Injection of Virulent Blood." *Journal Tropical Veterinary Science*, Vol. VI., No. 1.

[2] Gibson, A. (1910), " A Method of Dealing with Rinderpest in the Field." *Journal Tropical Veterinary Science*, Vol. V., No. 1.

[3] Dschunkowsky, E. (January 5, 1911), " ' 606 ' bei der Piroplasmose und Rinderpest." *Berl. Tierärztl. Woch.*, Vol. XXVII., No. 1.

[4] Theiler, A. (1905–1906), " Horse Sickness. The Result of the Inoculation in Practice." *Report of the Government Veterinary Bacteriologist, Transvaal Department of Agriculture.*

[5] *Idem* (1906–1907), " Immunisation of Mules with inadequate and adequate serum and Virus and the Immunity obtained therefrom." *Ibid.*

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more experiments on mules, to determine whether a polyvalent serum—*i.e.* a serum either composed of various monovalent sera obtained by mixing them, or by a serum obtained from a horse previously injected with a mixture of three or more viruses—could be used to greater advantage in practice, and would confer a greater protection against horse sickness than that given by a monovalent virus. The conclusion arrived at by Theiler was that the immunity obtained by a polyvalent virus afforded better protection than an immunity gained by the inoculation of an individual strain of virus.

In a further series of experiments Theiler [1] noted that animals immunised with a polyvalent virus and tested with the same virus, showed reactions when subsequently retested with the identical virus. He found that the best results were obtained by making a polyvalent virus from three different strains of virus plus the virus from a horse previously inoculated with these three viruses, together with relapse and spontaneous cases, the blood being collected in different districts and on the high veld. This virus Theiler named the CD (composite district) virus.

Theiler [2] has further shown that a virus may become inert in practice, and that the virulency of a particular strain of horse sickness is subject to a certain amount of variability. He noticed [3] certain fever reactions in horses simulating horse sickness, which he termed Ephemeral Fever. Investigations based on immunising experiments were carried out, and it was proved that there was no connection between this ephemeral fever and horse sickness.

Frei [4] has made a number of physical-chemical investigations in connection with horse sickness. He found that the surface tension of the serum of horses suffering from horse sickness was subnormal, and that, besides loss of erythrocytes, general impoverishment of the blood liquid took place, as shown by a decrease of the specific gravity and viscosity of the serum. This pointed to a diminution of colloids. There was also a decrease of the electrolyte-concentration.

Theiler [5] in 1905 successfully inoculated dogs with horse sickness virus. McFadyean [6] in four experiments, in which he used for his infective material the filtrate obtained by passing diluted blood through a Berkefeld filter, did not obtain results quite in accordance with those of Theiler. McFadyean considers that in view of the resistance which dogs offer to experimental infection with horse sickness virus, it is very improbable that animals of that species ever become infected in natural circumstances, or that they act as reservoirs of horse sickness virus in horse sickness districts.

Theiler [7] at a later date published an article replying to some of McFadyean's experiments, and for those who may be interested in the controversy on this subject the reference is given.

Bovine Pleuro-pneumonia. This contagious disease has been studied by Nocard and Roux, and later by Dujardin-Beaumetz. They showed by their experiments that the organism concerned could pass through Berkefeld and Chamberland filters. By means of the collodion sac method Nocard and Roux were able to cultivate the pleuro-pneumonia virus in broth inoculated with a trace of lung lymph previously passed through a Berkefeld filter. After several days incubation in the peritoneal cavity of rabbits a faint turbidity appeared in the broth, which was not present in the control collodion sacs. Microscopic examination of the turbid liquid revealed the presence of extremely minute granules. It was also found that these granules could be grown on a liquid medium containing serum. With material derived from a bovine pleuro-pneumonia culture obtained from the laboratory of M. Dujardin-Beaumetz, in which only amorphous granules were visible, Bordet [8] made subcultures on a medium containing defibrinated blood. No growth was visible to the naked eye on the cultures, but the medium became black along the needle track. Cover-glass preparations were made from the culture and stained with hot Giemsa stain. Examination of these showed the presence not only of the fine granules seen

[1] Theiler, A. (1906–1907), "Inoculation of Mules with Polyvalent Virus and Serum." *Report of the Government Veterinary Bacteriologist, Transvaal Department of Agriculture.*

[2] *Idem* (1907–1908). *Ibid.*

[3] *Idem* (1907–1908). *Ibid.*

[4] Frei, W. (1907–1908), "Physical-chemical Investigations into South African Diseases." *Report of the Government Veterinary Bacteriologist, Transvaal Department of Agriculture.*

[5] Theiler, A. (1905–1906), "Transmission of Horse Sickness into Dogs." *Ibid.*

[6] McFadyean, J. (March 31, 1910), "The Susceptibility of the Dog to African Horse Sickness." *Journal Comparative Pathology and Therapeutics.*

[7] Theiler, A. (December 31, 1910), "The Susceptibility of the Dog to African Horse Sickness." *Ibid.*

[8] Bordet, J. (November, 1909), "The Morphology of the Micro-organism of Bovine Pleuro-pneumonia." *Bull. Soc. Royale des Sc. Méd. et Nat. de Brux.* Quoted in *Journal Comparative Pathology and Therapeutics*, March 31, 1910.

Veterinary Diseases—*continued*

in previous cultures, but also of slender long spirochætes. These spirochætes were shorter than the treponema of syphilis, were often comma-shaped, and their spirals were not so close as those of the syphilis treponema.

Bordet's results are of interest, inasmuch as his experiments show that spirochætes develop from granules. Similar developmental changes have been observed by Leishman[1] in his observations in connection with tick fever. Balfour also confirmed Leishman's work when carrying out researches on the spirochætosis of fowls in the Sudan. He further observed the fowl spirochætes shedding granules[2] from either extremity when they were examined by the dark-field illumination method.

Ephemeral Fever, or three days Sickness in Cattle. Freer[3] has carried out some observations on this disease which is met with in South Africa. Its etiology has yet to be worked out. He noted that cattle of all breeds are susceptible to it, and that the injection of blood from a sick to a healthy animal produced the disease. The transmission of the disease in nature is probably through the agency of the night midge. The characteristic symptom is stiffness of one or all of the extremities, and usually of the whole body. There is a rise of temperature and watery discharge from the eyes and nose, together with an inability to swallow. The animal is usually convalescent at the end of three days. The disease is rarely fatal. The post mortem symptoms are typical, and consist of an enlargement of all the lymphatic glands in the body, particularly those in front of the sternum.

Infectious Anæmia, or Swamp Fever of Horses. Mohler[4] has investigated this fever, which is more commonly found in America than elsewhere. It has, however, been reported in Germany under the name of infectious anæmia and in France as infectious typho-anæmia. The cause has been definitely determined to be an invisible virus, chiefly confined to low-lying pastures. Swamp fever has also been found to exist at an altitude of 7,500 feet. It is a progressive anæmia in which the red blood cells diminish steadily in number, falling even as low as 2,000,000 per cubic millimetre. The most constant pathological lesion consists in the presence of petechiæ in the serous membrane and muscle of the heart. The characteristic signs and symptoms are insidious onset, emaciation, anæmia, staggering gait, and polyuria. The prognosis is unfavourable and the treatment somewhat unsatisfactory. Flies, mosquitoes and internal parasites are all suspected carriers of this disease.

Sarcocysts in the Camel. Mason[5] has studied this condition which commonly affects the older camels in Egypt. The sarcocysts were found distributed in the muscular tissue, chiefly in the œsophageal and gluteal regions, but they were also found to be present throughout the body. They were never found in the liver, spleen or kidney, nor were they present in the involuntary muscle of the stomach and intestine. The sarcocysts met with in the ox, buffalo and sheep have rows of cutical cells lining the basement membrane, but these are completely absent in the cysts of the camel. The mature cysts contained chlamydospores, differing in shape from those met with in sarcocysts of the ox, buffalo and sheep. Spherical bodies containing granules were also found.

Mason is inclined to think that the sarcocyst of the camel is a distinct species and suggests for it the name of *Sarcocystis cameli*. With the naked eye these cysts appear as small oval white bodies resembling abscesses. Sections of infected muscle exhibit, when stained and examined microscopically, three different zones: (1) A central area, showing disintegration of muscle fibres; (2) an outer zone of leucocyte infiltration; (3) and external to this a zone showing normal muscle fibres infiltrated with leucocytes.

Watson[6] is inclined to think that sarcosporidiosis is a frequent sequel to the disease of horses and cattle known as "*loco*" disease, and it may even complicate the diagnosis of dourine. He calls attention to the important fact that the crescentic spores of sarcocystis bear a strong resemblance to the crescentic bodies described as developmental forms of trypanosomata.

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[1] Leishman, W. B. (December 10, 1909), "Observations on the Mechanism of Infection in Tick Fever." *Transactions Society Tropical Medicine and Hygiene.*

[2] Balfour, A. (April 1, 1911), "The Infective Granule in certain Protozoal infections, as illustrated by the Spirochætosis of Sudanese Fowls." *British Medical Journal.*

[3] Freer, G. W. (1910), "Ephemeral Fever, or Three Days Sickness in Cattle." *Journal Tropical Veterinary Science*, Vol. V., No. 1.

[4] Mohler, J. R. (March 6, 1909), "Infectious Anæmia, or Swamp Fever of Horses." *Bureau of Animal Industry, Circular* 138. *Department of Agriculture, U.S.A.*

[5] Mason, E. (June 30, 1910), "Sarcocysts in the Camel in Egypt." *Journal Comparative Pathology and Therapeutics.*

[6] Watson, E. A. (March 31, 1909), "Sarcosporidiosis." *Ibid.*

Veterinary Diseases—*continued*

Moussu and Coquot[1] have described a case of sarcosporidiosis occurring in a horse. The administration of iodide of potash appeared beneficial although the animal eventually succumbed to the disease.

Camel Pox. This is a more or less benign disease in all the camel-breeding districts of the Punjab, and, according to Leese,[2] it is more severe in the rainy season. It has the usual character of variola in being highly contagious, easily inoculable and causing similar lesions. Most camels acquire the disease before the age of 2 years. In slight cases the lesions in the form of nodules are confined more or less to the skin of the lips, but in the severe cases they occur on the lips, sheath, head and feet, or all over the body, and the febrile symptoms are more marked. The mild cases usually last 3 weeks.

The camel men in the breeding districts practise a crude form of inoculation with the object of getting the young camels over the disease before the rains set in; a crust is taken from a case of camel pox and set aside till required, when it is emulsified in milk and rubbed on to a scarified surface, the disease then showing itself after an incubation period of four days. Only a few camels in a herd require inoculation in this way, as the disease soon spreads. Leese describes another condition occurring in young camels called *Girki* and *Giddah*. Girki means knuckling, and giddah, deformity. The fore and hind fetlocks knuckle at about 6 months of age, and if this progresses, the fetlock joints bend inwards and knock together. Leese considers it is brought about by the hard nature of the ground, which is covered with loose stones, is a condition quite apart from rickets, and can be prevented if the young camels are not allowed to move about in districts where such physical conditions exist.

Echinococcosis of the Camel. Hilbert[3] experienced this disease as an epizootic in Algeria, where more than one-tenth of the camels died. It commenced with loss of appetite and a violent cough, and in some cases there was a nasal discharge. The camels became profoundly anæmic. The autopsies showed a generalised echinococcosis of most of the organs. The infection was referred to drinking water.

Weinberg[4] has shown that the serum of animals suffering from echinococcosis contains specific antibodies which are easily demonstrated by deviation of the complement. This test has been employed with success in camels suffering from echinococcosis. The hydatid fluid may be obtained from the animal itself or from another animal. The hæmolytic serum used was that obtained from a rabbit immunised against the red corpuscles of a horse.

Miscellaneous. There is reason for considering that the camel is liable to tuberculosis. In India, Leese[5] and Lingard[6] have found lesions simulating tubercular infection, in which acid-fast bacilli were present, and Archibald[7] reported a similar condition occurring in the Sudan.

Webb[8] has described an outbreak of acute and fatal pneumonia which occurred in young horse and donkey stock in India. This observer isolated a bipolar-staining cocco-bacillus of the fowl cholera type from pus smears taken from the lungs. The disease is evidently a septicæmia, for Webb was successful in inoculating a pigeon with 1 c.c. of blood taken from the vein of a dying donkey filly. The bird died on the tenth day and examination of its blood showed the presence of large numbers of these cocco-bacilli. The type of pneumonia present during this outbreak was an acute suppurative one, usually ending fatally in one to four days.

Malkmus[9] gives a full description of contagious equine pneumonia, a type of pneumonia

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[1] Moussu, G., and Coquot (1908), "Sur un cas de sarcosporidiose du cheval." *Bull. Soc. Cent. de Méd. Vet.*, Vol. LXII. Quoted in *Journal Tropical Veterinary Science*, Vol. IV., Part 3, 1909.

[2] Leese, A. S. (1909), "Two Diseases of Young Camels." *Journal Tropical Veterinary Science*, Vol. IV., Part 1.

[3] Hilbert (March, 1908), "Sur l'échinococcose du chameau en Algérie." *L'Hygiène de la Viande et du Lait* Quoted in *Journal Tropical Veterinary Science*, January, 1909.

[4] Weinberg and Vieilard (1909), "Sur le diagnostic de l'echinococcose chez le dromadaire." *Bull. Soc. Cent. de Méd. Vet.*, Vol. LXIII.

[5] Leese, A. S. (December 31, 1910), "Acid-Fast Bacilli in Camel's Lung, with Lesions resembling those of Tuberculosis." *Journal Comparative Pathology and Therapeutics.*

[6] Lingard, A. (1905–1906), *Annual Report of Imperial Bacteriologist.* India.

[7] Archibald, R. G. (March 31, 1910), "Acid-Fast Bacilli in a Camel's Lung, the Gross Lesions of which simulated miliary Tuberculosis." *Journal Comparative Pathology and Therapeutics.*

[8] Webb, E. C. (June 30, 1909), "Bipolar Staining Bacilli of the Fowl Cholera Type as the cause of widespread, acute, and fatal Pneumonia in Horse and Donkey Young Stock in India." *Journal Comparative Pathology and Therapeutics.*

[9] Malkmus, B. (September 31, 1909), "Infectious Pleuro-Pneumonia of Horses." *Proceedings Ninth International Veterinary Congress at the Hague.* Quoted in *Journal Comparative Pathology and Therapeutics*, December 31, 1909.

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in which the inflammation is chiefly fibrinous. The actual causal agent of this disease has yet to be ascertained.

Of fowl diseases, mention may be made of the occurrence of an epizootic of fowl septicæmia in Calcutta reported by Chattergee.[1] Attempts to check the epidemic by isolation and disinfection failed and vaccine treatment was tried. The specific organism isolated was a very minute micrococcus.

Mathis and Leger [2] discovered a new parasite belonging to the order Trematodes and the family *Fasciolidæ* in the conjunctival cul-de-sac of the fowl. The name *Philophthalamus gralli* has been given to this fluke, which is fixed by its suckers to the ocular conjunctiva. It causes congestion and small erosions of the mucous membrane. The lachrymal secretion contains blood, eggs and actively motile ciliated embryos.

Malerba and Scacco [3] have recently been able to throw some light on the cause of the calcareous nodules so frequently seen in the liver of the horse. These nodules vary in size from a millet seed to a filbert nut, and are of a greyish-white colour. They prepared sections of the nodules, together with the adjacent liver tissue, and by suitable staining methods were able to demonstrate the eggs of *Distoma lanceolatum* in the centre of the nodule. Their presence sets up a local inflammatory hyperplasia with connective tissue formation, and, later, calcification occurs. No adult parasites were found in the nodules.

Bride and Nègre [4] have recently carried out some experiments in order to determine the nature of the cryptococcus of Epizootic lymphangitis. They utilised the method of deviation of the complement, using the serum of animals attacked by the disease. A dilution of the cryptococcus in normal saline solution formed the antigen. As a result of their experiments they come to the following conclusions :—

(1) That the serum of animals attacked by lymphangitis epizootica contains a "substance sensibilatrice."

(2) This manifests its action either in the presence of the cryptococcus or of a ferment.

(3) Another microbe, *B. coli*, is not sensitised by the serum.

(4) Neither the yeast nor the cryptococcus are sensitised by an anti-microbic serum, *e.g.* Plague serum.

(5) These observations are in favour of the contention that the parasite of epizootic lymphangitis is a blastomycelium.

As regards the treatment of epizootic lymphangitis, Freer [5] found that the administration of mercuric potassium iodide, combined with local antiseptic treatment, was effectual in 99 per cent. of cases.

Mention may be made of a disease known as otocariasis, which exists among the goats of the Congo. The external ear of the affected animals becomes plugged with matted filamentous material, in the midst of which are numerous acari. Gedœlst [6] examined some of this material sent by Dr. Broden, and came to the conclusion that the parasites were *Psoroptes communis*. The goats in the Pyrenees also suffer from this condition.

Piot [7] describes what he considers to be a new enzootic occurring in sheep and goats in the Egyptian delta. It is characterised by an intense fever, a confluent eruption on the muzzle and face and large, numerous and deep ulcers of the buccal mucosa. It has a duration of two to three weeks and causes a mortality of about 50 per cent. of the animals infected.

Montgomery [8] has recently discovered that the cattle in East Africa have been dying in large numbers from *Coccidiosis*. He found that the most pronounced clinical symptoms present were excessive lachrymation, a muco-purulent nasal discharge and fœtid diarrhœa often containing blood and mucus. Stomatitis, ulceration of the labial and lingual mucosa, gastritis, frequently with ulceration of the abomasum, enteritis, and often a marked

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[1] Chattergee, G. C. (February, 1910), "On the Occurrence of an Epizootic of Fowl Septicæmia in Calcutta, and Prophylactic Treatment of the Disease by Vaccine." *Indian Medical Gazette.*

[2] Mathis, C., and Leger, M. (April 13, 1910), "Douve oculaire de la Poule." *Bull. Soc. Path. Exot.*

[3] Malerba, C., and Scacco, P. (1908), "Contribution to the Study of Nodules of the Liver of Equines." *Clin. Vet. Mila*, No. 31, Quoted in *Journal Tropical Veterinary Science*, July 1909.

[4] Bride, M., and Nègre, L., "Sur la nature du parasite de la Lymphangite Épizootique. *C. R. de l'Acad. des Sciences*, t. 150. Quoted in *Journal Tropical Veterinary Science*, Vol. V., No. 4, 1910.

[5] Freer, G. W. (1909), "Treatment of Epizootic Lymphangitis." *Journal Tropical Veterinary Science*, Notes and Extracts, Vol. IV., No. 1.

[6] Gedœlst, L. (1908), "Le parasite de l'otocariase des chèvres du Congo." *Arch. für Schiffs-und Tropen-Hygiene*, Vol. XIII., No. 5.

[7] Piot, Bey, J. B. (March, 1909), "Enzootie encore inédite en Égypte sur des caprino-ovidés." *Bull. Soc. Path. Exot.*

[8] Montgomery, E. (May 11, 1910), "Coccidiosis of Cattle in East Africa." *Ibid.*

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proctitis were the main lesions present. The mortality was usually 10–20 per cent. of the sick animals. In young calves the disease frequently runs its course in three to five days; in older animals seven to ten days was about the average.

A scaly eruption of the neck and shoulders frequently occurred towards the end of the disease. Chronic cases lasted several months, the most common symptom being anæmia.

As regards its diagnosis, coccidiosis of cattle bears a strong resemblance to rinderpest, both in the clinical symptoms and in the pathological changes. Examination of the fæces and scrapings of the inflamed rectum will demonstrate either the presence of oocysts or merozoites. In the majority of the examinations carried out by Montgomery, only merozoites were present. They occurred either free or arranged within epithelial cells like the quarters of an orange. In fresh cover-glass preparations the merozoites appeared as comma-shaped bodies of a pale straw colour capable of flexion and extension, but of limited progression. The oocysts measured on an average 17 μ by 15 μ, were clear and transparent with a definite contour and contained fine granules frequently arranged towards the pole opposite to the micropyle. Montgomery's discovery of cattle coccidiosis in East Africa suggests the importance of looking for this disease in outbreaks of doubtful rinderpest occurring in Egypt and the Sudan.

Mention may be made of Cazalbou's [1] observations on choleraic diarrhœa of horses in the French Sudan. It is a disease which has a high mortality, and commences with the ordinary symptoms of colic. Death may occur within six hours of the commencement of the colic. The stools are abundant, greenish in colour, and very fœtid. Good results have been obtained by the use of a watery solution of potassium permanganate (1 in 1000) given by the mouth and by injection. Half-a-litre is given by the mouth and repeated every half-hour or hour according to the gravity of the case. At the same time injections are also given per rectum. Four to six doses and as many injections suffice to arrest the intestinal flux.

Suffran [2] and Edwards [3] have observed that common salt may act as a poison to poultry. Its action is evidently that of a caustic, for the pathological findings in Suffran's cases showed congestion and erosions of the intestinal tract, together with interstitial hæmorrhages. Suffran made a series of experiments on birds to determine the minimum toxic dose of common salt, and found that a dose of 4 grammes per kilogramme of body weight was sufficient to produce death.

Cameron [4] has an interesting paper on *sorghum poisoning*. The investigations of the scientific department of the Imperial Institute showed that prussic acid and cyanide of potassium were present in young sorghum (millet) plants in the proportion of 0·2 per cent. The prussic acid is present in dangerous amount only in certain stages of the growth (from five to seven weeks usually), and disappears gradually after the blossoming stage. When the seed is ripe no prussic acid is present. The prussic acid is found in increased quantity during dry seasons, and is almost absent in plants grown quickly on moist land. Stunted crops and crops which have had a check on their growth are very likely to contain poisonous quantities of this acid. Second growths are almost more poisonous than the first growth. As all varieties of the sorghum family are liable to contain poison, Cameron considers that the following preventive measures should be employed when feeding horses and cattle and other animals :—

(1) Never allow stock to have access to growing crops of sorghum, millet, amber cane, Dhoura or Egyptian corn, Kaffir corn or other plant of the sorghum family. Apart from the danger of poisoning, the practice of grazing the crop is a wasteful one.

(2) Never feed newly cut sorghum at any stage of its growth, but always allow it to dry or " wilt " for one or two days. If the atmosphere is dry and sunny, the danger will disappear more quickly.

(3) Never feed immature growth. Feed only in the green state crops which have blossomed and are forming again.

(4) Only use that sorghum as green feed which has been grown vigorously on moist land. Stunted crops off dry land should be made into hay or ensilage before use.

(5) Let the allowance be always moderate in amount with a due proportion of other foods.

Cameron recommends the use of ammonia stimulants in cases of sorghum poisoning. The *Liquor ammoniæ fortis* should be continuously inhaled, and one ounce of carbonate of ammonia dissolved in cold water should be given as a drench every hour where cattle are concerned. Half an ounce of the ammonium carbonate should be given for horses, and smaller

[1] Cazalbou, L. (April 8, 1908), " Diarrhée Cholériforme des Équidés Soudanais." *Bull. Soc. Path. Exot.*

[2] Suffran, F. (June 15, 1909), "Sur l'empoisonnement des Volailles par le Sel de Cuisine." *Rev. Gén. de Méd. Vet.*

[3] Edwards, E. R. (December 31, 1910), " Poisoning of Poultry by Common Salt." *Journal Comparative Pathology and Therapeutics.*

[4] Cameron, S. S. (May, 1908), " Sorghum Poisoning." *Tropical Agriculturist and Magazine Ceylon Agricultural Society.*

Veterinary Diseases— *continued*

amounts for the lesser animals, such as sheep and pigs. The tympanites which is frequently present can be relieved by the administration of baking soda if carbonate of ammonia is not at hand.

Müller [1] has reported cases of poisoning of cattle, horses and sheep due to the feeding of these animals with musty fodder. The symptoms consisted chiefly of a myopathic paresis or paralysis, and in the oxen and sheep there was excessive salivation. The fodder was subjected to examination and found to contain a black mycelium. The grain that was used was found to be covered with black spots which microscopically proved to be closely packed hyphæ containing spores.

Paralysis occurring in the ostrich has been studied by Robertson.[2] This condition causes a big loss to breeders of these birds. Robertson carried out numerous post mortem examinations on ostriches early affected with paralysis, and on those birds that had been paralysed for several months. The constant lesion present consisted of an inflammation of the duodenal mucous membrane accompanied by the deposit of inflammatory exudate on its surface. The submucosa was thickened and often infiltrated with a clear straw-coloured fluid. Robertson was successful in isolating the causal organism from the tissues under the inflamed mucosa. It is a short Gram-negative bacillus. Inoculation of broth cultures of this bacillus produced the disease in healthy birds. The symptoms of paralysis are believed by Robertson to be due to a toxin formed by this bacillus. He suspects that the source of infection is due to contaminated food and water.

Firket [3] has described a peculiar form of epizootic papillomatous stomatitis occurring among the goats in the Congo. It is characterised by the development of papillomatous vegetations in the mouth. Ulceration does not occur. Diarrhœa and marked wasting are concomitant symptoms and signs of this disease.

Tidswell [4] has met with pseudo-tuberculosis in sheep in New South Wales. The condition is really a lymphadenitis which may or may not lead to suppuration. Tubercle bacilli were never found. A bacillus was isolated which appeared from inoculation experiments to be the specific causal organism of the condition. This bacillus did not correspond to the *Bacillus pseudo-tuberculosis ovis,* Preisz, which is the cause of an apparently similar condition occurring in Europe.

Tidswell found in a turkey, that had succumbed to the disease known as *Blackhead*, the presence of rounded ovoid bodies resembling coccidia, and which are said to be the encysted form of the *Amœba melægridis.* These bodies were present in the inflamed bowel, in the exudate and in the liver. They are regarded as the cause of the disease.

In several cases of *Balanitis* (" Bad Pizzles ") occurring in sheep, the same observer found numerous bodies having the appearance of spirochætes.

Walker [5] has carried out some observations on *Gauw Ziekte,* a disease occurring in sheep, and which is characterised by acute œdema and hyperæmia of the lungs, with serous effusion into the pleural cavities. It seems to be influenced by meteorological conditions, as it commonly occurs in the summer months, particularly in wet seasons, and terminates shortly after the first frost. In acute cases the animal, without any premonitory symptoms, will describe one or two circles in its movements, or bleat, or leap into the air and fall dead. In the subacute cases Walker notes that the respirations are accelerated and abdominal in character, the ribs being fixed, and frequently an interval will be detected in the expiratory act or a distinct jerk will be noticed. The causal agent of the disease still remains to be discovered ; probably it is of the nature of a vegetable poison.

Frei [6] has investigated the cattle disease known as *Lamziekte.* The clinical symptoms commence with a stiffness of the forelegs followed by a paralysis of the hinder part of the body. Before death a complete paralysis, involving the forequarters, occurs. The chief lesions present are (1) an ulcerative or hæmorrhagic gastritis, (2) a catarrhal enteritis with

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[1] Müller, M. (July 30, 1908), " Beobachtungen über Vergiftungsfälle bei Pferden, Rindern und Schafen infolge Verfütterung rostpilzbefallenen Futters." *Berl. Tierärztl. Woch.,* p. 541. Quoted in *Journal Comparative Pathology and Therapeutics,* March 31, 1909.

[2] Robertson W. (June 30, 1910), " Paralysis in the Ostrich." *Journal Comparative Pathology and Therapeutics.*

[3] Firket, C. (1910), " Stomatite papillomateuse épizootique chez les chèvres du Congo" *Arch. f. Schiffs-u. Tropen-Hyg.,* Vol. XIV., No. 5.

[4] Tidswell, F. (1909), *Report of the Government Bureau of Microbiology, New South Wales.*

[5] Walker, J. (1908–9), " Gauw Ziekte : a Disease of Sheep." *Report of the Government Veterinary Bacteriologist, Transvaal Department of Agriculture.*

[6] Frei, W. (1908–9), " Investigations into the Disease Lamziekte of Cattle." *Ibid.*

Veterinary Diseases—*continued*

hæmorrhage and ulcerations, (3) an exudative leptomeningitis. A previous attack does not appear to confer immunity but rather predisposes to a second attack. Robertson and Spreull describe a bipolar-staining bacillus as the causal agent of the disease. This was not confirmed by Frei.

Numerous experiments were carried out by Theiler [1] to ascertain the infectivity of the blood of animals suffering from Chronic Glanders. As a result of these he found that the blood of animals suffering from chronic glanders is not necessarily infective, but may become so after large quantities have been withdrawn.

The question of adopting a dog ordinance ought to be seriously considered in those parts of the Tropics where rabies exists. Regulations should be made by municipalities to safeguard the public as well as the dogs themselves, and the list of recommendations given below as suggested in India [2] might well be adopted:—

(1) A dog is "at large" when it is away from its owner so far that the owner cannot exercise proper control.

(2) All *ferocious* dogs are nuisances. This has been held at law.

(3) All dogs must be registered and licensed, and, at certain times of the year, muzzled.

(4) All dogs should wear a metal tag or plate given to the owner when he pays his annual tax. There should be different coloured tags for males and females, and different colours for each year, so that by looking at the tag its colour indicates the year it was licensed.

(5) Registration need only be done in the different districts an animal is taken to. The licence should cover the whole country.

(6) All dogs without a tag should be seized, and diseased ones shot.

(7) A dog need not be licensed which is on leash on private property, but never out except in leash.

(8) The licence should be for dogs Rs. 5, and for bitches Rs. 3.

(9) Unmuzzled dogs, during the months the muzzling order is out, should be destroyed.

(10) A vicious dog should be defined as one which attacks any one on the roads or streets by chasing, biting, or attempting to bite. Such should be destroyed, and in certain cases the owner fined after warning.

(11) If a tag is lost, a new one should be given on payment of a certain small sum.

(12) Licences should be transferable on transfer of ownership of a dog.

(13) Muzzles should be defined as "a leather strap secured around both jaws of the dog of sufficient strength and tightness to prevent the dog from opening its mouth more than one and a half inches" or "a wire cage completely covering the mouth."

(14) An owner should be defined as "one who harbours or possesses a dog for 15 days or more."

(15) Puppies under five months may be exempted.

(16) In case of non-fulfilment of the ordinances, dogs may be seized by any policeman, magistrate, or member of a Society for the Prevention of Cruelty to Animals, or local poundmaster.

(17) Information of seizure should be given by publication in a newspaper, and owners may redeem the dogs on payment of a fine of Rs. 5 for each offence within a certain period; thereafter they may be sold.

(18) Any person interfering with a dog-catcher, or a policeman, or other authorised person while seeking to capture a dog on the streets should be fined.

In certain places abroad dog-catchers are provided with horse and wagon and nets.

In this way rabies would be stamped out, cruelty to dogs prevented, stealing of dogs rendered difficult, and a greater pride taken in looking after dogs engendered.

Speir [3] has an excellent illustrated paper on the construction of cow houses. The principal details requiring consideration in the building of a cow house are as follows:—

Site, including aspect and arrangement with regard to other buildings.

General Construction of the Building, including the walls, roof, floor, drainage, and water-supply.

Internal Design, including arrangement of stalls, stall divisions, bindings, feeding troughs, manure and urine channels, passages, etc.

Air-Space, including floor space.

Ventilation, including the various methods by which this is attained, and *Lighting*.

To those requiring full information on the subject this paper can be strongly recommended.

Additional Notes

Mention may be made of a paper by Manteufel [4] discussing the protozoal nature of the parasite of epizootic lymphangitis. The material examined was obtained from a horse and a mule.

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[1] Theiler, A. (1908–9), "The Infectivity of Blood of Animals Suffering from Chronic Glanders." *Report of the Government Veterinary Bacteriologist, Transvaal Department of Agriculture.*

[2] "Dog Ordinances." *Indian Public Health.* Quoted in *Journal Tropical Veterinary Science*, 1909. No. 1.

[3] Speir, J. (January, 1910), "The Construction of Cow Houses." *Agricultural Journal of India.*

[4] Manteufel (April, 1911), "Epizootische Lymphangitis bei einem Pferde und einem Maulesel." *Arch. f. Schiffs-u. Tropen-Hyg.*

Veterinary Diseases— *continued*

Dale [1] has a useful article entitled "Hints on Holding a Post Mortem Examination." A description is given of the method of conducting a post mortem examination on an animal, and a short account is forthcoming of the gross pathological lesions met with in the various organs of animals that have been affected with diseases common to South Africa.

Todd and Wolbach [2] have a paper entitled "The Swamp Fever in Horses." The etiology, pathology, symptomatology, diagnosis and treatment are discussed in this paper, which also includes the histories of two cases. The conclusions arrived at by these observers may be quoted :—

> Our cases were too few in number for it to be possible to draw definite conclusions from them. Our results do not differ from those obtained by previous observers; consequently, our observations will merely serve to confirm those of others who have preceded us in studying the disease.
>
> Swamp fever is a disease of horses which is widely distributed in the Western United States and in Western Canada.
>
> It is usually a chronic disease, and is characterised by emaciation, weakness, irregular temperature and anæmia.
>
> It is caused by an infecting agent which can be transmitted from horse to horse by the inoculation of blood taken from an infected animal.
>
> All search for a parasite which might cause the disease has been unsuccessful; although very large numbers of preparations of body fluids and tissues have been examined at all stages of the disease by microscopical and bacteriological methods.

Water. The subject of water is such a wide one, that in a review like this it is impossible to deal fully with all the research work that has been carried out in connection with it during recent years.

A good deal of research has been directed towards obtaining satisfactory and at the same time economical methods of sterilising water for potable purposes. Thresh's [3] experiments go to show that calcium hypochlorite is a satisfactory chemical agent for sterilising waters free from suspended matter and of fair organic purity. The bactericidal proportions of calcium hypochlorite were tested chiefly against the *B. typhosus* and *B. coli*. To the sample water three parts of hypochlorite per million were added—this representing 1 part of available chlorine—and at the end of the time required for effecting the destruction of the bacteria a little sodium bisulphite was added, which removed the remaining chlorine and prevented the palatability of the water from being impaired. The cheapness of this method recommends it, for Thresh estimated that 25,000 gallons of water could be sterilised at a cost of 1*d*. No special apparatus is required, the hypochlorite being added as the water enters a tank of suitable capacity, and the bisulphite as the water leaves the tank to flow into storage or service reservoirs. Thresh carried out experiments with natural waters obtained from different sources, and found that two parts of chlorine per million always sterilised them.

In a further series of experiments Thresh [4] found that the residual chlorine in the water left after sterilisation, could be got rid of by filtration through a thin layer of iron turnings or a thick layer of scrap aluminium. Wrought-iron turnings gave the best result. The iron which is held in solution and in suspension can be got rid of by filtration through sand or polarite.

Walker [5] has recently published a paper advocating the De-Clor system of purifying water for potable purposes. Chloride of lime is added to the water. The amount of chlorine used represents 1 part of available chlorine per million. The excess of chlorine present in the water is removed by subsequent filtration of the treated water through carbon.

The ozone process of sterilisation has been employed on a large scale in different cities, but the chief disadvantages appear to be due to the fact that the treated water acquires during the process a disagreeable taste and that considerable difficulty exists in the production of the ozone without at the same time producing nitrous acids. Further disadvantages are the initial cost of putting up the apparatus and that skilled supervision is necessary.

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[1] Dale, T. H. (April, 1911), "Hints on Holding a Post Mortem Examination." *Agricultural Journal of the Union of South Africa*, Vol. I., No. 3.

[2] Todd, J. L., and Wolbach, S. B. (January, 1911), "The Swamp Fever of Horses." *Journal of Medical Research*, Vol. XXIV., No. 1.

[3] Thresh, J. C. (November 28, 1908), "The Sterilisation of Potable Waters by means of Calcium Hypochlorite." *Lancet*.

[4] *Idem* (April, 1910), "Purification of Water for Potable Purposes by means of Chlorine or Hypochlorite." *Journal Royal Institute of Public Health*.

[5] Walker, L. (January, 1911), "The Effect of Chlorine upon the Micro-organisms of a River Water." *Ibid.*

Water—*continued*

Daske [1] gives a detailed description, with diagrams, of large ozone works and of works on a smaller scale, as for hospitals and houses, etc. He urges the use of ozone as a process for purifying surface water and the water contained in reservoirs.

Recently, advantage has been taken of the ultra-violet rays [2] as a sterilising agent for water. These rays are generated by means of a quartz mercury vapour lamp, the electric arc produced between the metal electrodes consisting of mercury. This mercury arc has been studied by Arons and Cooper Hewitt, the latter's work resulting in the Cooper Hewitt lamp.

The Westinghouse Cooper Hewitt Company, Ltd., now supply the apparatus for the process of sterilising by means of ultra-violet rays. This company supplies what are known as units ; each unit will sterilise 132,000 gallons of water in twenty-four hours.

Courmont and Nogier [3] carried out a number of experiments on the sterilising effect of the ultra-violet rays. They used a Kromayer lamp and they found that water inoculated with *B. coli* was completely sterilised at a point 10½ cm. away. The best results were obtained by immersing the lamp in the water. From the experiments of these observers it was found that water containing 1,000,000 bacteria, and 100,000 *B. coli* per c.c. was completely sterilised in one minute. The water to be treated must be clear, as the presence of floating particles nullifies the action, so that filtration is almost obligatory. The treated water undergoes no appreciable alteration as regards appearance, odour, or taste.

The apparatus is simple and cheap, and the working presents no difficulties whether the process is carried out on a large or a small scale.

Thresh and Beale [4] have also conducted a number of experiments with a small Cooper Hewitt quartz lamp, which was capable of purifying 50–200 gallons of water per hour. In their experiments they found that the ultra-violet rays had little or no effect on the chemical composition of water, nor did the treated water show the presence of ozone. The temperature of such a water was only slightly raised. They also credited the ultra-violet rays with deodorising properties. With a fairly clear water they found that the ultra-violet rays produced a sterilising effect sufficiently marked to convert a dangerously polluted water into a safe one. A faint turbidity in the water or the presence of colloid matter greatly retarded the action.

Many bacteria are killed after 5–20 seconds exposure to ultra-violet rays. *B. coli* was killed in 15–20 seconds, *B. typhosus* in 10–20 seconds, and the cholera vibrio in 10–15 seconds.

Henri [5] and others obtained equally successful results with the ultra-violet rays. Greater care has to be taken with the sterilisation of milk by this process owing to its opacity.

Smith [6] in a useful paper describes different methods for the treatment of water to prevent plumbo-solvency. The best results were obtained by adding finely-ground chalk, 1 grain per gallon of water, allowing the water to pass through filter beds of Trent sand, and then adding a clear solution of lime water.

Hungerford [7] found that the removal of iron from water was best accomplished by the addition of lime and subsequent filtration through sand. By this method iron, whether present as bicarbonate or sulphate, is eventually converted into the sesquioxide, and the latter, being insoluble in alkaline water, is readily removed by filtration.

Ruffer and Willmore [8] have carried out a bacteriological examination of the drinking-water supply of a large number of steamships, and, judging from their results, a very unsatisfactory and dangerous state of things exists.

Crimmin [9] has recently called attention to this, and it would be well if some form of

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[1] Daske, O. (1909), "Die Reinigung des Trinkwassers durch Ozone." *Deut. Vierteljahrsschr. f. öffentl. Gesundheitspflege*, Vol. XLI., No. 3.

[2] (December 17, 1910), "Sterilisation of Water on a large scale by means of Ultra-violet Rays." *Lancet.*

[3] Courmont, J., and Nogier, T. (June 30, 1909), "Sur la stérilisation de l'eau potable au moyen de la lampe en quartz à vapeurs de mercure." *Bull. de l'Inst. Past.*

[4] Thresh, J. C., and Beale, J. F. (December 24, 1910), "The practical Sterilisation of Potable Water by means of the Ultra-violet Rays of Light." *Lancet.*

[5] Henri, C., Helbronner, A., and Von Recklinghausen, M. (April 2, 1910), "Practical Sterilisation by means of Ultra-violet Rays." *Ibid.*

[6] Smith, C. C. (February, 1910), "Methods of Treating Water to prevent Plumbo-solvency." *Journal Royal Institute of Public Health.*

[7] Hungerford, C. (November, 1910), "Removing Iron from Water." *Ibid.*

[8] Ruffer, M. A., and Willmore, J. C. (September, 1908), "Drinking-Water of Steamships." *Journal of Hygiene.*

[9] Crimmin, J. (1909), "A Note on the Storage of Drinking-Water on Board Ships." *Transactions Bombay Medical Congress.*

Water—*continued*

international agreement was drawn up, and the suggestions of Ruffer and Willmore carried out on all ocean-going vessels. These suggestions are :—

(1) The source of the water must be above suspicion. Ships therefore should be allowed to take water only in places licensed by the medical officer of the port.

(2) The hoses, pumps, water-boats, etc., should be the property of the port sanitary authorities, who would then be responsible for the proper storing and cleaning of such apparatus. Should this be impossible, no apparatus or water-tank should be used until it has been examined and declared satisfactory by the said authority. All the apparatus should be examined and tested once a month.

(3) Intake pipes flush with the deck should be absolutely prohibited. They should be replaced by upright iron pipes, three feet high, of standard gauge, having their free ends bent downwards and fitted with screw cap chained to the pipe. When in use the cap should be removed and the hose screwed on. Some simple device would indicate when the tank was full.

(4) All water tanks on board ships should be made of iron, and coated inside with cement.

(5) All water tanks should be placed so as to allow inspection at any time during the voyage.

(6) All water tanks should be so closed as to avoid all chances of contamination during the voyage.

(7) All water tanks should be fitted with ventilating pipes, which should be carried up to a sufficient height to prevent contamination.

(8) One or more taps should be placed through the floor of tanks to ensure the latter being completely emptied at regular intervals. The tanks should be constructed with " round corners ; " the floor of the tanks should be sloping towards the taps used for emptying the tanks.

(9) The tanks should be completely emptied and disinfected after each voyage. The methods used at present for this purpose are extremely unsatisfactory. Some form of gaseous disinfection would probably give the best results.

Clemesha's[1] recent investigations on the bacteriology of drinking-water supplies in India show that the contamination of water-supplies in that country is chiefly due to animal excrement, and that the true *B. coli* of Escherich is by no means so common as many suppose in the fæces of man and animals in India. Clemesha and his co-workers carried out an extensive series of experiments and proved that the *B. coli*, Escherich, was extremely susceptible to the forces of nature inimical to most organisms and therefore that its presence in a water was strong evidence of actual and recent contamination. They further showed that the intestinal flora of both man and animals was a variable quantity at different seasons of the year, and that corresponding changes occurred in the bacterial contents of natural Indian waters. If systematic tests were carried out throughout the year on Clemesha's lines, important knowledge would be gained as to these seasonal variations in both excrement and water and it would be well for all interested in water-supply in the Tropics to adopt this procedure.

Clemesha adopted MacConkey's classification of the lactose fermenters which were found during the course of his investigations, dividing them into four groups according to their fermentative action on dulcit and saccharose. He further grouped these organisms into classes according to their powers of resisting sunlight.

Firth,[2] in an excellent memorandum issued to military medical officers in India, deals with the routine examination of Indian water-supplies, taking as a guide Clemesha's work on the resisting powers of fæcal organisms to sunlight. He makes the following tentative bacteriological standard for various water-supplies :—

A *good well or spring water* should contain no fæcal bacilli in 15 c.c., while an indifferent or usable water should contain no fæcal bacilli in 20 c.c. The presumptive evidence of fæcal bacilli is drawn from the initial reactions in the lactose bile-salt broth cultures. Further, a good water from these sources should yield a total colony count of under 50 per cubic centimetre.

Pond, tank, or *lake* waters should be condemned if they contain micro-organisms of the Madras Class I. in 1 c.c. or less. These are very difficult waters to judge, and much importance must be laid on the result of a critical personal inspection of the surrounding conditions, that is, where there is obvious evidence of fouling from local habitations or the recent occurrence of rain. Incidentally it may be remarked that the presence or absence of *Bacillus lactis ærogenes* is a valuable criterion, and the marked absence or scarcity of this particular micro-organism from waters of this class is to be taken as an indication for condemnation. Where a surface water contains more than five fæcal micro-organisms to the cubic centimetre, even if of the more resistant kind as included in the Madras Class, it must be regarded with suspicion. A *fair or usable pond water* should not yield more than 200 organisms per cubic centimetre on the total count. It should show no lactose fractors in less than 5 c.c., while a desirable feature is the considerable presence of *B. lactis ærogenes*. As a rule, the less resistant type of bacteria, as grouped in the Madras Class, should not be present in less than 15 or 20 c.c. On the other hand, a *good pond water* may be taken to be one which contains less than 100 total colonies per cubic centimetre. It should show no lactose fractors in 15 or 20 c.c., be rich in *B. lactis ærogenes*, and practically devoid of the Madras Class I. group in 50 c.c.

River waters are notoriously variable. A *bad river water* will yield as many as 1000 colonies on total agar count. The lactose fractors will be anything from 20 to 100 per cubic centimetre. This class of water should be

[1] Clemesha, W., Aiyar, T. S., and Mudaliyar, V. G. (1908), " A Study of the Bacteriology of Drinking-Water Supplies in the Tropics." *Annual Report, King Institute of Preventive Medicine, Madras.*

[2] Firth, R. H. (November, 1910), " Routine Examination of Indian Water-Supplies." *Journal Royal Army Medical Corps.*

Water—*continued*

condemned. A *usable river water* may be taken to be one which gives 200 to 300 colonies on the total agar count per cubic centimetre. The fæcal organism should not exceed 2 to the cubic centimetre, and should be mainly of the more resistant varieties, or those in the Madras Classes II. and III. If any of the less resistant type are present, or those of Class I., they should not be found in less than 15 c.c.

A *good river water* will not contain more than 100 colonies on total count on agar. If fæcal organisms are present they should be mainly of the Madras Classes II. and III. Those of Class I. should not be present in less than 50 c.c.

In all these cases it is assumed that the presence of cholera vibrios is tantamount to absolute condemnation.

Dolt [1] has carried out some experiments for the purpose of obtaining a suitable synthetic medium to be used in water analysis for the purpose of favouring the growth of *B. coli*, and inhibiting the growth of the other water organisms. Glycerin, ammonium lactate and malic acid all fulfil the purpose of inhibiting the growth of water organisms other than *B. coli*.

Dolt recommends :—

Purified agar	3 per cent. 500 c.c.
Glycerine	5 grammes
Ammonium phosphate	1 gramme
Distilled water	500 c.c.

Sodium hydroxide solution is used to neutralise, and 1 per cent. lactose added just before sterilisation.

Another medium recommended by him is—

Purified agar	3 per cent. 500 c.c.
Ammonium lactate	5 grammes
Disodium phosphate	1 gramme
Distilled water	500 c.c.

Sodium hydroxide and lactate are added as before. In preparing both media azolitmin solution is used in the ordinary way.

Wilson,[2] while carrying out some work on the characters of the pathogenic *B. coli* met with in the urinary tract in cases of pyelitis and cystitis, isolated six organisms of the *B. coli* type that did not ferment glucose. He suggested that the term *B. coli* "anærogenes" be given to the organisms that formed no gas in glucose.

Federolf [3] suggests what appears to be a useful method of precipitation for the detection of *B. coli* in the routine examination of water. By his method it is possible to detect as small a number of *B. coli* as seven per litre. Four cubic centimetres of a 10 per cent. sterile solution of NaOH are added to a litre of water, rendering it thus somewhat alkaline ; then there are added 3·5 c.c. of a 10 per cent. sterile solution of ferric sulphate, and the whole is mixed thoroughly. The flask is then placed in an ice chest, and the sediment collected and centrifuged. The supernatant fluid is propelled off and the sediment is dissolved by adding a sufficient amount of a sterile 25 per cent. solution of tartarate of potash. The dissolved sediment is then plated out in Drigalski-Conradi or Endo agar, and the colonies of *B. coli* picked off.

Rochaix and Dufourt [4] tested the action of a number of organisms upon neutral red, and they found that certain bacteria present in the urine other than *B. coli* gave a yellow colour with a green fluorescence. All these bacteria were ammonia fermenters. This neutral red reaction given by organisms other than *B. coli* is liable to introduce an error when searching for *B. coli* in water. To obviate this, Rochaix and Dufourt recommend the addition of glucose peptone to the neutral red. These observers lay stress on the fact that to observe the neutral red reaction it is necessary to use transmitted as well as reflected light in order to note the canary-yellow colour and green fluorescence.

Joseph [5] isolated the *B. anthracoides* of Hueppe and Wood from surface wells, sewage effluent, soil, dam-water and once from a deep bore hole. Apparently it is a resistant organism, for it survived in water after *B. coli* and other non-spore bearing organisms had disappeared. This observer considers that the detection of this organism is of considerable importance

[1] Dolt, M. (1908), "Simple Synthetic Media for the Growth of *B. coli*, and for its Isolation from Water." *Journal Infectious Diseases.*

[2] Wilson, W. J. (September, 1908), "Bacteriological Observations on Colon Bacilli infecting the Urinary Tract, with special remarks on certain Colon Bacilli of the 'Anærogenes' Class." *Journal of Hygiene.*

[3] Federolf, M. (1909), "Über den Nachweis des Bacterium coli in Wasser durch die Fällung. *Arch. f. Hygiene,* Vol. LXX., p. 311.

[4] Rochaix, A., and Dufourt, A. (November 5, 1910), "Signification de la réaction du neutral-rot." *C. R. Soc. Biol.*

[5] Joseph, F. H. (February, 1909), "The Bacillus Anthracoides in Water-Supplies." *Journal Royal Institute of Public Health.*

Water— *continued*

in the study of water-supplies, especially in those cases where pollution only occurs at comparatively long intervals.

Mention may be made here of the Mills-Reincke phenomenon. Mills observed that the general death-rate of the city of Laurence had considerably decreased when a filtered and purified water-supply had been established in that city. Reincke a few months earlier observed the same condition of things taking place in Hamburg, after a public water-supply had been installed there, and Sedgwick and Macmitt,[1] recognising the importance of this observation, termed it the Mills-Reincke phenomenon.

Houston [2] has carried out some important experiments in connection with the purification of raw river water by means of storage. He found that the biological benefits resulting from storage of water were due to vital reactions rather than to mechanical effects, and he believed that adequately stored water is probably incapable of causing epidemic disease. Some experiments carried out with *B. typhosus* and the cholera vibrio showed that beneficial results followed from storage of water artificially infected. The cholera vibrios succumbed very readily, 99·9 per cent. of them perishing at the end of a week's storage, and after three weeks no specific vibrios could be found in 100 c.c. water. He ascertained that typhoid bacilli survived for 5 to 8 weeks. In some further experiments carried out with a strain of *B. typhosus* isolated from the urine of a typhoid carrier, he concludes by stating that even a week's storage of river water is an enormous protection, and less than a month's storage an absolute protection against typhoid fever. As regards the method of storage Houston recommends the use of a series of small reservoirs rather than a single large one and advocates the "continuous flow" in preference to the "quiescent" method of working storage reservoirs. By doing so, the condition of stagnation which favours the growth of algæ is obviated. The length of time required for storage antecedent to filtration is 30 days.

The chief points quoted by Houston in favour of storage of raw river water are as follows :—

(1) Storage reduces the number of bacteria of all sorts.

(2) Storage reduces the number of bacteria capable of growing on agar at blood heat.

(3) Storage reduces the number of bacteria capable of growing in a bile-salt medium at blood heat, chiefly excremental bacteria.

(4) Storage reduces the number of coli-like microbes.

(5) Storage reduces the number of typical *B. coli*.

(6) Storage alters certain bacteriological river water ratios; for example, it reduces the number of typical *B. coli* to a proportionally greater extent than it reduces the number of bacteria of all sorts.

(7) Storage, if sufficiently prolonged, devitalises the microbes of water-borne disease (*e.g.* the typhoid bacillus and the cholera vibrio).

(8) Storage reduces the amount of suspended matter.

(9) Storage reduces the amount of colour.

(10) Storage reduces the amount of ammoniacal nitrogen.

(11) Storage reduces the amount of oxygen absorbed from permanganate.

(12) Storage usually reduces the hardness, and may reduce (or alter the quality of) the albuminoid nitrogen.

(13) Storage alters certain chemical river water ratios; for example, the colour results improve more than the results yielded by the permanganate test.

(14) Storage has a marked "levelling" effect on the totality of water delivered to the filter beds.

(15) Storage tends generally to lengthen the life of the filters. (Only under exceptional conditions is the converse true.)

(16) An adequately stored water is to be regarded as a "safe" water, and the "safety change" which has occurred in a stored water can be recognised by appropriate tests.

Frankland,[3] in a recent paper, endorses Houston's work on the storage of water.

Reference may be made to Don and Chisholm's [4] recent publication on the modern methods of water purification. The book commends itself on account of the practical descriptions given and the good technical illustrations.

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[1] Sedgwick, W. T., and Macmitt, J. S. (August 24, 1910), "The Mills-Reincke Phenomenon." *Journal Infectious Diseases.*

[2] Houston, A. C. (1909), *Research Reports Metropolitan Water Board.*

[3] Frankland, P. (March, 1911), "The Bacteriology of Water: Its present Position." *Journal Society Chemical Industry.*

[4] Don, J., and Chisholm, J. (1911), *Modern Methods of Water Purification.*

Additional Notes

Water—*continued*

Deeleman [1] has a paper describing a portable form of water steriliser, in which ultra-violet rays are employed. It is intended for use with existing available sources of electric current. The portable apparatus suggested by the author consists of the following parts :—

(1) A fixed 2½ h.p. petrol motor engine.

(2) A cylindrical or rotary pump of 25 to 40 litres (43 pints) per minute capacity.

(3) A shunt wound dynamo of 1·35 kilowatts at 135 volts.

(4) Two roughing filters.

(5) Two fine filters.

(6) Two sterilising chambers.

(7) A switch-board for the regulation of the dynamo and the electric fittings of the sterilising chambers.

(8) Tubes for water connection.

Volpino and Cler [2] have tried the complement deviation method as a means of detecting typhoid bacilli in water. The question of the minutest dose of typhoid bacilli that could be detected by this method had first to be settled, inasmuch as bacteria of the typhoid group are met with in water under natural conditions in only minute quantities. As a result of some preliminary experiments these observers found that the method employed by them was sensitive enough for the detection of 0·002 mgm. of bacteria.

The 10 litres of infected water having been subsequently concentrated to 10 c.c. in a water bath at a temperature of 100° C. during three days, 0·08 gr. of NaCl. was added to the residuum. The obtained fluid was rich in various salts, and had a turbid appearance. Nevertheless, preliminary tests showed that it did not possess any hæmolytic power by itself, nor did it interfere with the hæmolysis, even in a dose as large as 1·2 c.c. It was thought advisable to employ for the final test as small a quantity as possible, and, therefore, 0·1 to 0·6 c.c. was taken ; the results obtained were always positive. A similar experiment, which gave identical positive results, was undertaken with another 10 litres of infected water, which were concentrated according to the Weichardt's method (concentration at 70° C. until 100 c.c. were obtained ; these 100 c.c. again concentrated at 90° C., until a residuum of 10 c.c. were obtained). This method was proved to be specific, for *B. coli* and *B. paratyphosus B.*, employed in a dose similar to that of the typhoid organism gave but negative results.

The authors believe that under normal conditions a greater dilution of typhoid bacilli in water may be expected than that prepared by them, and that, therefore, much larger quantities of water would have to be concentrated. In such cases a prolonged filtration of many hectolitres of water, through Chamberland's F. filter, should be carried out. Several hectolitres of water could be filtered during twenty-four hours, and after that the surface of the filter should be thoroughly brushed, and all gathered substance should be dissolved in the smallest possible quantity of physiological salt solution. This solution would be used as the antigen, after having been preliminarily tested in the usual way. It should be remembered that all the dissolved salts would pass through the filter, thus leaving the residuum almost entirely consisting of bacteria and organic substances.

If this method can be proved by confirmatory results to be really as reliable as it is said to be, it will certainly facilitate the bacteriological control of drinking-water.

Mention may be made of a paper by Hall,[3] describing what he believes to be a supposed undescribed *coli*-form organism in drinking-water. It is an active fermenter of most of the carbohydrates, and produces large quantities of gas in certain media. It is non-pathogenic for guinea-pigs. A point of interest about this organism was the peculiar blue reaction produced on Conradi-Drigalski agar, while the reaction produced in lactose was evidenced by slight acidity and the production of gas.

Whooping-Cough. The organism discovered by Bordet and Gengou is now admitted by the majority of observers to be the specific microbe of whooping-cough. As described by Bordet [4] it is a small cocco-bacillus, resembling in size and shape the influenza bacillus. Examined *in situ* it is rather longer and plumper, but during the process of subcultivation it diminishes in size till finally it appears as a mere point when seen under the highest powers of a microscope. It is best grown in a medium consisting of defibrinated human or rabbit's blood mixed with an equal quantity of 3 per cent. agar containing a little extract of potato and glycerine. It is an obligatory ærobe, and grows well in liquid media such as serum broth and blood broth, provided that shallow vessels are used, so as to offer a large surface in contact with the air. If a subculture from blood agar be put on ordinary agar, no growth appears till the twelfth day, and even then it is faint, as the medium is not a favourable

[1] Deeleman, M. (March 20, 1911), "Ein fahbarer Uviol-Trinkwasser-Sterilisator für Feldgebrauch zum Anschluss an vorhandene Stromquellen." *Deut. Militär-Zeit.* Quoted in *Journal Royal Army Medical Corps*, May, 1911.

[2] Volpino, G., and Cler, E. (April 19, 1911), "Die Untersuchung der Wasser auf Typhusbazillen mit dem Komplementfixierungsverfahren." *Cent. f. Bakt.*, I. Orig., Vol. LVIII., No. 4. Quoted in *Journal Royal Institute Public Health*, May, 1911.

[3] Hall, G. N. (June, 1911), "The Occurrence of a Supposed Undescribed Coli-form Organism in Drinking-Water." *Journal Royal Institute of Public Health.*

[4] Bordet, J. (October 9, 1909), "The Microbe of Whooping-Cough." *British Medical Journal.*

Whooping-Cough—*continued*

one. Bordet has shown that the cultures obtained from growths in unfavourable media develop new traits and differences of a striking type from the mother culture.

In microscopic preparations from the exudate, taken at the beginning of the disease, the bacillus is present in enormous numbers. It grows by choice in the deep and remoter parts of the respiratory tract, seldom above the level of the larynx and more often below it. In the later periods of the disease the specific organism is not present in large numbers in the secretion from the respiratory tract. To obtain suitable material for cultural purposes it is essential to pick out of the phlegm a strip of viscid exudate rich in leucocytes coming from the depth of the bronchi, the expulsion of which marks the end of one of the violent fits of whooping in the early stage of the disease. The specific organisms found almost in pure culture are non-motile, Gram-negative, and stain but faintly with the usual basic dyes. Even on the most favourable media growth takes place slowly, colonies appearing after two or three days. As to the specificity of Bordet's bacillus, the conclusions of Bordet and Gengou, which are based chiefly on the serum reactions of whooping-cough patients have been confirmed by other workers, for cultures of this organism were specifically agglutinated by the serum of whooping-cough patients and deflected the complement with such serum. The agglutinative reaction was not very strong, complete agglutination in sixty-fold dilution of the serum being the highest found.

Bordet and Hceswijk found that if the bacterium of whooping-cough was subjected to special conditions of existence, such as growing it on ordinary agar, it lost certain of its characteristic elements, especially the property of reacting with an agglutinin capable of influencing the same germ when grown on a medium rich in blood; and further, they found that this property was regained when the agar germ was replanted in blood media.

They arrived at these results by discovering that the serum of a horse immunised against an organism grown on a blood medium agglutinated this organism to a higher extent than the same organism when grown on agar. They explained this by the fact that the organism grown on a blood medium possessed an antigen which was lacking in the organism grown on agar. The explanation accounts for some of the failures that occurred in the specific agglutinin tests carried out on pertussis patients, and were doubtless due to differences in the bacterial emulsions produced by different culture media being used. Freeman experienced some of these failures, and, acting on Bordet's suggestion, found that if the cultures were transferred to blood media satisfactory agglutination occurred.

Seiffert [1] examined sixteen cases of whooping-cough, and was successful in isolating Bordet's bacillus from the sputa of twelve of the cases. The sputum was washed several times in normal saline solution and a small particle placed in Bordet's blood agar plates. Suspicious Gram-negative colonies were picked off after incubation at 37° C. for twenty-four hours, and subcultured in sloped blood agar. If these subcultured bacilli again proved to be Gram-negative, the agglutination reaction was carried out with Bordet's horse immune serum, which agglutinated Bordet's bacillus in a dilution of 1 : 1000.

Seiffert found that the agglutination titre of whooping-cough patients was a low one, from 1 : 16 to 1 : 32.

In his hands experiments on the deviation of the complement gave positive results in the cases of whooping-cough that were convalescent.

Klimenko [2] has confirmed the results of Bordet and Gengou as regards the specificity of Bordet's bacillus of whooping-cough, and considers that the bacillus of Pfeiffer and the bacillus of Krause Joachman are not the true causal organisms of this disease. Klimenko isolated Bordet's bacillus from the sputum in five cases, and in one case he obtained the organisms from the blood of the heart and the lungs. He was successful in producing a cough in monkeys and in dogs, when these animals were inoculated with the specific bacillus. One of the monkeys contracted the malady after it had been in contact with another monkey which had its respiratory passages inoculated with the bacillus. This observer in a further series of experiments [3] on dogs produced in them a clinical picture of whooping-cough by applying cultures to the nose and trachea of these animals. The majority of the experiments ended fatally, and the post mortem findings consisted of tracheitis, bronchitis, and lobular pneumonia. Four monkeys were successfully inoculated. Bordet's bacillus was regularly cultivated from the animal during life, as well as from the post mortem lesions. Complement fixation experiments were successfully carried out in two dogs during the fifth week of illness.

[1] Seiffert, G. (January 19, 1909), "Über den Bordetschen Keuchhustenbazillus." *Münch. Med. Woch.*, No. 3.

[2] Klimenko, W. N. (February 18, 1908), "Über das Keuchhustenstäbchen von Bordet und Gengou." *Cent. f. Bakt.*, I. Orig., Vol. XLVI., pp. 218–219.

[3] *Idem* (November 19, 1908), "Zur Ätiologie des Keuchhustens." *Deut. Med. Woch.*, No. 47.

Whooping-Cough—*continued*

Klimenko [1] has recently endeavoured to apply the method of blood culture for the diagnosis of whooping-cough, but failed to detect Bordet's [2] microbe in the blood of patients during the spasmodic period of the illness. Whooping-cough infection, therefore, does not appear to be a bacteriæmia, but a local infection of the respiratory tract. This is more or less in accordance with the clinical picture of the disease, and with the opinion held by Bordet, who proved that the specific bacillus produced an endotoxin which accounts for the signs and symptoms of pertussis.

Ashby [3] has carried out some observations on the blood of nearly 100 children suffering from whooping-cough. The blood changes consisted of a slight anæmia, and a well-marked leucocytosis, 15,000 and 30,000 white blood cells being present per c.mm. Of the white cells, the lymphocytes were greatly in excess of the polymorphonuclears, the percentage of the former reaching about 60 per cent., and the latter about 40 per cent., with an occasional eosinophile cell. The lymphocytosis represented chiefly the small variety of lymphocytes, but at the same time there was a greater preponderance of large lymphocytes than is usually met with in normal blood, for these cells frequently reached 10 per cent.

In infants the lymphocytes normally form between 40 and 50 per cent. of the total white cells; but if the lymphocytes form nearly 60 per cent. of the white cells and there is a larger proportion of large lymphocytes than normal, Ashby considers that this is confirmatory evidence of the existence of the disease and a valuable aid to diagnosis in early cases where a child exposed to infection has developed a cough. After the whooping stage has passed the lymphocytosis persists for a short time and then disappears.

With regard to treatment, no specific drug has as yet been discovered.

Ker,[4] in his classical work on infectious diseases, advocates free ventilation and the treatment of the patients under open-air conditions. As regards diet, he is in favour of a fairly liberal dietary in all children who are able to be out of bed and who are over two years of age. Where the paroxysms are very frequent and the food ingested is vomited, he recommends milk and lime water, or small amounts of meat extracts, and also Sanatogen, sweetened and flavoured with vanilla. In bad cases the milk should be peptonised. As regards drug treatment, quinine appears to be efficacious towards the end of the paroxysmal stage; one grain for each year of the child's life being given twice daily. For the spasms, belladonna gives the best results in doses of three minims of the tincture every four hours, adding a minim daily till ten or twelve minims are reached. A mild expectorant often makes the cough easier.

Baedeker [5] claims that eulatin, a compound of amido-benzoic and bromo-benzoic acid with antipyrin, diminishes the number of paroxysms and also inhibits vomiting. His experience of this drug appears to be a favourable one, as the course of the disease is checked, and patients make a comparatively speedy recovery. The dose for a child of $1\frac{1}{2}$ years is 6–10 tablets daily, each tablet representing 0·25 gramme. Children of four years of age receive 12 of these tablets.

Biehler [6] strongly recommends fluoroform, and reports 232 cases of whooping-cough successfully treated with this drug. This observer claims that under fluoroform, recovery is complete in three to four weeks, and is most rapid in the older children, the attacks of coughing being lessened in all cases as soon as the patient begins to take the drug. The drug in the form of fluoroform water is well tolerated even by infants a few weeks old. The dosage recommended is 10–15 minims thrice daily and 5–10 minims after each attack of coughing, up to 200 or 250 minims in twenty-four hours for children of one year. Children of two or three years were given 20–25 minims thrice daily, and after each attack as many minims as the child numbered years.

Campbell Murray [7] has used euquinine (ethyl-carbonate of quinine) with marked success in whooping-cough. Its tastelessness renders it suitable for children.

Freeman [8] has employed vaccine treatment for this disease, giving 1000 test inoculations

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[1] Klimenko, W. N. (March 6, 1911), "Bakteriologische Untersuchungen des Blutes von Keuchhustenkranken Kindern und von mit Keuchhusten infizierten Tieren." *Cent. f. Bakt.*, I. Orig., Vol. LVIII., No. 1.

[2] Bordet, J. (October 9, 1909), "The Microbe of Whooping-Cough." *British Medical Journal.*

[3] Ashby, H. (May 7, 1910), "The Diagnostic value of the Leucocytosis occurring in Whooping-Cough." *Ibid.*

[4] Ker, C. B. (1909), "Whooping-Cough." *Text-book of Infectious Diseases.*

[5] Baedeker, J. (September, 1909), "Eulatin in Pertussis." *Therap. Monats.* Quoted in Epitome, *British Medical Journal*, January 1, 1910.

[6] Biehler (July, 1910), "Fluoroform in Whooping-Cough." *Arch. de méd. des enfants.* Quoted in Epitome, *British Medical Journal*, September 17, 1910.

[7] Murray, J. C. (October 15, 1910), "Euquinine in Whooping-Cough." *Therapist.*

[8] Freeman, J. (October 9, 1909), Discussion on Bordet's paper, entitled "The Microbe of Whooping-Cough." *British Medical Journal.*

Whooping-Cough— *continued*

of a vaccine prepared from Bordet's bacillus, and his statistics demonstrate an advantage of the vaccinated cases over the unvaccinated. His results showed that a larger dose of the vaccine conferred a greater benefit on the patient than a small one. The doses employed by him varied from two and a half million to twenty million bacilli.

Yaws. Two schools of thought still exist with regard to the specificity of yaws as a disease, but it is not within the scope of this work to enter into a discussion as to whether yaws and syphilis are one and the same thing, or two separate pathological entities.

A considerable amount of work has been carried out by competent observers in different countries where this disease is prevalent, and the concensus of opinion goes to show that yaws is not identical with syphilis, although the morphological similarity between the causal agents of both diseases is a very strong one.

Castellani, Neisser, Ashburn, Craig and other observers have carried out a complete series of experiments to establish the existence of yaws as a specific disease, and reference to their work was made in the previous review.

Many observers have studied the comparative morphology of the spirochætes of syphilis and yaws. Levaditi and Nattan-Larrier [1] published a paper, in which they stated that the *Treponema pertenuis* showed as a rule in stained preparations more irregular undulations than the *Treponema pallidum*, and that the former showed a greater tendency to curl up at one end into a loop. When fresh smears were examined *T. pertenuis* displayed whip-like lateral movements rather than translatory ones.

Russell [2] more or less confirmed these observations, for he found that (1) the *T. pertenuis* was slightly thicker than the *T. pallidum;* (2) the distance from crest to crest of the waves was greater; (3) the dip from the crest to the hollow was usually greater; (4) the waves were not quite so regular in height; (5) the number of forms showing longitudinal division were more numerous; (6) there was a greater tendency for the spirochæte to curl up at one end into a loop.

Similar appearances were observed by me (R. G. A.) in stained smears obtained from cases of yaws in the Sudan.

Prowazek, in some comparative studies on spirochætes, has come to practically the same conclusions. This observer also described a resting form of the treponema which is oval or round, and which is produced by a coiling up of the spiral.

Mention may be made of protozoal bodies which Robertson [3] found in films prepared from flies taken in yaws houses, and presumably infected. In addition to them there were also present spirochætes resembling the *T. pertenuis* of Castellani. Robertson was inclined to think that these so-called protozoal bodies represented the parent bodies of the spirochætes but this is extremely doubtful.

As regards recent experimental work in connection with this disease, Nicols [4] found that rabbits could be infected in the testicle with the spirochæte of yaws as well as with that of syphilis and the infection could be continued through successive generations in pure culture. The testicle became enlarged and showed the presence of a nodule. Microscopically, there was an apparent necrosis of the tubules with an infiltration of round cells, and the formation of œdematous connective tissue. With the material obtained from one of these rabbits the disease was reproduced in a monkey and continued in a second generation of rabbits. Nicols also obtained the complement fixation reaction in rabbits infected with the spirochætes of yaws, as well as in those infected with the spirochæte of syphilis.

McIntosh [5] has studied the histo-pathological changes present in experimental yaws, more especially in relation to the distribution of the *T. pertenuis* in the lesions produced, and his results more or less correspond with the description given by Shennan [6] and others of the distribution of this organism in human lesions.

There appears to be some difference in the distribution of *T. pertenuis* in the lesions

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[1] Levaditi, C., and Nattan-Larrier, L. (March 25, 1908), "Contribution à l'étude microbiologique et expérimentale du Pian." *Ann. de l'Inst. Past.*

[2] Russell, F. (1909), "The comparative morphology of the Spirochætes of Syphilis and Yaws." *American Society of Tropical Medicine.*

[3] Robertson, A. (November 2, 1908), "A protozoon in Yaws." *Journal Tropical Medicine and Hygiene.*

[4] Nicols, H. J. (November 1, 1910), "Experimental Yaws." *Ibid.*

[5] McIntosh, J. (January, 1909), "The distribution of the *Spirochæte pertenuis* in the lesions of Experimental Yaws." *Journal Pathology and Bacteriology.*

[6] Shennan, T. (January, 1908), "The localisation of Spirochætes in the papules of Yaws." *Ibid.*

Yaws—*continued*

of yaws when it is compared with the distribution of the *T. pallidum* in the primary lesions of syphilis. McIntosh and others consider that it is impossible to differentiate the *T. pertenuis* from the *T. pallidum* in sections stained by the silver method. Even if this is so, one must take into consideration that the relationship between yaws and syphilis is more or less the same as that existing between tubercle and leprosy.

In tubercle and leprosy the causal organisms strongly resemble each other, both morphologically and in staining reactions, and yet there can be no doubt as to the duality of these two diseases.

Considerable evidence has been brought forward as to the part played by flies as transmitting agents; doubtless other factors are also concerned.

Duprey [1] suggests that the abuse of the mango fruit as an article of diet may possibly account for the existence of yaws in the West Indies. His suggestion is not at all convincing. The treatment of yaws has advanced considerably since Ehrlich's preparation of dioxy-diamido-arsenobenzol was brought before the public as a specific for the treatment of syphilis. Strong [2] employed intramuscular injections in amounts of 0·3 gramme rubbed up with methyl-alcohol and distilled water, and finally dissolved in decinormal sodium hydroxide and injected into the buttock. Marked improvement was noticed in the granulomatous lesions in three to four days following this injection and in ten to twenty days the lesion had entirely disappeared. Large ulcerations healed up in three to four weeks.

Local treatment was unnecessary, except in cases of severe ulceration where organisms other than the *Treponema pertenuis* had invaded the lesions.

Castellani [3] also obtained excellent results by the intramuscular injection of this drug, the yaws lesions clearing up readily. It may be noted that one of his cases had a slight relapse which, however, yielded to a second injection.

Castellani recommends that the drug be injected into the external aspect of the thigh, as this is less painful than the injection into the gluteal region.

Alston [4] has employed the drug in doses of 0·6 gramme made into an emulsion with 5 c.c. of sterilised olive oil, and injected into the buttocks. This observer obtained some interesting results. He found that the serum of yaws cases treated with "606" was endowed with as efficient curative properties as the drug itself. Several cases of yaws were treated by injections of such serum, and rapid curative results obtained. The dose of serum used was 16 c.c. for adults. Alston found that boiling such serum did not destroy its efficacy. Further, he discovered that the serum of cases treated with the serum obtained from cases injected with "606" had also curative properties. He suggests that the milk of goats injected with "606" might be useful for children suffering from yaws.

Additional Note

Bowman [5] has carried out some work on complement fixation in yaws, and, as a result of his experiments, has been able to furnish additional evidence of the non-identity of syphilis and yaws.

Yellow Fever. In spite of the numerous investigations that have been carried out by scientific observers in the countries where this fever is endemic, our knowledge of its etiology has not advanced to any great extent. The part played by the mosquito *S. calopus* as a transmitting agent of yellow fever has been definitely established, although, according to Lacerda, Ybarra [6] and others, there appears to be a certain amount of evidence to show that this insect is not the only factor concerned in the dissemination of the disease. Quite recently Seidelin [7] has found what he believes to be the specific parasite of yellow fever in blood smears taken during life from yellow fever cases and in the capillaries of the kidney. This parasite is intracorpuscular, and bears a certain similarity to the malarial parasite. When

[1] Duprey, A. (December 15, 1910), "Yaws." *Journal Tropical Medicine and Hygiene.*

[2] Strong, R. (October, 1910), "The specific cure of Yaws." *Philippine Journal of Science*, B.

[3] Castellani, A. (January, 1911), "The use of Ehrlich's '606' in Frambœsia." *Arch. f. Schiffs-u. Tropen-Hyg.*, Vol. XV., No. 1.

[4] Alston, H. (February 18, 1911), "The curative effect of Salvarsan ('606') in Cases of Frambœsia." *British Medical Journal.*

[5] Bowman, F. B. (November, 1910), "Complement Fixation in Yaws." *Philippine Journal of Science*, B.

[6] Ybarra, A. M. F. (March 2, 1908), "Yellow Fever again in Cuba." *Journal Tropical Medicine and Hygiene.*

[7] Seidelin, H. (July 24, 1909), "The Etiology of Yellow Fever." *British Medical Journal.*

Yellow Fever—*continued*

stained by Giemsa it appears as multiple chromatin points with a pale blue staining protoplasm. These bodies have been found in nearly 90 per cent. of the cases. Seidelin considers them to be of a protozoal nature, and, owing to their complete lack of pigment and the frequent presence of two or more chromatin spots, he is inclined to associate them rather with the piroplasma than with the malarial hæmamœba. His observations in relation to this parasite being the specific cause of yellow fever require confirmation by other workers.

Mention may be made of Stimson's [1] discovery of a spirochæte in the cells and lumina of the kidney tubules in a fatal case of yellow fever. He suggested that this organism be called (*? Spirochæta*) *interrogans ;* the specific name being suggested by the form, somewhat resembling a question mark, which the organism frequently assumed in his preparations. Wolferstan Thomas,[2] in a series of experiments on guinea-pigs, rabbits, and chimpanzees, has given further proof in support of the part played by the mosquito in transmitting yellow fever. Guinea-pigs which had been bitten by infected *Stegomyia calopus* evidenced a reaction in 4½ to 13 days, while an animal which had already exhibited this reaction was immune to the bites of infected Stegomyia. The reaction in the guinea-pig was shown by the dull appearance of the animal, a rise of temperature and loss of appetite. The animal invariably recovered. Thomas further proved that Stegomyia which have fed on a guinea-pig during the period of fever could later on cause a reaction when allowed to bite a non-immune animal. The symptoms observed in those various animal experiments closely resembled the mild cases of an influenzal type so frequently seen in yellow fever epidemics and in young children living in endemic areas.

The recent epidemic of yellow fever in West Africa has been brought prominently before the public chiefly by the late Sir Rubert Boyce, who lately read a paper in which he stated that this disease was generally endemic on the west coast of Africa. This opinion is not, however, held by many medical officers resident in West Africa. The whole question seems to depend upon the differential diagnosis between yellow fever and malignant malaria. The supporters of the general endemicity of the disease on the coast hold the view that all cases of bilious remittent malaria have in reality been cases of yellow fever which have been wrongly diagnosed. Clinically there is often the greatest difficulty in saying whether a case is malaria—especially after quinine has been taken—or yellow fever. Lebredo [3] states that great stress should be laid on the following signs and symptoms of any suspicious or mild case of yellow fever : (*a*) date of invasion, (*b*) pains, (*c*) condition of the gums, (*d*) fever, (*e*) pulse, (*f*) jaundice, (*g*) albuminuria and diazo reaction, (*h*) vomiting. He also says that the presence of albuminuria on the third day of a febrile disease in a yellow fever country should always arouse one's suspicions.

Autopsies will assist materially in the diagnosis of yellow fever from malaria, for the appearance of the liver, kidney and spleen and the typical black vomit in the stomach are totally dissimilar from the pathological changes met with in malaria ; but here again a further difficulty arises, in cases where yellow fever occurs in patients who have had malaria. Wolferstan Thomas [4] has pointed out that the Brazilian child is susceptible to yellow fever, and the symptoms which present themselves are of such a character that a diagnosis can often only be made with the greatest difficulty. Albuminuria may or may not be present in these cases.

Mild attacks of yellow fever have also to be diagnosed from influenza and those gastric disturbances with fever of the types so well described by Marchoux and Simond.[5]

Mention must be made of Faget's [6] diagnostic reaction in yellow fever, as it is considered by many observers to be more or less pathognomonic of the disease. Faget from his studies of the New Orleans (1870) and the Memphis (1873) epidemics discovered that a falling pulse with a rising or horizontal temperature is a diagnostic reaction pathognomonic of yellow fever.

Fitzpatrick [7] has succeeded in obtaining Faget's reaction in eleven people, who were injected subcutaneously with killed mixed cultures of bacteria isolated from cases of yellow

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[1] Stimson, A. M. (December, 1909), " Notes on Stimson's Spirochæte found in the kidney of a Yellow Fever Case." *Transactions Society Tropical Medicine and Hygiene.*

[2] Thomas, H. W. (December, 1909), " The results of Inoculation Experiments by the bites of infected *Stegomyia calopus.*" *Ibid.*

[3] Lebredo, M. G. (December 15, 1909), " Diagnosis of Yellow Fever, with special reference to Mild Cases." *Journal Tropical Medicine and Hygiene.*

[4] Thomas, H. W. (June 1, 1910), " Yellow Fever." *Annals Tropical Medicine and Parasitology.*

[5] Marchoux, E., and Simond, P. L. (February, 1906), " Études sur la fièvre Jaune." *Ann. de l'Inst. Past.*

[6] Faget, J. C., *Yellow Fever.* Paris.

[7] Fitzpatrick, C. B. (1908–9), " Notes on the experimental production of Faget's diagnostic reaction of Yellow Fever." *Collected Studies from the Research Laboratory Department of Health, City of New York,* Vol. IV.

fever. The cultures that were used represented organisms of the colon group and consisted of two strains of *B. coli icteroides* and the *B. icteroides* of Sanarelli. When these killed cultures were mixed and injected subcutaneously the characteristic falling pulse and a rising or horizontal temperature was obtained. Yellow Fever—*continued*

Vargas and Seidelin[1] found that a positive diazo-reaction occurred in nine out of twenty-two cases of yellow fever. The reaction was positive only in those cases that had albuminuria, and frequently the urine gave an indican, but seldom a bile reaction.

Craig[2] has published quite recently an interesting paper showing the close similarity which exists between the virus of yellow fever, dengue, and pappataci fever. These three fevers resemble each other in having a sudden onset, a rapid course, and terminating by crisis rather than by lysis. Further, there is a certain similarity in their etiology, as the causal agent exists in the blood, but only during certain periods. The injection of both filtered and unfiltered blood from these febrile cases produces the disease, and all these three diseases are transmitted by insects. The causative agents are ultra-microscopical, and there is conclusive evidence to show that none of these three diseases is contagious. Craig concludes by considering that in time it will be proved that these fevers are due to closely-related species belonging to the same genus, and are probably protozoal in nature.

No specifie drug has yet been found for yellow fever, but a description may be given of the methods employed by Wolferstan Thomas[3] in its management and treatment.

The usual precautions with regard to the prevention of mosquitoes getting access to the patient are described, and do not require further mention.

Great stress is laid on the early examination of the urine and the patient should be made to urinate before the bowels move or a clyster is given.

As regards purges, fractional doses of calomel followed by sodium sulphate are strongly recommended, as the latter is an excellent diuretic, and with the calomel often allays the acidity of the stomach. After the preliminary purge, enemata should be used when required instead of further administration of purges by the mouth. After the purge has been given, a hot pack or mustard footbath is advised, and also the use of hot demulcent drinks.

Excessive sweating on the part of the patient should be avoided, and in fact, sweating should only be confined to the first twenty-four hours of the disease. As regards enemata, solutions of sodium chloride or sodium sulphate should be used, 600 c.c. to a litre of the solution being injected slowly, and retained as long as possible. The temperature of the solution should be usually about 60° to 70° F. Nourishment must not be given for the first three or four days, as the patient is able to do without food. His stomach obtains, therefore, the necessary rest. Even small amounts of milk increase the tendency to nausea, and should be discouraged. The patient should be encouraged to partake of such alkaline drinks as Vichy, Apollinaris, Mattoni; failing these, ordinary drinking-water with bicarbonate of sodium in it. At least three litres, distributed in definite quantities, at regular intervals should be given *per diem*.

The amount of urine passed increases, the kidneys being well flushed and the acidity of the stomach corrected. Venesection is indicated where the patients are plethoric, the congestion intense, the carotids visibly pulsating and the veins engorged. One hundred to a hundred and fifty cubic centimetres of blood can be removed with beneficial results in such cases as above indicated.

The application of ice bags to the head relieves the cephalalgia. The vomiting can frequently be checked by the use of ice bags, or a spray of ethyl chloride applied to the epigastrium.

If the temperature exceeds 101° F. sponging every two hours should be carried out. Cold baths are indicated if the temperature is above 104° F., but are only recommended if they entail no undue exertion on the part of the patient. If assistance is limited, cold packs could be substituted.

As inflammation of the gums and mouth is very likely to occur these should be carefully attended to. The tooth brush should be discarded and the teeth should be cleaned with pledgets of cotton wool soaked in a weak antiseptic solution. In order to harden the gums an antiseptic mouth-wash is useful. In addition to Vichy, fluid magnesia with benzoate of soda may be given.

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[1] Vargas, C., and Seidelin, H. (May 10, 1909), "Diazoreaktion beim Gelbfiebers." *Berl. Klin. Woch.*

[2] Craig, C. F. (February 25, 1911), "The nature of the virus of Yellow Fever, Dengue, and Pappataci Fever." *New York Medical Journal.*

[3] Thomas, H. W. (June 1, 1910), "Yellow Fever." *Annals Tropical Medicine and Parasitology.*

Yellow Fever—*continued*

Wolferstan Thomas recommends cachets of sodium bicarbonate in doses of 1 to 2 grammes every three to four hours. By this alkaline treatment the acid reaction of the urine is replaced by a neutral or alkaline one.

If in spite of this alkaline treatment the amount of urine is decreasing and failure of the renal system appears imminent, caffeine citrate in the form of hypodermics should be administered, failing this, theobromine in 2–3 gramme doses should be given daily. It is preferable to administer this drug in cachets of 0·3 to 0·5 gramme for a dose. Hot hip baths and poultices to the loins may be tried. Carroll suggested that a hypodermic or rectal injection of urea might be given if anuria is impending. The patient should be trained to use the urine bottle every three or four hours. Catheterisation may be necessary if the bladder becomes paralysed.

Alcohol in the form of champagne, or a good Rhine wine with Vichy added to it, is a useful stimulant. For hiccough, iced champagne gives very satisfactory results.

The distressing symptom known as black vomit can be treated by stopping the administration of all fluids by the mouth, and exhibiting adrenalin in the form of 20 to 40 drops in a teaspoonful of water. If collapse of the patient is threatened through attacks of vomiting, ether is useful. For cardiac weakness, caffeine, spartein and strychnine are of use.

During convalescence the patient requires careful treatment, more especially in severe cases, owing to the tendency to recurrent vomiting. Fatal relapses are generally due to indiscretions of diet. In mild cases, nourishment can be given on the fourth day. Milk mixed with lime water or Vichy, or toast water and barley water, can be taken in small amounts. For the first week of convalescence, chicken jelly, raw eggs and fish are indicated. Convalescent cases are very erotic, and patients should be warned of the dangers incurred by sexual intercourse while their heart muscle is degenerated. Wolferstan Thomas does not recommend the use of coal-tar products in the treatment of the disease. This experienced observer concludes his excellent paper by stating that "the first and most indispensable thing for success in the treatment of yellow fever is that it be begun as soon as the disease has declared itself."

Additional Notes

The late Sir Rubert Boyce [1] recently published a paper relating to the question of yellow fever in the black race and its bearing on the question of the endemicity of yellow fever in West Africa. A historical description of the disease is given, and he comes to the conclusion from the evidence obtained that (1) The negro can contract and die from yellow fever; (2) he has, as a rule, yellow fever of a much milder type than that met with amongst whites who have recently arrived in a tropical country. Boyce considers that yellow fever occurs amongst the natives of West Africa in a mild form difficult of recognition, just as it did amongst the Creoles of the West Indies and the indigenous inhabitants of New Orleans, Cuba, Rio, and other places. The natives apparently suffer in early childhood, and may acquire subsequent attacks. This explains why fatal or severe yellow fever is rare amongst the native population, as the latter is partly immunised. The natives contain the virus in their blood, and can infect Stegomyia. If, on the other hand, these same natives are removed in childhood from a yellow fever endemic area and protected, they rapidly become non-immunes, as shown in Barbados, and as has been proved many times amongst the Creoles and Indian-Spanish races. As regards the West Coast of Africa Boyce says:—

> The evidence is overwhelming that yellow fever is endemic in West Africa, and that the reservoirs are the natives of West Africa. How far the natives of all coast towns in West Africa are reservoirs of the virus I am not prepared to state, as we require more evidence, but the facts warrant us in stating that in many places yellow fever is endemic amongst the native inhabitants in a particularly mild form very much as malaria occurs amongst them. Unfortunately, we have so far no blood or animal test which will prove the presence of the virus, and have only to rely upon a severe case occurring in a non-immune to prove the existence of the disease. In West Africa the non-immune who serves as the test appears to be the Syrian, who happens to live most in contact with the native. From these facts it follows that the great practical lessons to be learnt are that segregation of the non-immunes and Stegomyia destruction are the absolute remedies against yellow fever, also that the answer to the question propounded in the beginning of this paper, viz., why have not the native races in the large towns been decimated or completely wiped out ? is that they are completely immunised by mild attacks of yellow fever from childhood. It must be borne in mind, however, that a considerable proportion of the infantile mortality in the native races may be due to mild yellow fever as well as malaria.

In a more recent paper Seidelin [2] published a fuller account of the protozoon-like bodies which he found in cases of yellow fever. Two coloured plates demonstrate the morphological and staining characters of these parasites which strongly resemble *Babesia*.

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[1] Boyce, R. (April 20, 1911), "Note upon Yellow Fever in the Black Race and its bearing upon the question of the Endemicity of Yellow Fever in West Africa." *Annals Tropical Medicine and Parasitology*, Vol. V., No. 1.

[2] Seidelin, H. (January, 1911), "Protozoon-like bodies in the Blood and Organs of Yellow Fever Patients." *Journal Pathology and Bacteriology*, Vol. XV., No. 3.

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