REVIEW OF SOME OF THE RECENT ADVANCES IN TROPICAL MEDICINE

LEISHMANIOSIS.

A.Balfour and R.G.Archibald.

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pp. 95–99.

REVIEW

OF SOME OF THE

RECENT ADVANCES IN TROPICAL MEDICINE

HYGIENE AND TROPICAL VETERINARY SCIENCE, WITH SPECIAL REFERENCE TO THEIR POSSIBLE BEARING ON MEDICAL, SANITARY AND VETERINARY WORK IN THE ANGLO-EGYPTIAN SUDAN

BEING A SUPPLEMENT TO THE

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KHARTOUM

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constipation. There is then a rise of temperature, the globes of the eyes become tender and there is a characteristic injection of the conjunctiva, hence the name "Dog disease" applied to the condition from the fancied resemblance of the affected eye to that of a dog. Mild bronchitis, gastric tenderness, cramps and epistaxis are the chief symptoms, together with a rash like urticaria or erythema multiforme. The disease lasts two to four days and terminates by crisis, but convalescence is slow and there may be considerable anæmia. A lasting immunity to further attacks seems to be conferred by the disease. It has been attributed to the bites of certain gnats but there seems more reason to believe that bed-bugs may be the vectors. Insects—*continued*

King[1] has described a very tiny blood-sucking *Hemipteron*, which he found in Khartoum. It attacks without provocation, but only causes slight local irritation.

As hornets are common in the Sudan, though apparently for the most part quite inoffensive, attention may be directed to a note wherein MacWatters[2] details three cases in which serious symptoms of collapse followed the sting of a hornet (*Vespa orientalis*).

Wellman[3] draws attention to the noxious larvæ of Coleoptera and Lepidoptera above mentioned, some of which may cause severe pain and skin eruption, while nervous symptoms may follow contact with stinging caterpillars. He has also a note on two species of Myriapods, and states that their poisonous secretion is probably from the foramina repugnatoria which are at the sides of the segments and look like trachael stigmata. One has had Myriapods sent from the Southern Sudan, some of which are said to be much dreaded by the natives. They are being determined by Professor Werner of Vienna.

Jaundice (*Infectious*). *See* Weil's Disease, *page* 231.

Kala-azar. *See* Leishmaniosis (*below*).

Leishmaniosis. Various reports have shown that this deadly disease is of much wider distribution than was at first thought to be the case. Assam, Bengal, Southern India, Ceylon, Burma, China, Arabia, Egypt, Sudan, Tunis, Algeria, South Africa and Crete are the places where it has been known to occur.

Most of the facts presented in various papers, together with original matter, are to be found in Rogers' work.[4] We can only quote some of the more important points to which he refers and supplement them from more recent papers.

In speaking of a certain epidemic, he explains the peculiarity of its course by the fact that the disease travelled through the virgin soils of a certain northern valley in Assam, previously unaffected by the sporadic form of the disease, and there found a population fully susceptible to its deadly influence. Hence it was able to work terrible havoc. This, if confirmed, is interesting in the light of a similar state of things probably existing in Central Africa as regards Sleeping Sickness, which invaded Uganda from the west with such dire results.

The early stages are very hard to diagnose, the differentiation from typhoid and paratyphoid being especially difficult. Rogers says the high continued type of fever, especially with a slow pulse, is almost conclusive evidence of typhoid as against early kala-azar, while the high remittent type is almost equally rare in the latter disease. Some typhoids, however, show the slow remittent type which is common in kala-azar, and if a negative serum test has also been obtained, the blood changes must be turned to for help.

Three of the most important early signs are:—

1. Double remittent type of pyrexia.
2. Persistent remittent fever with absence of severe constitutional disturbance and of abdominal or respiratory symptoms.
3. Enlargement of spleen down to the navel.

Rogers has shown that a marked relative leucopænia, say less than 1 white to about 1000 red corpuscles, is practically diagnostic of the disease and is of bad prognostic significance. There is nothing special to note as regards general symptoms, except possibly

[1] King, H. H. (December 15th, 1906), "Blood-Sucking Hemipteron." *Journal of Tropical Medicine*, p. 373, Vol. IX.

[2] MacWatters, R. C. (June, 1908), "Some Effects from Stinging by a Hornet (*Vespa Orientalis*)." *Indian Medical Gazette.*

[3] Wellman, F. C. (June 1st, 1907), "Notes on some Noxious Larvæ from Angola." *Journal of Tropical Medicine and Hygiene*, p. 185, Vol. X.

[4] Rogers, L., "Fever in the Tropics." (*Loc. cit.*).

Leishmaniosis— *continued*

that the majority of cases begin with rigors, but a good account is given of the changes in the spleen and liver. The former is usually hard and, in very chronic cases, its firm edge may project so as to be evident to sight through the abdominal wall. The rapid increase, and the still more striking rapid decrease, which may occur in the size of the spleen are described. In very chronic cases an actual cirrhosis of the liver may occur. The surface of the organ is smooth, and microscopically there is a very diffuse intra-cellular cirrhosis in the fibro-cellular tissue of which shrunken parasites of kala-azar may still be visible with a high power. Advanced cases are accompanied by ascites.

The chief blood change is a great relative reduction of the leucocytes which may be extreme even at a very early stage. There is usually also a marked increase in the percentage of the large mononuclears. This, be it noted, rarely occurs early in typhoid, and hence is a useful diagnostic aid.

Possibly improved technique will be able to demonstrate parasites in the peripheral blood even early in the disease. As regards the general course of the fever, many charts are given showing the different types of fever. A double remittent passing into a low fever is common, while the low continued type also occurs. Both high continued and the high remittent forms are much more rare.

Blood changes.

1. Marked anæmia is only characteristic of the later stages.

2. Relative leucopænia is very marked and may be pathognomonic. It is less marked during high fever than during remissions or low intermittent pyrexia. It is important to note that a great degree of leucopænia may be absent in kala-azar, (*a*) during any inflammatory complications such as pneumonia, dysentery, cancrumoris, meningitis, phthisis, etc.; (*b*) during high remittent pyrexia occasionally; (*c*) during the very earliest stages of the disease such as the first month of fever, or in recovering patients who have been free from fever for some time.

3. Increase in the large mononuclears. Note that kala-azar differs from malaria in that this increase seems to occur more frequently when there is high remittent fever than when it is intermittent or absent or when the temperature is normal. In malaria it is less marked or even absent during pyrexia. An increase of the large mononuclears in typhoid during fever is very rare, hence this sign is valuable in early kala-azar with high remittent fever which closely simulates that of enteric.

4. Decrease in the polynuclears. This, which is marked, is of significance in two directions. (*a*) As a prognostic sign, the prognosis becoming progressively worse as the polynuclears become fewer and fewer. (*b*) As a factor predisposing to the secondary inflammatory complications, often coccal or bacterial in origin, which so often prove fatal. This is easily understood when it is remembered that there may be a loss of nine-tenths of the phagocytic polynuclear leucocytes.

5. There is increase of the lymphocytes and decrease of the eosinophiles, but these changes are of no special import.

As regards treatment, Rogers upholds the utility of quinine given in large doses and for months together if necessary. He has repeatedly seen a high remittent fever reduced to a comparatively harmless low intermittent one by increasing the quantity of quinine given, say, up to 60 grains or even 90 grains a day. He also points out that a considerable number of cases wholly recover.

The parasite is then fully considered. It may be found in practically every organ of the body, but is most numerous in the spleen, bone-marrow and liver. Christophers' work is mentioned. It showed that the parasites multiplied mainly in the large endothelial or macrophagic cells of the spleen and bone-marrow, especially until the invaded cells bulge into the lumen of the vessels. Hence, when splenic puncture is performed, the larger capsulated forms are obtained.

It has been found that the parasite is absent from the body in diseases other than kala-azar.

The flagellated stage of the parasite is then discussed and its resemblance to Herpetomonas noted. These discoveries and observations are so well known that there is no need to refer to them here at any length. One important point, however, is the optimum temperature for the cultivation and development of the parasite. This is between 20° C. and 22° C. Hence, in working with bed-bugs, it is well to carry out the feeding experiments during the cold season. It was Rogers who determined that the reaction of the fluid in the stomach of the bed-bugs, after they had sucked human blood, was distinctly acid, and this led him to employ an acid medium (citrated human spleen blood plus sterile citric acid) for observing the development of the parasite. Prophylaxis on plantations and in villages in India is fully considered. Segregation of the sick, building of new lines and the destruction of old houses and purification of old sites by fire are advocated, as is the destruction of bed-bugs by sulphur fumigation, washing beds with strong boiling carbolic lotion, boiling clothes in the same or destroying them altogether and burning blankets.

Rogers,[1] in a recent paper, enters more fully into the question of the cirrhosis of the liver present in cases of kala-azar, and concludes that:—

1. The most chronic cases of kala-azar not infrequently terminate their course with ascites due to cirrhosis of the liver.

2. The cirrhosis is of a peculiar intralobular type of uniform distribution, and with a smooth surface to the organ.

[1] Rogers, L. (July 1st, 1908), "A Peculiar Intralobular Cirrhosis of the Liver produced by the Protozoal Parasite of Kala-azar." *Annals of Tropical Medicine and Parasitology*, Series T.M., Vol. II, No. 3.

3. It is due to the protozoal parasite of kala-azar, which may be found in the liver and other organs after death. **Leishmaniosis—** *continued*

4. This form of cirrhosis of the liver is much commoner in Lower Bengal than a true malarial cirrhosis, with which it has probably hitherto been confused. It is, however, much less common than atrophic cirrhosis due to unknown causes.

Patton,[1] who has done the work on the development of the parasite in the bed-bug, records his latest work from which we cull a few notes and his conclusions. The large endothelial cells mentioned above, which contain the parasites in large numbers and are found in the liver, spleen, bone-marrow and lymphatic glands, occur in the peripheral blood of patients some days before death. "It seems most probable," says Patton, "that the rupture of these cells and the liberation of the parasites they contain, explains the occurrence of the large numbers of parasites in the peripheral blood of patients suffering from ulceration of the large intestine. Once the parasites are set free in the plasma they are immediately taken up by mononuclear, eosinophyl or polymorphonuclear cells."

It is suggested that the brawny swellings met with in the course of the disease, and *cancrum oris*, which is so common, both owe their origin to hæmorrhage caused by the blocking of a small vessel by one or more of these large cells.

Attention is drawn to large, non-nucleated, parasite-containing, blue-staining (with Giemsa) bodies, also found in the peripheral blood. Some believe them to be altered red blood corpuscles, others, detached buds of macrophages or mononuclear cells.

The general evidence seems to be against the occurrence of parasites in the red cells.

In continuation of his last report,[2] Patton gives more confirmation regarding the development of the parasites in *C. rotundatus*. After the early stages of development, *i.e.* increase in volume of protoplasm and in size of micronuclei which show signs of commencing division, one or other of two things takes place: (1) the parasite may rapidly pass on to flagellation; or (2), what is more important, they further enlarge and by consecutive division of the macro- and micronuclei produce a rosette of from four to eight parasites. "The single flagellates enlarge and begin to divide longitudinally to result in oval or spindle-shaped cells, while the rosettes, after flagellation, begin to divide up into separate, elongated flagellates. The oval or spindle-shaped parasites divide repeatedly . . . . and result in smaller and more irregular forms. All these changes may be seen in the bug during the first three days. Still later, longitudinally division of the oval and irregular flagellates progresses rapidly, so that by the fifth day the majority have become small or spirilla-like flagellates."

Patton also deals with temperature requirements and concludes that the disease usually begins in the cold weather, but this is not to say that infection can only take place during this season.

The final stages of development and the method of re-entry into the human body have not yet been determined, but the conclusions on this very valuable work so far are as follow:—

1. Though kala-azar is a chronic disease lasting many months and often years, it occasionally runs an acute course terminating in from four to five months, as illustrated by the case described above. In these acute cases, as well as in the chronic ones terminating with ulceration of the large intestine, the parasites are found a few days before death in large numbers in the peripheral blood in the leucocytes and endothelial cells, and the latter are probably the source of all the parasites seen in the circulating blood.

2. Though the parasites are most abundant in the peripheral blood towards the end of the disease, they are also found in the early stages, as a case recently seen clearly illustrated.

3. In the female as well as in the male bed-bug *(Cimex rotundatus)* the parasites have by the third day passed through all the intermediate stages of development described above up to the formation of the mature flagellates. Rapid multiplication by rosette formation is a "characteristic feature of the development of the parasite in the bed-bug." As the male bug sucks blood, it probably plays as important a rôle in the transmission of the disease as the female bug.

4. The infection acquired by the bug varies considerably, some ingesting large numbers of parasites, others only a few; and there is no evidence at present to show that the development in the bug depends on variations in the temperature.

5. The tendency that the disease has to linger in a house for a long time is probably explained by the fact that the parasite may remain in the midgut of the bug for several days before beginning to develop, and, as the nymphs, which take from seven to ten weeks to arrive at maturity, may ingest the parasites shortly after hatching, and as a rule feed only once between each moult, the infection may remain for a considerable time in a house; there is no evidence at present to support the view that the infection is inherited by the bug.

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[1] Patton, W. S. (1907), "The Development of the Leishman-Donovan Parasite in Cimex Rotundatus." *Scientific Memoirs of the Government of India*, No. 31.

[2] Patton, W. S. (1907), "Preliminary Report on the Development of the Leishman-Donovan Body in the Bed-Bug." *Scientific Memoirs of the Government of India*, No. 27.

Leishmaniosis— *continued*

Leishmaniosis was recently discussed[1] in London. Bassett-Smith referred to the occasional similarity of the temperature chart to that of Malta fever, the occurrence of hæmorrhages (epistaxis), the benefit resulting from atoxyl treatment, the drug being pushed to 12 grains a day, and the danger of splenic puncture. Liver puncture, he thought, was safe.

Precautions for puncture are: (1) Warn patient to avoid movement. (2) Thoroughly sterilise the skin. (3) Use a small needle and withdraw the blood quickly. (4) Apply a firm binder and make patient lie quite still in bed for several hours afterwards.

Manson described a case in a European which seemed to be about to terminate fatally and then markedly improved. This may or may not have been due to the atoxyl used in treatment.

Others spoke to the value of change of air and a sea voyage. The general impression was that when cure resulted, nature had been the successful physician.

Low mentioned a case clinically indistinguishable from kala-azar in which no parasites were found on spleen and liver puncture and in which, post mortem, double tumours of the adrenals were found, although there was no bronzing of the skin. He also mentioned other conditions, such as splenic anæmia, closely resembling kala-azar, and pointed out that for a certain diagnosis the parasite must be demonstrated.

Leishman mentioned Cummins' suggestion to produce artificial pustulation and thereby obtain polynuclears without having to resort to splenic or hepatic puncture.

Woolley[2] has described cases in the Philippines with symptoms of splenomegaly, rheumatic pains, œdema, diarrhœa, with or without hepatic enlargement, and remittent fever, but in which no Leishman-Donovan bodies could be found. He believes they may be associated with a chronic infection or intoxication originating in the intestinal tract and that, while a certain number of cases of tropical splenomegaly may be due to infection with the Leishman body, it will be found that various organisms are associated with the clinical picture and that the symptoms will depend chiefly on intestinal conditions and pathological changes in the intestinal walls.

Nicolle and Cassuto[3] have an interesting paper on three cases of splenomegaly in children at Tunis, in which cases the Leishman bodies were observed. There is a good coloured plate showing amongst other things a capillary of the liver with parasites in the endothelial cells and the forms met with in culture. The authors conclude:—

1. That there exists in Tunis an illness of infants with symptoms similar to those of kala-azar and apparently identical with certain cases of infantile splenic anæmia, described more especially in the south of Italy. It usually seems to terminate in death, but treatment by atoxyl may possibly prove beneficial. The etiology is unknown and the diagnosis can only be made with certainty by splenic puncture.

2. The pathogenic agent is a protozoan indistinguishable from the Leishman body. Its habitual site appears to be the endothelium of the vessels, and it is found in the blood and liver and more rarely in the lymphatic glands and in the blood.

3. This parasite is easily cultivated at 22° C. in the condensation water of blood-agar (Novy and McNeal's medium). The culture forms are identical with those of the Leishman parasite in citrated blood.

4. Until the identity of this parasite either with the Leishman body or the organism of oriental sore described by Wright, is established, it is proposed to group the following under the generic name Leishmania.

Leishmania wrighti, the cause of oriental sore.

Leishmania donovani, the cause of kala-azar.

Leishmania infantum, the cause of an infantile splenic infection closely resembling kala-azar, observed in Italy and in Tunis.

One's impression is, however, that the three cases recorded were merely examples of kala-azar affecting infants, and that there is no need to accord them special distinction.

In a later paper, Nicolle and Comte[4] mention the very interesting fact that they have found the parasite in a dog in Tunis. They also state that the children whom they found

[1] "Kala-azar" (March 16th, 1908). *Journal of Tropical Medicine*, p. 85, Vol. XI.

[2] Woolley, P. G. (June, 1906), "Tropical Febrile Splenomegaly." *Philippine Journal of Science*, p. 533, Vol. I.

[3] Nicolle, C., and Cassuto, E. (February 1st, 1908), "Sur Trois Cas d'Infection Splénique Infantile à Corps de Leishman observés en Tunisie." *Archive de l'Institut Pasteur de Tunis*, p. 3.

[4] Nicolle, C., and Comte, C. (April 11th, 1908), "Origine Canine du Kala-azar." *Archive de l'Institut Pasteur de Tunis*, p. 59.

infected had been in habitual contact with dogs. They are inclined to think that infection may be derived from the dog, and that in this animal the disease runs a benign course. Their work, which is of a preliminary nature, requires confirmation, but is at least suggestive. Leishmaniosis—*continued*

The presence of Leishmaniosis in the Sudan was first determined by Neave, who reported a case in a child from Meshra-El-Rek. For a considerable period thereafter no further cases were recorded, but recently, thanks to the work of Captains Cummins and Bousfield, of the Egyptian Medical Service, a considerable number of instances of the disease have been brought to light. In addition, as already mentioned, Dr. McTier Pirrie fell a victim to it, and I have found the parasites in the splenic smears of several cases sent me for diagnosis from Wad Medani. A second fatal case in a European has recently occurred.

As Captain Cummins furnishes a special paper on this important subject there is no need to enlarge upon it here.

Its distribution has yet to be fully worked out, but it seems commonest in the Kassala and Sennar Provinces, at least at the present time. So far *C. lectularius* is the only species of bug found in the Sudan, but it is possible that *C. rotundatus* will be discovered in the regions where kala-azar is endemic.

I have little doubt but that the disease is much more common than is generally supposed and that hitherto it has been overlooked or not recognised. Every effort will have to be made to arrest its spread should it show signs of extending beyond its present known limits.

Leprosy. In looking over the recent literature relating to leprosy, one notes the tendency to attribute the disease in the first instance to the bites of insects.

Thus Mugliston[1] of Penang suggests that *Acarus scabiei* may be the carrier of infection. He found that of 77 lepers, 44 had itch on admission, 11 of the others remembered having itch, and from the remaining 22 no history was obtainable. He thinks it possible that the bacillus of leprosy may be conveyed either *in* or *on* the insect.

Bassewitz[2]* also cites a case where in all probability leprosy was conveyed by the parasite of scabies from a leper to his attendant. The incubation period was two and a half years.

Goodhue[3] of the Leper Settlement at Molokai, Hawaii, reported the finding of the bacillus of leprosy both in the female mosquito, *Culex pungens*, and in the bed-bug, *Cimex lectularius*. He is inclined to think that the bug is a greater factor than the gnat in the spread of leprosy.

Smyth[4] of Lebombo states that in his diocese there are tribes which till quite recently have been free from European influence. The cases of leprosy amongst them are sporadic. These natives eat and drink out of the same pots; if there be food, no matter of what kind, they all share alike. They practically live altogether, with one exception—no healthy person ever sleeps with a leper, or one suspected of leprosy. In the case of married people, they have intercourse, but it is always in the daytime if one is a leper. The children of such parents appear to be normal. The sick are isolated in a hut or huts quite close to the village, but no healthy man or woman sleeps there. Smyth argues with some force that if the intermediate host were winged, it would fly from hut to hut, and therefore leprosy would spread in the villages in a way that it does not seem to do; if it were infectious, like some other diseases, people would catch it from the common spoons and cups; if it were due to food, all who eat that food would be liable to get it. Therefore we are driven to the conclusion that the *Cimex lectularius*, or some similar wingless parasite that feeds at night, is the means of conveying it from man to man.

Hutchinson[5] adduces the following arguments against the insect theory:—

1. If such conveyance were possible, how account for the disappearance of the disease in the fifteenth and sixteenth centuries from England and from Europe?

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[1] Mugliston, T. C. (July 15th, 1905), "On a Possible Mode of Communication of Leprosy." *Journal of Tropical Medicine*, p. 209, Vol. VIII.

[2] Bassewitz, E., *Münch. Med. Woch.*, 1905, No. 41.

[3] Goodhue, E. S. (August, 1906), "The Bacillus Lepræ in the Gnat and Bed-Bug." *Indian Medical Gazette*, p. 342, Vol. XLI.

[4] Smyth, W. R. (December 8th, 1906), "Leprosy." *British Medical Journal*, p. 1670, Vol. II.

[5] Hutchinson, J. (December 22nd, 1906), "Mosquitoes and Leprosy." *British Medical Journal*, p. 1841, Vol. II.

* Article not consulted in the original.