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TROPICAL DISEASES.

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Malaria: mosquito theory.

Although we may chronicle no very important advance in the therapeutics of tropical disease during 1898, some important advances in the etiology of malaria, which in the not very distant future may have important practical issues, demand a brief notice.

In the "Year-Book" for 1898 Ross's observations on the malaria parasite in its relation to the mosquito were briefly described. It was pointed out that in the stomach wall of a certain species of mosquito, fed on crescent-containing blood, pigmented cells, which were presumed to be a developmental stage of the malaria parasite, were found. In the *Brit. Med. Journ.*, Feb. 26, 1898, **Ross** published additional observations which enabled him to state positively that these cells were certainly pathological as regards the insect, and also to convince him that his conjecture that they were malaria parasites was correct.

Since that time Ross has turned his attention to the study of the proteosoma of birds. Proteosoma, which occurs in several species of birds, is an intracorpuscular blood parasite closely allied in appearance, structure, and habit to the malaria parasites of man. By feeding a certain species of mosquito ("grey" mosquito) on sparrows infected with proteosoma, and subsequently dissecting the insects, Ross found that he could, without fail, obtain a crop of pigmented cells in the stomach wall of the mosquito experimented with. These pigmented cells closely resembled the cells he had previously seen in the mosquito above referred to as having been fed on human malarial blood. They were lodged among the muscular fibres forming the outer layer of the stomach wall. On the second day after feeding, the pigmented cells were still very minute (6μ), but day by day they increased in size, until at the end of a week they measured from 30μ to 60μ in diameter. With increase in size the cells in question acquired a capsule of some thickness and showed evidence of structure, some being granular, some being hyaline with the

appearance of vacuoles, some containing peculiar sausage-shaped black rods. As the cells increased in size they came to project from the outer surface of the stomach, giving that viscus, as seen through a low power of the microscope, the appearance of being studded over with warts. At this stage of their development, if the cover-glass overlying the preparation were lightly pressed down so as to rupture the cells, a vast number of very minute, somewhat flattened, spindle-shaped, motionless bodies were forced out from a proportion of the cells into the body cavity of the insect. These spindle-shaped rods (germinal rods, Ross calls them) are apparently taken up by the blood of the mosquito, and are ultimately filtered out, at least in part, by the cells of the veneno-salivary gland situated in the head of the insect and communicating by a duct with the proboscis. The secretion of this gland is instilled by the mosquito when it bites. Ross found that by causing a healthy sparrow to be bitten by an infected mosquito he could communicate proteosoma, the characteristic intra-corpuscular parasites appearing in the infected sparrow's blood in great profusion some five to eight days after it had been bitten. This experiment was successfully repeated thirty times. It is therefore absolutely conclusive as to the possibility of communicating proteosoma disease to healthy sparrows by means of the grey mosquito.

Seeing that certain species of mosquito, fed on human blood containing malaria parasites, present pigmented cells in the stomach wall; that certain species of mosquito fed on proteosoma containing bird's blood also present similar pigmented cells; that mosquito-infected proteosoma can convey proteosoma disease to sparrows; Ross concludes that human malaria is communicable in the same way by mosquitos.

Recent observations made in Rome confirm this conclusion. **Grassi** (*Il Policlinico*, vol. v., 1898), who has made an extensive study of the mosquitos of Italy (upwards of fifty species), finds that only three species (Anopheles claviger, Culex malariæ, Culex penicillaris) constantly occur in, and are confined to, the worst malarial districts. Believing that one or all of these three species was an active agent in conveying malaria to man, Grassi placed specimens at Bignami's disposal for experimental purposes. For a time repeated attempts at infecting man by the bite of these insects were futile. Quite lately, however, and under circumstances which seem to exclude all sources of fallacy, Bignami has succeeded in conveying malaria to a man by one or other of these three species of mosquito. The subject of the successful experiment was an old soldier who had been in San

Spirito Hospital, Rome, for upwards of six years, and who, during all that time, had never suffered from fever. Some days after he had been bitten he showed a rise of temperature at midday, and at 3 p.m. had a rigor. At 4 p.m. the temperature was 102° F.; it continued rising, and on the third day reached 105° F. On the morning of that day the unpigmented amœba form of the æstivo-autumnal parasite was detected in the blood. In the evening the parasites were mostly unpigmented, but a few showed initial pigmentation, and brassy red corpuscles were seen. Quinine was then administered, and by next morning the temperature had become normal. This experiment seems conclusive, although, unfortunately, Bignami cannot say which of the three species of mosquito was responsible for conveying the infection. This, however, is a point which will be easily determined by further experiment.

2. Quinine and blackwater fever.

The uncertainty which has for so long hung over the ætiology, nature, and treatment of blackwater fever has not been dispelled by **Professor Koch's** recent utterances on the subject. In an experience of sixteen cases observed by him at Daressalam, he ascertained the presence of the malaria parasite only in two. As bearing on the use of quinine in, and on its relation to, the disease, he writes of one patient, "that he had not been more than eight months in East Africa; at home, it is alleged, he had never been ill, but caught the fever a few months after his arrival, and up to the time of his reception into the hospital, with shorter or longer interruptions, the attacks had always returned to him. About a month before he had an attack of blackwater fever. During his first week in the hospital he was free from fever and seemed to recover; no malaria parasites were discovered in his blood. Suddenly there occurred a rise in the temperature, which aroused the suspicion of a malaria relapse. The blood was examined, and now the presence of tropical parasites (æstivo-autumnal) was ascertained. He was given 1 gramme of quinine during the time of his freedom from fever, and a few hours later he had a pretty strong attack of blackwater fever. I at once conjectured that there existed here a causal nexus between quinine and blackwater fever. Of course, that might at first only be a conjecture, but soon it was to become a certainty. To prevent a relapse, the patient had to take further doses of quinine, and thereby it would soon become evident whether it was a mere coincidence or a case of blackwater fever caused by quinine. The patient received the next quinine dose after the complete disappearance of the hæmoglobinuria, the fever temperature, and

also of the parasites. A few hours after the quinine was taken another typical attack of blackwater fever, with a rise of temperature, hæmoglobinuria, and slight icterus, took place. To make every doubt impossible, a third dose of quinine was given, which could be done without hesitation, as the previous attacks had never taken a threatening character, and the patient received the quinine doses on the fifth day of the complete disappearance of his malaria. The effect was absolutely the same as after the previous quinine doses. Precisely at the same hour a typical blackwater fever attack again made its appearance. Afterwards the patient declared that before the attack of blackwater fever which he had gone through previous to his admission to the hospital, he had taken quinine."

In this case the parasite present in the patient's blood was what Koch calls the "tropical," that is the æstivo-autumnal of the Italians; in the following case the parasite was the benign tertian. "The patient had been for a year and a quarter in East Africa; he had his first fever three weeks after his arrival. After three months in Africa, he noticed for the first time bloody urine after having taken quinine a short time before. Since then he has had, as he told me himself, ten attacks of blackwater fever, and that, each time after taking quinine. His last attack he had a month ago, when he had taken quinine on account of a tertian fever. As the quinine had to be stopped after this one dose the fever returned and the patient was treated with arsenic, but without result; so that there was nothing left but to return to quinine. This time a dose of half a gramme was given subcutaneously. The patient received it at 8 a.m., the fever attack regularly taking place between twelve and one. Two hours after the injection there was violent ague shivering, which lasted for about half an hour. Soon after, 250 c.cm. of bloody urine was passed, the patient complained of pains in his limbs, a feeling of uneasiness, great weakness and nausea. He vomited several times. From twelve o'clock onward, the skin assumed an icteric hue which soon turned to a deep yellow. Towards two o'clock, a further evacuation of 150 c.cm. of black-red urine took place. After this, the weakness of the patient increased, and he fell into a sleep out of which he could not be aroused. Death came at ten o'clock in the evening, twelve hours after the injection."

That the administration of quinine provoked the blackwater explosion in these cases seems a reasonable enough conjecture; but to say that blackwater fever is caused by quinine, is "quinine poisoning," as Koch asserts, is a very different matter. As reasonable would it be to say that in a case of Bright's disease, opium injudiciously given caused uræmia. Did quinine cause blackwater fever, why is it that this disease is not an every-day occurrence in India, where quinine is given in vastly greater quantity and in bigger doses probably than in Africa? It is well known that blackwater fever may supervene on exposure, chill, fatigue and other causes of physiological strain. But to say that these things are the cause of blackwater fever would be absurd. Such things do not give rise to blackwater fever in Europe or in India. Why should they do so in Africa? Manifestly because there exists in Africa a specific germ of some sort—be it a variety of the malaria germ, or something quite different—which is the real cause of blackwater fever. In persons infected with this germ, chill, exposure, and many other things—among them perhaps quinine—provoke, on occasion, the symptom "blackwater." If the malaria parasite be not the true cause of blackwater fever, it is certainly a powerful agent in provoking the blackwater manifestation, a much more powerful agent than quinine. As a practical corollary from this, the practitioner will be right, in the presence of an attack of blackwater fever, or in those who have suffered from blackwater fever, to administer quinine, if by microscopical examination of the blood, or from other reasons, he knows that the malaria parasite is present, and especially if it is active, in the patient. We think that Koch has been much too sweeping in his assertions about the danger of giving this drug, whether in blackwater or in other African fevers, and that he has presented his views to the public in a way so incautious that their expression is calculated to do an incalculable amount of harm. We believe that Bastianelli, as pointed out in the "Year-book" for 1898 (p. 425), has correctly formulated the indications for the use of quinine in blackwater fever, namely, to give it if there are malaria parasites ni the blood, to withhold it if there are no malaria parasites in the blood. It seems to us that, under any circumstance, in such a country as Africa, it would be culpable to withhold quinine in the presence of an active malarial infection. If quinine be an evil, it is manifestly an infinitely smaller one than malaria, and infinitely less likely to provoke the "blackwater" symptom than a neglected malarial infection.

Soon after the publication of Koch's views, the writer had a conversation on the subject with a missionary who had passed twenty years in one of the worst blackwater districts of Africa. It had been this missionary's practice, while in Africa, to take every day a five-grain dose of quinine. Only three times had he suffered from blackwater fever, and these three attacks he confidently attributed to his having given

up for a time his accustomed daily dose of quinine. **Dr. Crosse**, formerly P.M.O., Royal Niger Company, who has spent as many years in Africa as Professor Koch has spent months, says: "My experience is that those who take quinine, and take it freely, do not get blackwater fever. In my own case I attribute my attacks—and I have had at least ten severe ones—partly to my neglecting to take quinine, which I dislike very much, and to the fact that very often when unwell I had to be about attending to others who were more ill than I was myself." Dr. Crosse refers to Mr. Stanley's opinion, one founded on personal experience of the disease. Mr. Stanley considers that blackwater fever yields to quinine; in his own attack he did not get well till he took 60 gr. of quinine in a single dose. I would not go so far as to say that this, in my opinion, unjustifiably large dose cured Mr. Stanley's attack; but, as he got well after taking it, it is evident that it was not the cause of blackwater, in his case at all events. Equally emphatic is **Dr. Moffatt**, P.M.O., Uganda Protectorate, in condemning Professor Koch's sweeping assertions about the pernicious effects of the free use of quinine. Dr. Moffatt "has never seen a man die of malaria when quinine has been given early"; and he adds, "fatal cases, whether complicated with hæmoglobinuria or not, have been those in which quinine has not been administered, or was given in very small doses, or else resorted to only when the case was practically hopeless." Of nine cases of blackwater fever treated by him, two were fatal, the administration of quinine having been neglected until too late; the cases which recovered were all treated with quinine, six of them with heroic doses, 60–120 gr. in twenty-four hours.

Drs. Crosse and Moffatt deplore the effect that Koch's statements about the danger of giving quinine is having on the public, many people now absolutely refusing to take quinine under any circumstances.

It seems to me that Koch would have been wiser had he said that although, in some instances, quinine may have seemed to provoke blackwater, yet this drug cannot be held to be the cause of blackwater; and that as neglected malaria is a much more powerful provocative of the symptom than any other known agency, it is good and proper treatment to give quinine to all patients who are the subjects of active or latent malarial infection, unless in cases in which a blackwater idiosyncrasy in regard to quinine had by past experience been ascertained to exist.

PUBLIC HEALTH AND HYGIENE.

By Edward F. Willoughby, M.D. Lond., D.P.H. Lond. and Camb.

1. Legislation.—Except so far as the Local Government (Ireland) Act (1898) may be considered as bearing on the public health of that kingdom, the session of 1898 was unusually barren in sanitary legislation. The long-cherished hopes of a consolidation and revision of the laws relating to adulterated and unwholesome foods have again been doomed to disappointment, though in Mr. Kearley's Bill of the previous session there were ready to hand all the materials of an almost perfect statute; and the sanitary administration of the whole of England and Wales outside the metropolitan area is still carried out under the imperfect provisions of the Public Health Act of 1875, with the Public Health (Amendment) Act of 1890, and the Infectious Diseases (Notification) Act of 1889 and (Prevention) Act of 1890, the optional character of which creates local anomalies that ought long since to have been removed by consolidation and incorporation, as they have been in London in the Act of 1891.

The Royal Commission on Vaccination having completed its labours and issued its report, the Government introduced a Bill for the amendment of the laws relating to vaccination, which in its original form was, to say the least, disappointing, since the only amendment really needed was the legal enforcement of re-vaccination, as has long been the practice in Germany and Scandinavia, and is now adopted by Austria, Hungary, and Servia. The Bill, however, raised the age for the primary operation to six months, as in Scotland, abolished repeated convictions in respect of a single offence, and made provision for the performance of domiciliary gratuitous vaccination—matters of minor importance, though not without some advantages. But when the Bill reached the stage of being committed, the Government—who up to that time had firmly resisted all attempts at tampering with the principle of compulsion, and in so doing had had the hearty support not only of their own party but of many Liberals, as well as of the Irish Nationalists, and could easily have overpowered all opposition in the Commons and have relied on the unanimous votes of the Peers—surprised both sides of the House by a sudden