certain gardens since 1898, and he finds no less than 132, or 26.4 per cent., recovered completely and permanently. It is possible that the more favourable results obtained at the Calcutta European Hospital and by Dr. Price in Assam may be due to another factor, for in view of what has been said above as to marked improvement taking place as long as only low intermittent fever is present, and the fact that in Calcutta it has been repeatedly found that the temperature runs up to the remittent type the moment quinine is left off (a point which will shortly be illustrated by Captain Clayton A. Lane, I.M.S.), there is good reason for believing that the much more favourable results of Dr. Price and myself than those reported by Major Donovan are causally related to the firm belief in, and the practice of, giving large doses of quinine in cachexial fever and kala-azar by the former, in opposition to the view of Major Donovan and others that quinine is useless in even the milder endemic form of the affection. At any rate, it can hardly be maintained that quinine does any harm, when it is considered that 60 gr. and upwards have frequently been given daily for long periods in some of the favourable cases recorded above, with much better results than any yet reported by those who deny the value of the drug; so that the proof afforded above, that even a reduction in the fever curve makes all the difference between deterioration and improvement, appears to me to render it inadvisable to deny these unfortunate patients the benefit conferred by quinine, combined with the administration of red medulla tabloids, or their equivalent in uncooked marrow mixed with other food to render it palatable.

Finally, I have to express my great indebtedness to my colleagues Lieutenant-Colonel G. F. A. Harris and Major F. J. Drury, the Physicians of the Medical College Hospital, and to Captains Clayton A. Lane and R. P. Wilson, of the European General Hospital, all of the I.M.S., for their kindness in allowing me to examine and make use of their cases.

CONCLUSIONS.

1. A very marked decrease in the leucocytes is always found in uncomplicated cases of cachexial fever, and when they number below 2,000 per c.cm. this is almost diagnostic of the disease, but may rarely occur in true malarial cachexia.

2. In cachexial fever the white corpuscles are reduced to a greater degree than the red, so that the ratio falls below 1 to 1,000 in all uncomplicated progressive cases. This is rarely so in true malarial cachexia, while a reduction in the ratio to below 1 to 1,500 appears to be quite diagnostic of cachexial from other Indian fevers.

3. The most marked degrees of reduction of the leucocytes, and especially of the polynuclears, is of bad prognostic import, and vice versa.

4. Red marrow tabloids are of great value in increasing the leucocytes, and this increase may take place during the continuance for months of intermittent fever, and be then followed by cessation of the fever and complete recovery.

5. High remittent fever is accompanied by progressive deterioration of the blood and general condition, but it may be often to a large extent reduced to the less injurious intermittent form by continued large doses of quinine, combined with red marrow. The best results yet reported have been obtained by those who carry out vigorous quinine treatment.

REFERENCE.

¹ Quart. Jour. of Micros. Science, November, 1904.

THE EXPERIMENTAL TRANSMISSION OF MEDITERRANEAN FEVER.

BY

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(Communicated by the DIRECTOR-GENERAL R.N.)

[PRELIMINARY NOTICE.]

It having been suggested to us, by Professor Ronald Ross, that Mediterranean fever is possibly conveyed from person to person by the mosquitoes *Stegomyia fasciata* or *Culex pipiens*, and bearing in mind the work of the Commission of the United States Army on yellow fever,¹ we have made some experiments in the hope of ascertaining the true nature of the transmission of this disease.

Experiment 1.—Transmission by Direct Contact, Fomites, etc.

A case of Mediterranean fever was treated in the sick berth of a ship for a period of one month, while she was at sea or

anchored in open roadsteads. The fever was fairly severe, the serum reaction was positive, and the micrococcus melitensis separated from the blood of the patient.

He was nursed by three non-immunes, who took no special precautions to avoid contracting the disease, and who twice slept in the bedclothes which had been used by the patient. The disease was not conveyed to these non-immunes.

This experiment was then repeated in another ship with another but more severe case of Mediterranean fever, and nursed by other non-immunes. The result was the same as before.

In both these cases the Mediterranean fever was obviously contracted before embarkation. No cases of the disease had occurred before in the ships and none were contracted afterwards.

Experiment 2.—Transmission by Inhalation, Infected Dust, etc.

The urine of a case of Malta fever, passed on the fifth day of the disease, with fever of 103.8° F., was mixed with some dust, making a thick paste; part of this was allowed to dry slowly in the shade for five days and powdered.

The dust was then inhaled, sniffed up the nostrils, and a considerable quantity swallowed by two non-immunes (E. H. R. and Mr. C.). The remainder of the infected dust was kept for six days, then dried in the sun and powdered, and this also inhaled, sniffed up the nostrils, and swallowed by the same non-immunes. The disease was not conveyed by these means.

A living culture of micrococcus melitensis, grown on agar for seven days, was spread on a glass plate, it being kept moist meanwhile, and was inhaled for one hour by one of us (E. H. R.); the culture was then allowed to dry, and finely powdered; this was then inhaled for three hours, and ultimately sniffed up the nostrils, and some of it swallowed by the same non-immune. The disease was not contracted by him.

Experiment 3.—Transmission by Infected Water.

Ten ounces of the urine of a case of Malta fever, in the sixth week of the disease, was mixed with five gallons of ordinary drinking water; a tumblerful of this mixture was then drunk by two of us (E. H. R. and G. M. L.). When the urine was passed the patient's temperature was 102.4° F., and when mixed with drinking water, an hour later, was neutral to litmus. The disease was not contracted by either of us.

Experiment 4.—Transmission by Mosquitos.

Two female mosquitos of the species *Stegomyia fasciata*, Fabricius (var. *Culex mosquito*, R. Desvoidy), and one female *Stegomyia pseudotaeniata* (Giles), were allowed to bite a patient suffering from Mediterranean fever in the third week of the disease, whose temperature at the time was 103° F. The mosquitos were then allowed to bite the two non-immunes (E. H. R. and Mr. C.) alternately on the sixth, twelfth, seventeenth, and twentieth nights after.

These same mosquitos were then reinfected from a fresh case of Malta fever, in the sixth week of the disease—temperature 101.6° F.—and again allowed to bite the same two non-immunes alternately as before, twenty-four hours, fourth, sixth, eighth, eleventh, thirteenth, and fifteenth days after. Two of these mosquitos then died; the remaining one, a *Stegomyia fasciata*, was then again reinfected from a fresh case of Malta fever, with a temperature of 103° F., who was in the eleventh week of the disease. This mosquito then fed on the blood of Mr. C. twenty-four and again forty hours after. The mosquito then died.

The disease was not conveyed by these means.

The possibility of the transmission being due to mosquitos infected in the early days of the disease having been suggested, another *Stegomyia* was allowed to distend herself with the blood of a very severe case on the second day and again on the eighth day of the illness, the patient's temperature on the two occasions being 102.4° F. and 103.2° F. respectively. This mosquito was then allowed to bite two other non-immunes—G. L. M. and Mr. D.—alternately on the third, sixth, tenth, twelfth, fourteenth, sixteenth, and seventeenth days afterwards.

The disease was not contracted by these non-immunes either.

Similar experiments have been attempted with other gnats—*Culex pipiens* (Linneus), *Culex fatigans* (Wiedermann), and the sea-water bred species, *Acartomyia zammitii* and *Theobaldia spathepalpis* (Rondani), but these have up to the present failed owing to the difficulty of making these species feed on blood when in captivity.

We have described ourselves as non-immunes, for none of us have had Mediterranean fever, and we have only lately been exposed to the disease for short periods during the last few months. None of us have had a day's illness during that time, with one exception—the case of G. M. L., who had three attacks of spring tertian malaria, contracted in Sardinia, when the parasite was found in his blood. The attack gave way readily on the exhibition of quinine. Moreover, we have all been tested with the serum reaction for Malta fever, which has given uniformly negative results.

The greatest care also has been exercised by all of us concerned to prevent the possibility of the accidental occurrence of the disease among us. Thus, the contact with cases, or the handling of living cultures of the micrococcus melitensis have been avoided, drinking water carefully examined, mosquito netting utilized when necessary, and we have refrained from sleeping on shore. Places where the disease is known to be endemic have been avoided as far as possible.

Up to the present, therefore, these experiments have failed to reproduce the disease, but we trust that our efforts will be ultimately rewarded, and that the true nature of the transmission of Mediterranean fever be fully ascertained, and its prevention practised.

We publish these, our preliminary results, with the hope that they may prove to be of use to those now engaged in investigating the disease, and that, with the kindly help of others, we may have better opportunities for the furtherance of our researches.

REFERENCE.

* Reed, Carrol, Lazear, and Agramonte, *Journal American Medical Association*, 1901, vol. xxxvi.

INTERMITTENT FEVER IN MALTA.*

BY

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THIS is the first time that the existence of intermittent fever has been noticed in these islands. At least this is the first time that cases of ague contracted in Malta have been dealt with by the medical profession. There has always been a vague notion amongst us that there was a time when malarial fever was not an unknown disease in this island. Abela, a knight of the Order of St. John, mentions in his history of Malta, published in 1647, that a certain type of malignant fever was known, against which a certain powder was administered. Many places in old times were marshy and probably malarious. The valley beyond Naxar, on the way to St. Paul's Bay, was marshy for a great extent, and that district was called "Bûr-Marrôd," pronounced now "Benwarrad." Bûr-Marrôd means literally "unhealthy plain." The Marsa was known, in quite recent times, to be marshy and the whole district to be malarious. In the Capuchin convent at Floriana, which overlooks the Marsa, malaria is said to have been endemic at one time, and the friars were even forbidden to go down to church before daylight for fear of contracting the disease. This is what can be gathered from written and unwritten history, but it is a fact that, so far, nobody has demonstrated that a case of ague had been contracted in these islands.

During the month of August, 1904, cases of fever of a type unknown here, came to the notice of medical practitioners at Rabat. All the cases could be traced to a certain district not far away. On September 13th we visited the locality and collected information from the peasants of the neighbourhood.

Wied-il-Kligha is a deep ravine, distant about a mile from Rabat. In 1887 a portion of that ravine was dammed, with a view to collect the rain water for agricultural purposes. The length of the ravine between the two dams is 1,430 ft., and it was hoped to collect about 1,000,000 gallons of water at a time. Water collects there during the rainy season, and is then gradually conveyed as required in pipes to the eastern part of the country. On the western side of the ravine several groups of huts are seen, and a few rock caves have also been turned into habitations. The inhabitants of this cluster of huts number about 50, and they all sleep there on week days, to be ready in their fields early in the morning. On Sunday they generally go to Rabat where they have their proper dwelling houses.

Early last summer some of these peasants had a sudden rise of temperature, preceded by fits of shivering and followed by profuse perspiration. As they felt quite well soon after, medical aid was not immediately asked for, and it was only when children were attacked that the district medical officer was consulted. All the cases yielded readily to quinine treatment.

When we first visited the locality we saw two persons who had had a rigor about an hour before:

One, a man over 30, was lying in bed, hot and perspiring; the temperature in the mouth was 103° F. He had been ill twice during that week, and had taken a small dose of quinine. We made a good number of preparations from his blood, and Laveran's parasite was found in fair quantities.

The second patient was a woman of about 40, who was found sitting in the middle of a field, where she had been at work. She had been attacked there an hour before, and was not capable of moving a limb. That was her first attack, but nearly all the members of her family had been down with the fever. A good number of films were prepared from the blood of this woman, and the parasites were abundant.

On September 16th we visited once more the small community and found that other persons had been attacked, and that some of those who had been infected before had recurrences.

A young girl was found in bed with high fever, but she did not complain of having had fits of shivering. We took blood from the lobe of one of the ears, and the films showed the parasite in a fair quantity.

In all the cases the parasite was of the same type, globular, with the infected blood corpuscle hypertrophied.

We showed the preparation to Major Horrocks, R.A.M.C., and some films were sent to Professor Leishman, R.A.M.C., who kindly undertook to examine them for us. We all agreed that the cases were of benign tertian. Having satisfied ourselves as to the clinical symptoms and as to the presence of the parasite, it was natural that an attempt to find the mosquito that spread the disease should be made. We knew that so far nobody had found *Anopheles* in Malta. Indeed, the conditions of our land service are not very favourable to the breeding of those mosquitos. Experience, however, had shown elsewhere that mosquitos can readily adapt themselves to conditions which seem unfavourable to their species. The suspected ravine with its collection of rain water was not an unfavourable place for this species of mosquitos.

When we inspected the place in September the rainy season had not yet set in, but pools of water covered with green vegetation were numerous all along the bottom of the ravine. At the lower end of the same a considerable amount of water was collected, teeming with animal and vegetable life. At a superficial inspection on the first day of our visit we could not discover any larvae, but on the second day we went over the ground very carefully and succeeded in collecting both larvae and pupae. We were so lucky on that day that in one of the huts close by we found, by the help of an acetylene lamp, two female mosquitos in a dark corner. Although the characters of these insects were clear enough, we preferred to have an expert opinion on the same, and we therefore sent the mosquitos to Mr. F. V. Theobald, of the Zoological Department. That expert, with his usual kindness, was not long in informing us that the mosquitos sent to him were *Anopheles maculipennis*, a species common along the shores of the Mediterranean.

Our inquiry was then complete, and the only problem that could present itself was as to how the fever was brought to that distant part of the island. Undoubtedly the *Anopheles* have been among us from time immemorial, and surely the artificial lake at Wied-il-Kligha offered a good breeding ground.

The erection of the great military camp on Mtarfa hill, which overlooks and is not distant half a mile from the collection of water, brought with it the elements of infection. The regiments stationed there were bound to have in their ranks men who had contracted the fever in India, in Africa, or in Crete. The passage of the parasite from the infected men to the *Anopheles* in the valley below was simply a question of time. Last summer the circuit was closed and malaria in an epidemic form spread for the first time among the peasants of the Kligha district.

Fortunately, so far, the disease has not extended beyond its endemic focus, and considering that the collection of water in the ravine is artificial and fully under the control of the authorities, it is more than probable that the infection will not spread and will be also eventually eradicated.

THE Berlin Municipality has made a grant of £4,000 to be applied towards the prevention of infantile diseases.

* Read before the Malta and Mediterranean Branch.