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MALARIA COMMISSION.

Fourteenth Session.

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Sub-Committee 3.

1st Meeting held on the 27th June, 1928 at 5.30 p.m.

Professor ASCOLI in the Chair.

The CHAIRMAN said the first question the Sub-Committee was asked to discuss was the dose of quinine and the duration of treatment.

Professor NOCHT asked whether the Sub-Committee were going to discuss these questions from the point of view of the clinical treatment of malaria, or were they going to discuss, i.e., the distribution of quinine by an imperfectly trained personnel,

The CHAIRMAN said that the question before the Sub-Committee was the employment of quinine as a social problem, but that the conclusions of the Sub-Committee would necessarily be based on clinical experience.

Professor NOCHT thought it would be interesting to hear first of all the experience of his American colleagues with standard treatment in America.

Dr. COLLINS, in reply, described two experiments carried out in the United States, which were designed to test the efficiency of quinine administration as a prophylactic measure. Bass' method was used, and endemic areas were selected for the experiments.

In each of these experiments ten weeks treatment was administered to each member of a group of children, another similar control group being left untreated in each case. Each child was visited daily, and the blood, spleen and haemoglobin were examined

once a month. The treatment succeeded in quickly ridding the peripheral blood of parasites. Enlarged spleens were reduced promptly in size, more especially very large spleens. After the termination of treatment, however, the parasites soon made their reappearance in the blood and the spleen became re-enlarged, with the result that three months after the termination of treatment the conditions of the treated and untreated control groups of children were identical. When smaller doses were used, not even this temporary improvement was observed. Nothing less than standard treatment rids the blood of parasites. For more effective treatment, the cost and the necessity for a large trained personnel, make the measure almost prohibitive in most circumstances. Other methods of malaria control are considerably cheaper.

Professor NOCET emphasised the fact that too long application of quinine may lessen the body's resistance to the parasite. This difficulty could be overcome by intermittent administration. He drew attention to the occasional occurrence of pseudo-relapses, febrile attacks which are caused by quinine intoxication.

Professor de BUEN said he could only speak from experience acquired in Spain, but he thought the explanation of the American results might be found in insufficient dosage. In his own experience eight to ten days treatment of 1.5 gr. of quinine a day was sufficient to cause the disappearance of parasites, although in malignant tertian crescents might still be found, and in benign tertian relapses were liable to occur.

Dr. COLLINS referred to the difficulty of comparing results in different countries. In the United States the experiments which he had described were carried out in an endemic area. In Spain it was possible that

there was more extensive infection and more active transmission. In the areas in Georgia referred to no parasites were found in the blood during the administration of Bass' treatment.

Professor de BUEN agreed that quinine appeared to give better results in some regions than in others.

Professor NOCHT referred to the importance of making a distinction between infections and relapses. Treatment cannot prevent re-infections. His own personal opinion was well known. One does not cure malaria with quinine; the patient cures himself in response to the stimulus of quinine. The problem before them was to determine what treatment was most effective and most useful in the prevention of relapses.

Professor SCHUFFNER endorsed the importance of Professor Nocht's observations. The question of re-infection was most important in serious outbreaks. He thought that the severity of the disease was a most important factor to be taken into consideration when discussing dosage. Small doses were sufficient in mild outbreaks, but one gram a day may not be sufficient if re-infections and super-infections are common. In such conditions one was occasionally near the limits of the use of quinine. In general, however, a dose amounting to 3 gr. a week was usually successful in many parts of the Netherlands East Indies.

The CHAIRMAN laid stress on the fact that the type of the parasite was important in determining the dose. In general, bigger doses were required in the treatment of malignant tertian fever than of other forms. He also wished to call Dr. Collins's attention to the fact that there may be a fallacy in drawing general conclusions from experiments on children owing to the fact that malaria is more apt to

become a chronic disease in children. One often found that if insufficient doses were given to children relapses occurred immediately after the cessation of treatment.

Professor de BUEN also laid stress on the importance of the differentiation of parasites. His experience in Spain had shown him that efficient consecutive treatment caused the disappearance of quartan fever, but that it sometimes failed to reduce the incidence of benign tertian. This question of relapses, or reinfection was likewise one of importance.

The CHAIRMAN, in summing up the conclusions arrived at, said that he also agreed that for malignant tertian a daily dose of $1\frac{1}{2}$ to 2 gr. of quinine during the attack was sufficient; that for benign tertian a dose of 1 to $1\frac{1}{2}$ gr. a day during the attack sufficed, and that for chronic cases a daily dose of 1 gr. was enough.

Col. JAMES drew attention to the fact that the recommendation of the Malaria Commission, contained on page 73 of its Second General Report, appeared to be almost universally supported by the Sub-Committee. The daily dose recommended by the Commission was from 1 to $1\frac{1}{2}$ gr.

The CHAIRMAN agreed that this opinion might be endorsed. This proposal was adopted.

The CHAIRMAN opened the discussion on the duration of treatment.

Professor NOCHT expressed the opinion that the condition of the individual was the chief factor in determining the duration of treatment. Consequently it was very difficult to make a general pronouncement on this question. Good and suitable food, confinement to bed etc., were most important

auxiliaries to treatment. On the other hand it is difficult to get results from treatment of ill-fed populations.

Professor SCHUFFNER agreed that it was difficult to lay down a general dose. The salt of quinine used was another important factor; but he agreed that no matter whether hydrochloride, sulphate or bi-sulphate of quinine was given, a dose not exceeding 1.5 gr. a day, given by mouth, was nearly always sufficient. He also expressed the opinion that quinine acts indirectly, and not directly, on the parasite. Quinine in high concentration does not kill the malaria parasite. In large doses the drug may even paralyse the defensive forces of the body.

Professor NOCHT thought that for consecutive treatment $1\frac{1}{2}$ gr. a day was too high a dose, and entailed waste of quinine and waste of money. He agreed that it was difficult to lay down a general rule, but he thought that 3 grs. a week might be considered amply sufficient. He thought that consecutive treatment should not be too prolonged. Three or four weeks was generally sufficient.

Col. JAMES referred to recent experiments he had carried out with regard to the treatment of artificially induced malaria in cases of general paralysis of the insane. Exactly similar results were obtained if one gave a dose of 0.33 gr. of quinine once a day as with the administration of a similar dose three times a day. In general, treatment for five days was not sufficient to cause the disappearance of all parasites, but ten days treatment sufficed. It was interesting to note that the disappearance continues during the day on which the dose was given and also on the following day, so that at present quinine is given only on alternate days. In other

words stimulation occasioned by a dose of quinine appears to last forty eight hours.

Professor SCHUFFNER agreed that a dose of 1.5 gr. was adequate in most cases, after which three grs. a week was in general sufficient.

At this point the meeting was adjourned.