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RECENT RESEARCH ON PROPHYLAXIS AND TREATMENT OF MALARIA*

REPORT FOR 1935

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As a member of the Committee on Medical Research, I have been requested by the Chairman to prepare a summary of prophylaxis and treatment of malaria during the year ending September 1, 1935. Undoubtedly many of the present year's records will not be included in this summary, since we have not access to all of the world's literature filed during this period of time and we hope the authors of papers not abstracted will understand why they do not appear in this summary. It will also be taken for granted that the membership of the National Malaria Committee and the readers of this report are well acquainted with the efficacy of quinine and the various methods of using it as an anti-malaria drug. It is still our number one drug for the masses. However, the small space allotted for this review will be given to the new drugs that have been given field trials.

Studies in Untreated Malaria.—It seems worth while, at the very beginning, to record a brief statement from Lowe,[1] who calls our attention to the fact that the relation of the numbers of parasites to the course of untreated fever is not the same in benign tertian and subtertian. The parasite counts made by him ranged from 20 to 202,000 per cu. mm. In benign tertian malaria, a minimum count of 500 parasites per cu. mm. is usually necessary to cause fever. On an average, only some 20 per cent of the young trophozoites reach maturity.

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In subtertian malaria a count of 600 to 1,500 parasites is usually necessary to cause fever. The increase or decrease in the parasite count is not necessarily followed by an increase or decrease in the fever of subtertian malaria, but in benign tertian the fever generally rises and falls with the number of parasites. The author considers that the destruction of parasites occurs in two ways: (1) by lysis or phagocytosis of free merozoites; (2) by ingestion of infected red cells by the reticulo-endothelial system. It seems to be more or less generally held that our anti-malarial drugs do not kill parasites by direct action, but they simply stimulate the reticulo-endothelial system. If this be true, then the possibility of blocking this system by over treatment with any drug must be given our consideration.

Kritschewski and Demidowa[2] reach the conclusion that the therapeutic activity of anti-malarial drugs is greatly lowered by blocking the reticulo-endothelial system with trypan blue. Others experimentally produce the same result with india ink. May we not also induce the same condition by the overdose of any of the anti-malarial drugs?

NEW DRUGS

White and Adhikari[3] report that a single course of quinine and plasmochin given at the beginning of the malaria season to all children living in an area under anopheline control caused no permanent improvement.

Green[4] considers that it will be necessary to have the results of prolonged and well conducted experiments before forming any opinion on the use of atabrine as a clinical prophylactic. He does not think that it would be safe to give subcurative doses of atabrine, say 0.1 gram daily, over long periods, because of the possible cumulative effects. He reports 4 per cent relapse under atabrine treatment and 38 per cent relapse under quinine treatment. His period of observation, however, was only 27 days for atabrine and 18 days for quinine.

Manson-Bahr,[5] in discussing the prognosis in malarial infection, states very definitely that relapses in subtertian malaria can be entirely prevented by atabrine. The life span of the benign tertian parasite is given by him as 3¼ years, that of subtertian at about nine months and of quartan at six years. We like the conclusions of Williams and Bhattacharyya,[6] who re-

gard atabrine as a more suitable drug for those who can afford it, but consider that it cannot replace quinine in general use in a poor country like India. The usual curative course of quinine on the tea gardens consists of 20 grains daily for seven days. The small reduction of malaria which followed prophylactic treatment with atabrine and plasmochin was not sufficiently satisfactory to compensate for the expense in curred.

TOXIC EFFECT OF THE NEW DRUGS

Chopra and Chandhuri[7] have recorded some observations on the toxicity of synthetic anti-malarial remedies and they conclude that plasmochin and atabrine should not be given together and that neither plasmochin nor atabrine should be used for prolonged periods for prophylactic purpose. No one should be allowed these drugs except under direct medical supervision. Kingsbury[8] reports seven cases of psychosis following the use of atabrine in cases of malaria. These occurred among several thousands of cases of malaria treated with atabrine. Perhaps it would be well for us to consider other causes for these few cases. They may have been the direct result of malaria. Furthermore, the incidence of a psychosis due to other causes among that number of people should also be considered.

OTHER NEW DRUGS

Mosna[9] reports the use of "quinoplasmine" in malaria prophylaxis. He used an administration twice weekly of the drug (2 centigrams to adults with doses proportionately less for children) to the entire population of 771 in a community where malaria is endemic. This treatment extended over a period of about five months, May 18 to October 21. His results are tabulated as follows:

(1) A marked reduction in malaria incidence among the population in general.

(2) Marked reduction in incidence among those born during the year.

(3) Absence of infected anopheles throughout the period of experiment.

(4) Absence of symptoms of toxicity or intolerance of the drug.

Russel,[10] in his discussion of malaria and its control in the Philippines, offers some complimentary remarks

on totaquina. He advocates the local cultivation of cinchona and the manufacture of totaquina. He believes there is a potential market in the Philippines alone for some 33 tons of totaquina annually, without competing at all with the quinine and synthetic products now imported. Totaquina is less bitter than quinine, has no bad effects and is equally efficacious. It would meet the need for an effective and much cheaper remedy. There would be a market for it in South China and, possibly, in the southern United States.

PERSONAL EXPERIENCE IN PANAMA

Komp and Clark[11] reported their fourth year's observations on malaria in Chagres River villages with reference to control with atabrine and plasmochin. No mosquito control nor house screening has been in use at any time during this period. Various combinations of anti-malarial drugs were used, including quinine sulphate alone or with plasmochin, and with atabrine alone or with plasmochin. None of the methods used was so successful as we had hoped in reducing the parasite rate. Monthly blood surveys over four years indicate the presence of cyclic variations in the malaria parasite rate extending over several years. If treatment of any sort happens to be given during the down-swing in rate success is almost sure to follow, but if it is given on an upswing in rate apparently nothing can stop the natural course of the cycle. The control towns show too little difference in parasite rates to warrant such methods of survey and drug control. There has been a very slow decline in town parasite rates over these years to a point where we thought only chronic cases and relapses accounted for most of the parasite index, but since the fourth year's report was made an epidemic of the disease has occurred that carried our rates to an average of about 30 per cent and many of these cases were in persons who had been on our negative list for a long time. This is all the proof we need to establish the fact that we did not control the oöcyst rate even over these five years of treatment efforts. From the standpoint of a commercial organization operating under such conditions we have no doubt that we have accomplished much good in the way of building up the general health of these villages. The number of chronic infections has been reduced and the people are now prompt in taking treatment when the disease shows actively, a business man's

control, but not a scientific control. In our opinion, the question of preventing relapse, in any species of malaria, and the question of a drug to kill the gametocytes and sterilize the mosquito are confronting us almost as much as they were twenty years ago.

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