THE EFFECT OF MALARIA ON LEPROSY AND FILARIASIS[1]

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Malaria has always been regarded as a serious complication in leprosy. Long experience has shown that protracted weakening febrile diseases, by lowering the power of resistance, usually aggravate the condition of a leprous patient. The stimulus produced by a malarial infection can mobilize latent leprous processes and, by activating them, cause an outbreak of an acute form of the disease (1, 3).

On the other hand it has been repeatedly observed that not only a marked improvement but sometimes even cure has occurred in leprosy after periods of fever arising from various causes, as secondary infection or protein shock (milk or vaccine injections) and also from a rise in temperature produced by hot baths, as in Kusatzu, Japan. For this reason Nocht (2) recently recommended the treatment of leprosy with artificially produced fever (pyrifer).

The author, from observation of a number of malaria cases in the Bethesda Leprosy Colony in Surinam, was also convinced that the short attacks of fever in this secondary infection had by no means as unfavorable an effect on the leprosy as was to be expected from the literature on the subject. The reason for the contradictory reports on the effect of this condition are dealt with more fully below.

The infections were spaced fairly evenly over the whole year. There is no clearly-defined malarial period in Surinam, as the rainy and dry seasons are not distinct and the conditions necessary for development of the anopheles are, on the whole, favorable throughout the year.

Of the 132 patients in the colony, 38 contracted malaria during the period of observation from December 1, 1933, to April 1, 1935. Three cases also occurred among the 7 nonleprous Europeans belonging to the staff. Of the lepers who came down with malaria 27 were Creoles, 10 Negroes and 1 a Malay. The types were as follows:

[1]From the Leprosy Colony, Bethesda, Surinam.

Diagnosis	*Number of cases*
Tertian	17
Subtertian	16
Quartan	3
Undetermined	5
Total	41

The treatment was as follows: Every malaria patient, freshly infected and relapsed alike, received altogether 1.5 gm. of atebrin 1.5 gm., or atebrin 1.5 gm. plus plasmoquine 0.15 gm. The daily dose was always 0.3 gm. of atebrin or 0.3 gm. of atebrin with 0.03 gm. plasmoquine. Treatment was as intensive and vigorous as possible. During the course and afterwards the results were constantly checked microscopically.

Atebrin was given for five days in all 41 cases, orally or parenterally, either alone or in combination with simultaneous or successive oral doses of plasmoquine. Orally one tablet of 0.1 gm. of atebrin was given three times daily. For parenteral treatment the author used for injection atebrin (Musonat) in dry-ampules of 0.1 gm., the daily dose being 0.3 gm. injected intramuscularly or intravenously once or twice daily. Oral atebrin treatment carried out in the manner prescribed showed no noteworthy characteristics; as the course of treatment is generally known it is unnecessary to give the details here. Although there was no special reason for adopting the parenteral route in these patients (oral administration of atebrin being adequate for all uncomplicated cases), some of them were nevertheless treated in this manner so that the staff should be familiar with the details and mode of action of the method in case of need. Three cases of subtertian and four of tertian malaria were so treated. In three patients the whole daily dose of 0.3 gm. was injected intramuscularly at once. Although it is generally advised not to give more than 0.1 gm. as a single dose intravenously, we saw no circulatory disturbances through fall in blood pressure or other by-effects after intravenous injection of the full daily dose of 0.3 gm. at once, even in two patients of over sixty who had had leprosy for over thirty years. Two other patients received the daily dose divided, morning and evening 0.15 gm. intravenously. The intravenous injections were always given slowly. The parenteral treatment was easily carried out in spite of the often primitive conditions prevailing in tropical practice.

No difference was observed in our few cases in the speed and duration of the atebrin action on the parasites and clinical manifestations with intramuscular, intravenous and oral treatment. The effect of the drug was particularly noticeable during an acute attack. Temperatures returned to normal after two to three days. Plasmodia could no longer be detected after the fourth day of treatment. Tolerance was always good. In two Europeans a yellow discoloration of the skin occurred after completion of the cure, which disappeared completely only after two to three weeks. In our colored patients traces of this were seldom seen.

All cases of subtertian malaria were treated with atebrin with plasmoquine, in view of the unique gametocidal action of the latter preparation on *Pl. falciparum*. Plasmoquine was always given orally for five days, either

simultaneously with atebrin or following the atebrin treatment after an interval of 2 days. The tablets were taken after meals with a fairly large amount of fluid; the dosage used was 0.01 gm. three times daily. Simultaneous administration of the two drugs in the proportion of 10:1 led in some cases to abdominal pain. This by-effect was not observed when plasmoquine was given after an interval of two days following the atebrin treatment.

Flu, Urchs (4) and others have already stated that cerebral symptoms occur relatively often in Negroes in Surinam during the course of a malarial infection, independently of whether treatment is carried out or not. In two of our patients (Creoles) conditions of excitation arose during treatment. As these nervous manifestations were presumed to have no connection with the use of atebrin under the circumstances, treatment was not interrupted. The symptoms disappeared completely after twelve hours.

Atebrin and plasmoquine affected the leprous condition in these patients neither favorably nor unfavorably. To our surprise it was clear, on the other hand, that the secondary malaria infection, contrary to expectation, had very little influence on the clinical picture of leprosy. Following the malaria treatment definite aggravation occurred in only 2 cases; 33 remained unchanged and in 3 the leprous processes improved considerably.

The loss in weight, which averaged 1.5 kgm. during the malarial infection and treatment, was as a rule not only made good in two to three weeks, but in 10 cases the patients continued to put on weight considerably. Only in 2 cases was there a loss in weight six weeks after completion of treatment. The weight of the 26 other patients remained unchanged.

The good results of the malaria treatment on leprosy were no doubt favorably influenced by the patients' comparatively good state of nutrition and by the fact that treatment was always begun as early as possible, i.e., immediately after the type of the parasite had been ascertained. In only 5 cases was the laboratory finding not awaited, for clinical reasons.

In these patients it was clearly shown that the extent to which the clinical course of leprosy was affected depended in general on the duration and intensity of the malaria. An acute infection with few short attacks of fever had a different effect than a chronic one; leprosy in a quiescent state was again influenced differently from that in the exacerbative stage. Whereas a protracted malarial infection, particularly when it reached the cachectic stage, always affected leprosy unfavorably, a few short attacks of fever can sometimes have a beneficial action, especially in torpid cases.

Of the total of 41 cases of malaria, 7 contracted the disease again during the first six months after completion of treatment. It cannot of course be decided whether these were fresh infections or relapses, as the patients were exposed to the same external risk of infection after treatment as before. In one case the patient contracted subtertian malaria three weeks after completion of treatment for a tertian infection.

Five of the leprous malaria patients were carriers of *Microfilaria bancrofti*. It is noteworthy that in all of them the microfilaria disappeared from the peripheral circulation after the first or second attack of fever, and were only found again in increasing numbers on an average four weeks later. This success was at first attributed to atebrin-plasmoquine treatment, but a test treatment of two malaria-free filaria carriers clearly showed that these drugs are not capable of reducing the number of microfilaria to any marked extent. Their temporary disappearance from the peripheral blood resulted from the action of the fever alone. Similar phenomena have already been repeatedly noticed in other febrile conditions.

A chance observation led the author to treat gonorrhoea experimentally with the medicaments in question. Oral doses of 0.1 gm. atebrin with 0.005 gm. of plasmoquine given three times a day for 5 days had a striking effect in nine fresh, untreated cases of gonorrhea free from malaria. In view of the relationship between atebrin and acridine the possibility of an action in this direction was considered. In all cases the symptoms were relieved by administration of the tablets; the burning sensation on urination and the purulent secretion disappeared. The number of gonoccoci rapidly decreased, but unfortunately disappeared completely in none of the cases. When the tablets were no longer given, the gonorrheal manifestations immediately returned.

SUMMARY

Malaria in 38 lepers and 3 persons free from leprosy was treated with atebrin and plasmoquine. Although some of the patients had been in an advanced stage of leprosy for more than 30 years and two of them were over 70 years of age, the treatment was carried out successfully and without complications in every case.

The atebrin-plasmoquine treatment had no influence on the leprosy.

In contrast to chronic malaria, an acute infection seldom leads to aggravation of leprosy. The more quickly the intercurrent malaria is treated, the less the danger of such aggravation. The most rapid effective treatment of malaria with atebrin or atebrin and plasmoquine therefore merits being given preference over all other methods in the case of lepers.

In 5 leprous carriers of *Microfilaria bancrofti*, the embryos disappeared from the peripheral blood after the first two attacks of malaria fever and only reappeared in increasing numbers after an average of four to five weeks.

Oral treatment with atebrin caused the clinical symptoms to disappear during treatment in 9 fresh gonorrheal patients.

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