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EPIDEMIOLOGY OF DISAPPEARING MALARIA

II. THE IMPORTANCE OF ASYMPTOMATIC PARASITE CARRIERS IN MALARIA ERADICATION¹

by

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The last few years showed clearly that the achievement of malaria eradication in a large territory depends to a great extent on our ability to deal effectively with "symptomless parasite carriers" - the invisible sources of infection. Whereas earlier, during the period of high malaria morbidity, parasite carriers were an important, but undoubtedly only a supplementary, source of infection of secondary epidemiological significance, the part they may play today in residual malarious foci becomes of greater importance, when compared with the quickly detected and easily treated cases of overt malaria.

The problem of malaria parasite carriers was studied in former years quite intensively, but unfortunately much of our knowledge was obtained during the period marked by intense and prolonged transmission of the infection and consequently when there was every likelihood of super-infection and re-infection. Parasite carriers studied during that period were a direct and close consequence of malaria epidemics. Today, in the last stages of malaria eradication we must consider, possibly qualitatively, special types of parasite carriers. In any case, the epidemiological conditions leading to the occurrence and maintenance of parasite carriers in the community have become different and less complex. This permits

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more extensive studies of the carrier phenomenon in malaria under field conditions. Before considering the trend of research on this problem, the terms "symptomless infection" and "parasite carrier" must be defined, since different authors give them different meanings.

According to one extreme view, symptomless parasite carriers are those subjects who have plasmodia in the blood but at the moment of examination show no signs of fever; this view does not take into account the duration of such a condition, or whether it is connected in time with acute manifestations of the infection. According to the opposing view, only carriers of gametocytes of Plasmodium falciparum represent the pure phenomenon which approaches closest to a symptomless condition. An intermediate position is held by authors who consider that only those persons who have plasmodia in the blood and in whom no acute manifestations of the infection are detected during a certain period of time before and after the discovery of the parasites, should be considered symptomless parasite carriers. The presence of parasites during this period is considered to be directly connected with the acute manifestations of the infection and not with the parasite-carrying phenomenon proper. Usually any parasite-carrying capacity is due to the increasing resistance of the macro-organism to the parasite during the course of infection. Some research workers also consider the possibility of "parasite carriage" in persons who have not suffered from malaria before ("primary parasite carriage").

With a view to studying the problem of parasite carriage and working out adequate counter-measures during the final stages of malaria eradication, we propose the following definitions of various concepts connected with malaria parasite carriers:

Symptomless parasite carrier: a subject with parasites in his blood, but without obvious symptoms of fever at the moment of examination and for at least three days before it. He may be a primary parasite carrier if the presence of parasites was not preceded by acute infection, or a secondary parasite carrier if his parasitaemia is in direct connexion with a former acute infection. In falciparum malaria the phenomenon can take the form of gametocyte carriage: real gametocyte carriers are treated subjects whose schizonts have been destroyed by schizontocidal

drugs, and only surviving crescents remain for some time; and apparent gametocyte carriers are untreated or incompletely treated subjects whose schizonts are undetected, but existing schizonts continue to produce crescents without interruption.

In all cases of parasite carriage in tertian and quartan malaria, and in some instances in falciparum malaria, the production of schizonts and gametocytes takes place.

Two groups of research problems can be singled out in connexion with parasite carriage: the nature of the phenomenon, and its epidemiological significance.

1. THE NATURE OF PARASITE CARRIAGE

1.1 Primary Carriage

This problem, which is important from the theoretical and practical standpoints, has often been solved in practice before attracting the attention of epidemiological research workers. If some organisms, on their first encounter with the parasite, do not react to its presence and activity, it is a fair assumption that they possess a congenital anti-febrile immunity to malaria. If the possibility of primary carriage in malaria could be successfully demonstrated, then the nature of secondary ("acquired") carriage would become more intelligible. Investigation of this problem requires observations of non-immune volunteers infected with small doses of sporozoites of various ages of different strains of plasmodia in different seasons of the year.

1.2 Duration of carriage in blood-induced and sporozoite induced infection

Comparative research on tertian and quartan malaria would help to find out to what degree the phenomenon of parasite carriage in untreated or inadequately treated patients is due to continued schizogony and to what degree it is connected with repeated entry into the blood of secondary tissue stages of the parasite. Elucidation of this problem would help in finding the correct method of treatment of parasite carriers. Observations should be carried out on volunteers or on patients undergoing malaria therapy.

1.3 Therapeutic response of acute and symptomless infections

The view is quite widely held that subjects partially immune to malaria respond to treatment relatively better than non-immunes. Consequently the response to treatment of symptomless infection should also be better than that of acute infection. But does "symptomless parasite carriage" necessarily occur in persons with a relatively high level of immunity? Would it not be more correct to say that it is evidence of the rapid development of one aspect of immunity - "anti-febrile" immunity - accompanied by the slow development of its other aspect - "anti-parasitic" immunity? Some stubborn parasitic relapses in a number of carefully treated cases of tertian malaria can be more satisfactorily explained from this point of view. It would be advisable to determine in two parallel and comparable groups the respective response to schizontocidal and radical treatment of acute and symptomless infection. It seems that more attention should be paid to the treatment of asymptomatic carriers than to the treatment of those with acute symptoms.

1.4 Possibility of detecting parasite carriers by means of other symptoms

It would be advisable to carry out, in various conditions, careful clinical observations on the "micro-symptoms" of parasite carriage in groups of persons left without treatment. If some characteristic micro-symptoms of this condition could be discovered, the task of detecting "invisible" carriers would become easier. An obvious success would have been achieved even if it were possible to sort out subjects suspected of being carriers, so that this selected group could be subsequently examined for the presence of parasites in the blood. In particular, it is important to discover how often parasite carriage occurs in persons without any enlargement of the spleen.

2. EPIDEMIOLOGICAL SIGNIFICANCE OF PARASITE CARRIERS

2.1 Large numbers of gametocytes in symptomless infections

The epidemiological importance of parasite carriers depends largely on the production of infective gametocytes during the carrier phase. The solution of several problems would allow us to assess the potential epidemiological danger from

parasite carriers. When is the gametocyte output greater; in the initial or terminal phase of parasite carriage? How does it compare with gametocyte production during acute attacks? What is the relationship between gametocytes and schizonts at various stages in the carrier state, particularly in the terminal phase?

2.2 The infectibility of mosquitos from parasite carriers

Numerous researches in the USSR (Shishlyayeva-Matova, Remennikova, Yakusheva) and in other countries (Jeffery, Shute and Maryon, etc.) have proved beyond doubt that parasite carriers can infect mosquitos, even if their blood contains only scanty parasites. The point that remains obscure is the infectivity in the terminal phase of carriage, or in other words, the maximum duration of the infective period in parasite carriers. Most probably the duration of the infective period will be equal to the duration of carriage, but this still remains to be proved.

2.3 Parasite carriage and blood donors.

Parasite carriers represent a double danger: as direct sources of infection for mosquitos, and as indirect sources of infection if they act as blood donors (infection of the recipient, who becomes a new source of infection). In the last few years many new facts have accumulated showing the extreme difficulty of timely detection of parasite carriers among blood donors and proving the infection of recipients with transfused blood which probably contained a very small number of parasites. The sufferers are mainly weakened children who are given multiple blood transfusions. It would be of interest, (a) to organize the collection of information on all cases of blood-transfusion malaria in localities with a very small residual incidence of the disease; (an analysis of this material might facilitate the detection of parasite-carrying blood donors with particularly low, "sub-microscopic" parasitaemia), and (b) to discover and introduce into practice more sensitive methods of blood examination for parasites which will detect donors with sub-microscopic parasitaemia (the method of fractionated centrifugation might be tried out for concentration of infected erythrocytes in a blood sample prior to microscopic examination).

2.4 Disappearance of parasite carriage in foci with varying degrees of endemicity in the terminal phase of malaria eradication

It seems that during malaria eradication, parasite carriers in foci of low endemicity disappear very quickly, almost as fast as the cases of acute malaria. No special investigations of this have been made, however. It is possible that the longer persistence of parasite carriage in foci of high endemicity is connected with residual cases of re-infection. It would be advisable to carry out special observations on the dynamics of disappearance of parasite carriage in foci of varying degrees of endemicity, particularly in those countries where malaria eradication is proceeding under conditions of the almost complete temporary eradication of the vector.

2.5 Features of parasite carriage in different age-groups

There is little information available concerning the presence, frequency and degree of parasite carriage in different age-groups in conditions when the collective immunity is gradually decreasing. It would be advisable to carry out comparative observations on the following points: (a) the frequency of primary parasite carriers; (b) the duration of parasite carriage; (c) response to treatment; (d) the abundance of gametocytes; (e) their infectivity to mosquitos; and (f) the course of disappearance of parasite carriage in foci with different degrees of endemicity.

3. CONCLUSION

The problem of parasite carriage in the terminal phase of malaria eradication is of sufficient importance to be considered as a matter for research under the auspices of the World Health Organization. Observation should be arranged on volunteers and in field conditions in various geographical areas in accordance with a plan specially drawn up and recommended by the World Health Organization.