

OBSERVATIONS ON "HEALTHY" PLASMODIUM VIVAX CARRIERS.

-BY-

DR. W. de GRAAF, CAPTAIN, NETHERLANDS EAST INDIES ARMY.  
DOUGLAS N. GILLIES, M.B., B.S. (Syd.), D.T.M. (Syd.)

By a "healthy" plasmodium carrier we mean a person who has plasmodia in his blood stream, as revealed by microscopic examination, but who exhibits no clinical signs of infection and who is able to carry out his normal work. "So-called 'healthy' parasite carriers play a very important part in the transmission of malaria". This statement was made by Prof. N. H. Swellengrebel after fifteen years work on malaria in Europe, and especially as a result of his experience in the country north of Amsterdam where malaria is endemic.

In "Malaria in the Netherlands" by Swellengrebel and de Buck, one can find a typical example of the influence of "healthy" carriers on the anophelene infection rate. These workers during the year 1935 kept 92 houses in an endemic area in Holland under continuous observation. Some of these houses harboured "healthy" carriers, some contained people who suffered from malarial fevers, and in other houses both types of persons lived. These 92 houses were divided into two groups:

- (a) a first group of 43 houses, which had 83 "healthy" carriers,
- (b) a second group of 49 houses, from which "healthy" carriers were absent.

Group (a) consisting of 43 houses contained 23 houses with a total of 48 cases of malaria fever.

Group (b) consisting of 49 houses contained 33 houses with a total of 75 cases of malaria fever. Thus the proportion of cases of malaria fever is practically the same in both groups.

During the late summer and autumn of 1935 Swellengrebel captured a total of 1329 infected anopheles mosquitoes in the 92 houses. 1279 (or 96%) were found in the 42 houses containing "healthy" carriers, and 50 (or 4%) in the 49 houses without "healthy" carriers. In reference to this finding Swellengrebel makes the

following statement: "All this may seem difficult to believe. Surely a person with numerous parasites in his blood, with quite a few gametocytes among them, is better able to infect anophelens than one with few parasites and fewer gametocytes. Of course he is, so long as man does not interfere by giving drugs. But he does interfere and so effectively at that, that the malaria patient simply has no chance to infect anophelens. So there remain the "healthy" carriers as the only source of anophelene infection, and the above figures are there to show that they are quite successful in infecting numerous mosquitoes".

Whether or not one agrees with this statement in its entirety, it would seem that Swellengrebel and de Buck have effectively demonstrated the importance of the "healthy" carrier as an important reservoir of infection. This reservoir of infection is naturally still more important in tropical countries among native populations, where the treatment of clinical attacks of malaria is either non-existent or so often insufficient, due to many causes with which this article has no concern. These notes will, we hope, show how this state can arise in white men in the tropics.

Evidence that carriers with few parasites in their peripheral circulation are able to infect anophelens was also produced by Swellengrebel. He found that "healthy" carriers with one parasite per 100 leucocytes could infect 60% or more of anophelene mosquitoes which had fed on them only once; even if no gametocytes could be detected in the patient's blood on the day of feeding. Furthermore "healthy" carriers with one parasite per 1000 leucocytes or less could likewise infect anophelens, but at a much lower rate.

Two main questions arise:

- (1) Under what conditions does a malaria infected person develop into a "healthy" carrier?
- (2) Is a "healthy" carrier really healthy?

The writers submit that the following observations made in Mater Dolorosa P.O.W. Hospital, Batavia, during 1943 and 1944 throw some light on these questions.

OBSERVATIONS ON "HEALTHY" CARRIERS IN A P.O.W. HOSPITAL.

In early 1943 the Japanese Army set aside two hospitals in Batavia for the treatment of the more seriously sick of the P.O.W. One was for the treatment of general medical and surgical cases, and the other, Mater Dolorosa, mainly for the treatment of infectious diseases, which included malaria, the dysenterys, diarrhoea, tuberculosis and leprosy. Almost all of these cases suffered from varying degrees of malnutrition, "burning feet" syndrome and beri-beri on admission. Due to the fact that recovery from malnutrition and the avitaminoses took a considerable time owing to inability to supply the right type and quantity of food, we were able to retain in hospital quite a few of the chronic malaria patients when their febrile attacks had ceased.

Most of the patients admitted suffering from malaria had had clinical relapses with typical chills and fever every 14 to 21 days for some time. Patients with malaria fever were given a standard treatment of quinine gr. 30 per day for five days if they had B.T. malaria, and those with M.T. malaria were given the same daily dose for seven days.

It was decided that in certain uncomplicated cases of B.T. malaria, as soon as their general condition had improved sufficiently to stand the strain, they should be allowed to have a couple of febrile attacks without treatment in order to stimulate their immunity, in accordance with the League of Nations recommendations. This proceeding was never tried in cases of M.T. malaria, tuberculosis, dysentery or any serious intercurrent condition. The parasitaemia was controlled by means of a thick blood film examination made every second day stained by the Giemsa method. The patient was closely observed by the ward orderly and the ward doctor, and if he showed signs of unfavorable reaction to his infection such as vomiting, rigors, etc. quinine treatment was instituted immediately and maintained for five days. Likewise if the parasitaemia, as revealed by the number of parasites per leucocyte, showed signs of marked increase, quinine treatment was also instituted.

During these experiments it was noticed that some patients who had many attacks of malaria before entering hospital (always more than ten) did not develop a second paroxysm. At the same time the number of parasites in the blood film diminished to a low level or disappeared. These patients did not receive any treatment, and in all of them the number of parasites in the blood stream increased in two to three weeks and a few developed a febrile reaction. However in most cases the parasites remained below the pyrogenic level and the "healthy" carrier state developed. A typical example of this process is the following history:

B., a Dutch patient, was admitted to hospital on 7.7.1944. In June 1943 he had been sent to Flores by the Japanese. While there he suffered 17 attacks of malaria. For each attack he received from 3 - 5 days quinine (1 - 2 gm. per day). On admission a thick blood film was positive for B.T. malaria. He was given quinine gr. 30 per day for five days. On 25.7.44 his blood film was again positive for B.T. malaria, and on 28.7.44 he developed a fever. No treatment was given and within a few days his fever subsided and did not recur up to the time of his discharge from hospital on 1.11.44. His parasite counts, expressed in parasites per number of leucocytes in a thick film, for the last two months of his stay in hospital were as follows:

<u>Date</u>	<u>Parasitaemia</u>		
28.7.44	125	per 100	leucocytes
30.7.44	100	"	100 "
1.8.44	52	"	100 "
3.8.44	12	"	100 "
17.8.44	1	"	500 "
19.8.44	8	"	500 "
21.8.44	20	"	500 "
23.8.44	25	"	500 "
25.8.44	25	"	500 "
27.8.44	50	"	500 "
29.8.44	50	"	500 "
31.8.44	40	"	500 "
2.9.44	10	"	500 "
4.9.44	10	"	500 "
6.9.44	5	"	500 "
10.9.44	1	"	1000 "
13.9.44	1	"	1000 "
14.9.44	1	"	2000 "
16.9.44	1	"	1000 "
18.9.44	2	"	1000 "
20.9.44	12	"	1000 "
22.9.44	8	"	1000 "
24.9.44	17	"	100 "

<u>Date</u>	<u>Parasitaemia</u>
26.9.44	10 per 1000 leucocytes
28.9.44	10 " 1000 "
30.9.44	5 " 1000 "
2.10.44	0 " 1000 "

A number of "healthy" carriers were detected only by routine blood examinations. As a routine every malaria patient had a thick blood film examined for malaria twice a week. If parasites were found he was so examined every second day.

It was noticed that if the number of parasites either stayed constant or increased only a little, the patient either did not develop a fever, or if he did it was very slight.

In 412 patients treated in the malaria ward (which was reserved for malaria uncomplicated by dysentery, tuberculosis, etc.) a total of 31 carriers was found. Of these 12 were Australian, 11 Dutch and 8 English. They had been infected on Flores, Timor and Ambon while prisoners of war living under the usual conditions of poor food, unhygienic surroundings, and lack of medical supplies. On Flores many men had died from malaria, and on Timor and Ambon, although the death rate from malaria was not high, the morbidity was exceedingly high. Amongst these the number of treated attacks of malaria before admission varied from 10 to 26. We did not find the carrier state developing in a person who had suffered from less than 10 treated attacks.

The general rule was that first the parasitaemia diminished gradually to a very low level (in some cases to less than 1 parasite per 6000 leucocytes, which is less than 1 per cubic m.m.) and then increased in every case but one. After increasing to a certain level, varying from 25 to 125 parasites per 100 leucocytes, the number of parasites decreased again. If the patient was given quinine they disappeared and very often reappeared after 2 - 3 weeks or longer. One of our patients repeated this procedure three times. Only once did parasites disappear from the blood stream without any treatment and not reappear within the observation period of two months, after which the patient was discharged. The extreme limits of the carrier state, uninterrupted by treatment, varied in our cases from 2 days to 3 months.

In one case the carrier state lasted for one year, but this period was interrupted by several treatments of five days quinine. This case was an English sergeant who was admitted to hospital as a patient but subsequently became a volunteer member of the staff. His history is as follows:

Admitted on 12.11.42. Temperature 40°C. Five days quinine given. Blood film B.T.+

25.12.42	Relapse, five days quinine
23. 1.43	Relapse, five days quinine
3. 2.43	B.T.+
4. 2.43	Fever
6. 2.43-13.2.43	Apyrexial until the latter date when five days quinine was commenced.
31. 3.43	B.T.+ No fever. No treatment.
25. 4.43	Five days quinine.
30. 9.43	B.T.+ After five months of negative films.

From then on this patient had positive blood films without treatments or ill-effects until -

28.12.43 Five days quinine treatment.  
Routine blood films until 13.2.44 were all negative.

Evidence was collected which shows that the patients were so little affected by their infection that they might well be described as healthy; particularly in view of their poor diet. The weight, haemoglobin estimation and the spleen were constantly observed in most cases (figures for weight and haemoglobin are lacking in 7 cases). As a general rule the haemoglobin did not fall, the weight remained constant, and the spleen did not become enlarged. The first two findings were probably due to the fact that the food in the hospital was (despite its poorness by normal standards) better in quality and greater in quantity than that in the other P.O.W. camps in Batavia. Furthermore most of these patients had recently arrived from Flores, Timor and Ambon where the diet was appallingly deficient, and it was a general experience in P.O.W. camps that a small increase in the rice or vegetables supplied by the detaining power resulted in an increase in weight and well-being, although the diet level reached was well below minimum standards for healthy living.

The lowest haemoglobin percentage found in our series of 24 cases was 72% and the highest 105%. In not one case did the haemoglobin decrease while the patient was a "healthy" carrier, and some of them increased.

No carrier lost weight and most increased by one or two pounds per month. The English sergeant previously mentioned increased in weight from 57 kilogrammes in December 1942 to 68 kilogrammes on the date of his discharge in February 1944.

A surprising fact was that the spleen was not usually enlarged on admission despite repeated attacks of malaria before admission, and, furthermore, did not become enlarged during the observation period. Immediately on admission the ward doctor examined the patient and entered the absence or presence of splenomegaly on the history sheet. The figures for spleen examinations cover the total of 31 carriers.

SPLEEN SIZE IN 31 CARRIERS.

<u>On Admission</u>	<u>Subsequently as carrier</u>
14 no enlargement	One became enlarged after 20 days then became non-palpable.
14 were palpable on deep inspiration	None became enlarged after periods from 60-90 days.
3 were Schuffner 2 (2 fingers)	No further enlargement after 21, 30 and 41 days respectively.

Most of these carriers felt sufficiently well to volunteer in the hospital working party which was used to help keep the hospital clean, to cook, etc. This is a good indication of their subjective sensation of well-being. Sometimes when their parasitaemia was at a relatively high level they had headaches or a feeling of heaviness in the legs, but usually were quite well in one or two days. However no direct relationship could be found between the parasitaemia level and the subjective sensations of the carriers. In a few cases there was a slight rise in temperature, but never above 37.8°C. One of the best examples is the following history:

A Dutch patient, H., was admitted to hospital on 23.5.44 with a history of having had 15 attacks of malaria while in Flores. His first attack was on 1st July 1943. After admission he had relapses of B.T. malaria on 13.6.44, 3.7.44 and 7.8.44. On each occasion he received five days quinine treatment. On 2.9.44 his blood film was positive for B.T. malaria and from then on until discharge his parasitaemia kept below the pyrogenic level. His record is as follows:

<u>Date</u>	<u>Parasitaemia</u>		
2.9.44	B.T.++		
4.9.44	15 per	100	leucocytes
7.9.44	38 "	100	"
9.9.44	28 "	100	"
11.9.44	6 "	100	"
13.9.44	8 "	100	"
15.9.44	6 "	100	"
17.9.44	B.T.+		
19.9.44	12 per	100	leucocytes
21.9.44	14 "	100	"
23.9.44	7 "	100	"
25.9.44	1 "	300	"
27.9.44	1 parasite	to every 40 fields	
29.9.44	1 "	"	20 "
2.10.44	1 per	600	leucocytes
4.10.44	2 "	100	"
7.10.44	24 "	100	"
9.10.44	20 "	100	"
12.10.44	7 "	100	"
14.10.44	1 "	150	"
16.10.44	1 "	250	"
18.10.44	1 "	100	"
20.10.44	B.T.+		
22.10.44	1 per	100	leucocytes
24.10.44	5 "	100	"
26.10.44	6 "	100	"
28.10.44	3 "	100	"
30.10.44	1 "	3000	"
1.11.44	1 "	2000	"
3.11.44	1 "	300	"
5.11.44	1 "	1500	"
7.11.44	1 "	100	"
9.11.44	2 "	100	"
11.11.44	16 "	100	"
13.11.44	2 "	100	"
15.11.44	1 "	300	"
17.11.44	1 "	500	"

On the above date the patient was given five days quinine and discharged from hospital for reasons divorced entirely from the terms of the management of his carrier state. (Note: If a carrier had to be discharged owing to shortage of bed space he was given quinine gr.30 per day for 5 days). This man was well accustomed to his carrier state and apart from headaches, usually very mild and occurring in the afternoon or evening, was in perfectly normal health. He remained a carrier for 78 days, and during this period his weight remained constant at 68 kilogrammes and his spleen was not enlarged. The last figure we have for his haemoglobin is 90%.

At the commencement of these notes we put two questions:

- (1) Under what conditions does a "healthy" carrier arise?
- (2) Is a "healthy" carrier really healthy?

As regards the first of these the chief factors would seem to be heavy infections due to constant reinfection, and the subsequent occurrences of many relapses in spite of treatment with usually



insufficient quinine. One of us spent seven months on Dutch Timor in a P.O.W. camp where no more than 5% of the prisoners possessed mosquito nets. In seven months well over 90% of the P.O.W. became infected with malaria, and these people became well-known for their tendency to relapse when taken to Java, the previously mentioned writer having more than 20 relapses.

Question (2) can in our opinion be answered in the affirmative. The carriers with whom these notes deal are healthy generally speaking. The only objection one can raise to this is that the patients did suffer from time to time from headaches and lassitude, but these symptoms are very mild in view of the rigors of their life before admission and their poor diet for over two to three years of prisoner of war existence.

We suggest that healthy adult carriers may be of some importance in the spread of malaria to areas where it is at present rare or non-existent.

We regret that our notes are incomplete and unsatisfactory in many ways and most especially that we can give no figures for the presence of gametocytes in the thick films examined. Furthermore the figures regarding the weight of the carriers are also incomplete, and it would have been of advantage to have been able to give more detailed information about the subjective and objective well-being of the carriers. Our only excuse is that we also were prisoners, and we gleaned what information we could under the disadvantages of such a life.

#### SUMMARY.

- (1) A series of 31 "healthy" *plasmodium vivax* carriers is described.
- (2) The manner in which their condition arose is described.
- (3) Some evidence to show that they are healthy is given.

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