War Medicine Series

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MALARIA IN WARTIME

BY

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Malaria in wartime is a large subject, and may be a serious problem. It was so in the war of 1914-18 and probably it will play a part in the present conflict. Then, in the "side shows"—Iraq, Salonika, East Africa, and Palestine—malaria may be said to have been decisive—much more so than enemy action. The admission rates to hospitals which were published in the *Medical History of the War* give impressive figures. In the East African Expeditionary Force there were annually more hospital admissions than troops in the field; that for Salonika was 500 or 600 per thousand troops. Therefore it behoves us more than ever to try to keep in mind what malaria may be like in a war of movement.

There are four different species of intracorporeal parasites causing malaria, but only two are really important in war; the others do not really matter, just being curiosities. The first causes benign tertian; the second, which may be predominantly important, causes subtertian or malignant malaria.

Unfortunately, scientists have given these parasites many names. I need not bother you with the scientific terms, but I should like to point out how the parasites differ, and how the fevers which they produce also can be distinguished from one another, for there is no doubt that different parasites produce different clinical types of disease. It is of no use at the present time saying that someone has got malaria, and leaving it at that. Research has shown that these fevers differ considerably not only in their clinical appearances but in their treatment also.

The Benign Tertian Parasite

First we have the benign tertian parasite. The ring form becomes attached to the blood corpuscles and then enters them, gradually occupying the whole; but the host cell enlarges when the parasite attains its maximum development as the sporulating form. Moreover, within the substance of the red cell there is produced a degeneration of the protoplasm known as Schüffner's dots, which are peculiar to this and to the *ovale* parasite alone.

Multiple infections of the corpuscle by more than one parasite are rare in benign tertian, although common in subtertian malaria. The sporulating body consists of eighteen to twenty-four spores, and breaks up and sheds the spores (merozoites) into the plasma. It is at this stage that the malaria rigor, or fever, takes place. In the case of the benign tertian parasite this recurs every forty-eight hours. There is another stage, the gametocyte or sexual form, in which the development runs parallel with the former, or asexual, cycle.

There is nothing else quite like a chart showing the classical appearances of the fever. Rigors recur on alternate days at exactly the same time. If the rigor began at 2 p.m. on one day the second rigor will also take place at the same time within forty-eight hours. It was Manson who suggested that any fever which began in the forenoon or early afternoon was more likely to be malaria than anything, more especially if it started with explosive suddenness. The classical features of a malaria attack are the cold, the hot, and the sweating stage, the last taking place when the temperature begins to fall. It is possible to get temperatures of considerable height—

104°, 105°, or even sometimes 106° F. When a temperature suddenly shoots upwards so as to cause alarm it is much more likely to be benign tertian malaria than any other kind of fever. Moreover, it falls as abruptly, and afterwards drops to subnormal. The reaction to quinine given intramuscularly may be dramatic, but a subsequent attack cannot be prevented or aborted by one injection of this specific. It just depends upon the stage of development the parasites have attained when the quinine is given whether any further rigors take place.

The classical tertian periodicity is not observed in every case of benign tertian. One must expect fevers, especially in primary infections, which are atypical, resembling tuberculosis or typhoid. Quotidian rigors were formerly held to be due to two generations of parasites running concurrently, but that is not really the case. Rather they are due to the response of the body to a primary infection, because we now know that in experimentally produced malaria we do not get the typical tertian periodicity till the fever has lasted several weeks.

Subtertian Malaria

Benign tertian malaria may be likened to the ordinary rifle bullet, whereas subtertian (*Plasmodium falciparum*) may be likened to a high-explosive shell. The illness the latter produces is different; that is why it is misleading to use the term "malaria" as embracing all these diseases. This parasite does not enlarge the red blood corpuscle in which it lives; and, again, owing to some adhesive properties in the infected corpuscles, they tend to agglomerate, so that development mostly proceeds in the capillaries of the internal organs, and thus the parasite does not freely circulate in the peripheral blood as does the benign tertian. By taking blood slides from the finger one cannot see the complete cycle of development of this parasite in human blood, because a number of stages develop in the sinuses of the spleen, pancreas, brain, intestinal capillaries, and other internal organs of the body. The clinical appearances of the fever depend upon in which organ the maximum multiplication takes place. There is no more protean infection than subtertian malaria. It is a sort of conjurer, continually producing new tricks out of the hat. The parasite at the start somewhat resembles a very small flattened signet ring; next we find it plastered on to the edge of the blood corpuscle, and multiple infections of the cell are common. Irregularity in outline of the corpuscle will be observed, and there are differences in the staining properties of its protoplasm. The sporulating stage takes place almost entirely within the internal capillary vessels; the affected corpuscles agglutinate, forming thrombi, and in the security of their retreat the sporulating form develops. When this last stage is seen in the peripheral blood prognosis is grave, because it means that the patient has been overwhelmed with this parasite.

I will now describe what a blood film looks like in fatal cases such as were frequently encountered during the last war. We see here rapid multiplication of the parasite inside the red cell, and the two bifid nodules of chromatin which usually indicate a severe infection. We can see also large hyaline mononuclear cells which devour defunct malaria parasites. Thus one often finds in subtertian malaria pigmented corpuscles, and nearly always they are mononuclears.

With the subtertian parasite we do not get any dots in the protoplasm of the red cells, but little fissures or holes, which are known as Maurer's dots, or clefts, and they are distinctive.

With regard to the fever, subtertian malaria usually has a quotidian periodicity, but may produce almost any variety of temperature chart. Every now and again there is a sudden drop in temperature, and then it rises once again. In the benign tertian one may see what may be termed a "Salisbury Cathedral" type of chart, but in this case one frequently observes a double rise of temperature—that is, with a dicrotic notch. That is a very important point, and when you see a temperature chart of this description you should always think of this kind of malaria.

I mention this because many years ago I was summoned to a nursing home in London to see a young official who had travelled from West Africa via Barcelona and Paris. There he had partaken of oysters, and was overcome by vomiting and diarrhoea with grave weakness which had been diagnosed as "food-poisoning." With this diagnosis he arrived in London,

and there, every day for three weeks, he produced rigors with a double crisis. He had been examined by several doctors and as many diagnoses had been suggested, till a blood culture was taken, and on a streptococcus being isolated he was given the appropriate serum; but still he did not improve. When I was called in I suggested that he must have malaria, to which the objection was raised that he had no enlarged spleen (but many cases of subtertian malaria do not exhibit this) and that no malaria parasites had been found in his blood. I was informed that thirteen blood examinations had been made already and therefore it was no help to suggest malaria. But in the first blood film I was able to demonstrate three parasites within one corpuscle. He took quinine and atabrin that night, and the fever defervesced and soon he was quite well.

Another curious feature of the subtertian malaria chart is that you may not get any fever at all. It is possible to find people in apparent perfect health walking about with this parasite in their blood, and many return from West Africa with this parasite lying dormant, ready to spring into activity and produce the most dire symptoms at the first opportunity on exposure to cold or exertion.

The Mosquito Problem

Now we come to the mosquito problem. What is an *Anopheles*, and what are you to do when you see one? The first characteristic of the *Anopheles* mosquito is its posture; it is said to stand on its head. Actually it does appear to stand in this uncomfortable position with abdomen raised in the air, while all other kinds of mosquito carry it in a horizontal position. This mosquito is usually found in nooks and crannies of the wall and ceiling. In wartime it can be discovered inside canvas tents, and whenever you see an *Anopheles* mosquito the best thing to do is to "swat" it. There are all sorts of minor marks of differentiation between this and other species. The egg of the *Anopheles* is one of the wonders of Nature. It resembles a primitive float, and, unlike those of other species, is laid singly. The larva on emerging lies with its body parallel to the surface of the water and has a short respiratory siphon. The *Anopheles* also has spotted wings, whereas other species generally have not, as exemplified by Ross's provisional description, "the dappled-wing mosquito." Several species of *Anopheles* in Great Britain have been described; indeed, there are probably just about as many individuals of this genus in Great Britain at the present time as ever, so that it is difficult to know why endemic malaria disappeared from this country. But there are different races even of the same species. Some prefer feeding on cattle or horses, others on humans; and it is only those which prefer biting human beings to biting cattle that are dangerous to man.

Next the elaborate cycle inside the mosquito's stomach must be considered; this, as is well known, was worked out by Ross at the instigation of Patrick Manson. It must always be insisted that had it not been for Manson's original hypothesis this would probably not have been worked out at that time. The copulation of the sexual forms of the parasite takes place inside the stomach cavity of the mosquito, and is known as the sexual cycle. Manson's original hypothesis was that there must be one particular type of mosquito in which this took place; so that time and further work have not upset that original idea—that is, it is only in the genus *Anopheles* that this development may occur.

We have drugs which act upon this parasite in various stages. There are drugs which act upon the sporozoites from the salivary glands and others which act upon the sexual cycle, so that it is becoming more and more important that we should know of these researches because we may in that way eventually find the ideal malaria prophylactic. It is quite obvious that quinine does not fulfil this ideal, because it has been found to have no effect on the sexual cycle and has no influence on the sporozoites. On the other hand, there is plasmoquine, which, although it may not produce such startling results in man, can knock out sporozoites and destroy the sexual stages of the parasites. Then there is atabrin (quinacrine or mepacrine), which acts mainly upon one species (the subtertian), so that we have selective drugs for different stages of malaria parasites.

The Incubation Period

One of the great difficulties in studying malaria is the varying length of the incubation period. In benign tertian malaria it is not unusual for this fever to commence one year to fifteen months after the primary infection; therefore, one commonly meets patients who have been in India and have not had fever there, yet who a year or fifteen months after their return fall sick with an abrupt attack which proves to be malaria.

How long can the malaria parasite persist in the body? The old soldier will assert that he can feel malaria "in his bones." His colonel avers that the only thing is to "drown" it with whisky; he is convinced that he still has malaria thirty or forty years after quitting the Tropics. Are we to believe these stories? I say distinctly they are not true. The parasites have their limited cycle in the body of man. They have their life span just as any other creature. The shortest for subtertian malaria is one year: that of benign tertian is from three to three and a half years at the maximum. The statistics of the Ministry of Pensions show that the benign tertian malaria parasite disappeared within three years from the end of the last war. The quartan parasite is the toughest, because apparently it can hang about in the blood for a very long time. A fatal case was recently reported in London in a child transfused with blood from its father, who had quitted Ceylon twelve years previously. One German observer has even discovered it in the blood nineteen years after primary infection. How are we to explain these long latent periods?

The theory has been developed, backed up by some evidence, that sporozoites do not all immediately enter red blood corpuscles, but lie dormant in the skin, and then infiltrate into the blood stream from time to time, causing malaria. That is a plausible explanation, and may indeed be true.

The Sexual Stage.

Next we must briefly consider the sexual stage of the subtertian parasite, or crescent. This looks like a miniature Zeppelin developing inside the red cell, the free edge of which may be clearly visible. It is the black pigment within the parasite that attracts attention, and it was really due to this that the malaria parasite was discovered by Laveran in 1880. While watching one of these parasites, then thought to be dead pigmented cells, he found that when the crescent was abstracted from the blood stream and chilled it underwent an amazing transformation known as exflagellation. This is really a sexual process, and it was due to Manson's explanation of this phenomenon that it was discovered to be a vital process in the life of the parasite. It is not, indeed, as formerly thought, a sort of swan-song of the malaria parasite, but from this amazing act the whole scheme of development of the malaria parasite in the mosquito was formulated.

There are two varieties of crescent—male and female. The latter simply becomes rounded off into a sphere, but the former becomes transformed into this flagellated body. It was Manson, too, who first demonstrated that the flagella broke away, abandoning the defunct body of the parasite, and that each flagellum had a definite structure; but it was McCallum who in 1897 saw the free flagellum impregnating the female. Thus was a vital stage in the elucidation of the life history of the malaria parasite demonstrated.

(This paper will be concluded in next week's issue.)

The National A.R.P. Co-ordinating Committee is arranging a one-day conference at Caxton Hall, Westminster, S.W., on Sunday, Oct. 25, starting at 10 a.m. There will be two parallel sets of lectures—one on organizational topics, including post-raid welfare and war damage, and one on more technical subjects, including anti-gas measures, fire defence, casualty services, and industrial defence. There will also be a show of the latest civil defence films from the Ministry of Information. The speakers include Prof. J. B. S. Haldane, F.R.S., Prof. J. R. Marrack, M.D., and Dr. K. W. C. Sinclair Loutit, former A.R.P. medical officer for Finsbury. Inquiries and applications should be sent to the Conference Secretary, A.R.P. Co-ordinating Committee, Faraday House, 8, Charing Cross Road, London, W.C.2.