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OBSERVATIONS ON MALARIA IN THE GOLD COAST COLONY, WEST AFRICA

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PLATES I-II

INTRODUCTION

The Gold Coast shares with the rest of West Africa the unenviable reputation of being an unhealthy country, and although in recent years great improvement has been observed in the health of European officials, the latest (1914) return shows that the percentage of deaths to the average number resident was 1·70, a figure which must be considered high when it is remembered that it refers to individuals of an age with which death deals sparingly in Europe, who are moreover repeatedly subjected to searching medical examination.

From a purely medical point of view the reason for this is somewhat obscure, as many of the most serious diseases of other tropical countries are either unknown or are but rarely encountered in West Africa. Cholera, for example, has never yet broken out on the Gold Coast, and plague, although it has visited the colony, is not an established disease; kala-azar and other *Leishmania* infections, undulant fever, and tick fever are very rarely seen; typhoid fever is uncommon, and the trypanosomiasis that does occur is of the relatively mild type due to infections with *T. gambiense*. Dysentery, indeed, is prevalent, but it is mainly amoebic and is now-a-days fortunately amenable to treatment, and yellow fever and cerebrospinal meningitis periodically occur in fatal outbreaks.

Malaria, however, is exceedingly common, and is mostly of the sub-tertian variety. Official statistics are of little value in estimating

the incidence of this disease, because it is, as a rule, only the graver attacks that come to the notice of Medical Officers, the Europeans treating with quinine, and the natives ignoring, the milder manifestations; but, so far as they go, the annual returns for the four years 1911—1914 show that 10 per cent. of the admissions to Government hospitals, and 5 per cent. of the total attendances at Government dispensaries were attributed to malaria. In 1914, of a total of 499 on the sick list out of an average number of 646 resident European officials, malaria accounted for 180 and 'pyrexia' for 57. Amongst the natives other diseases such as pneumonia, tuberculosis, and ankylostomiasis are of great importance, but so far as the Europeans are concerned malaria dominates the field to such an extent that it must be concluded that the unhealthiness of the country is largely due to its prevalence.

THE RELATIVE FREQUENCY OF OCCURRENCE OF THE DIFFERENT MALARIA PARASITES

During the last three and a half years (1913 to June, 1916) a careful record has been kept of the results of the blood examinations made at the Accra laboratory, and some idea of the prevalence of the different malaria parasites in this district may be gathered from these figures (see Table I). Malaria parasites were found in 250

TABLE I.—The incidence of the malaria parasites in the blood of European and Native patients examined at the Accra laboratory.

	Europeans			Natives		
	Malignant tertian	Simple tertian	Quartan	Malignant tertian	Simple tertian	Quartan
1913	27	2	—	36	2	5
1914	42	2	3	18	1	1
1915	18	—	—	40	5	5
1916, Jan. to June ...	14	—	—	24	1	4
Totals ...	101	4	3	118	9	15
Percentages ...	40·4	1·6	1·2	47·2	3·6	6·0

cases, namely in 108 Europeans and 142 natives, and of these 219 (87·6 per cent.) showed sub-tertian parasites, 13 (5·2 per cent.) benign tertian, and 18 (7·2 per cent.) quartan. In both European and native patients sub-tertian parasites were by far the commonest, but in the former benign tertian and quartan parasites were relatively rarer than in the latter. The fact that all Europeans were adults but a considerable number of the natives young children, may account for this, as it has been recorded by Statham (1915) that at Freetown, Sierra Leone, benign tertian and quartan infections were very rare in adults, but amounted to as much as 20 per cent. in children.

The Investigators' Reports published by the Yellow Fever Commission (West Africa) furnish some interesting and at the same time puzzling statistics as to the occurrence of malaria parasites (see Table II). The Reports by the investigators in the Gold Coast

TABLE II.—The prevalence of the malaria parasites, according to various observers, in Sierra Leone and the Gold Coast.

Locality	Observers	Number of cases	Malaria parasites in percentages		
			Sub-tertian	Benign tertian	Quartan
Freetown, Sierra Leone	Statham	676	98·5	?	?
Freetown, Sierra Leone	Butler	201	95·0	0·5	4·5
Freetown, Sierra Leone	Dalziel and Johnson	221	77·7	0·4	21·9
Sekondi, Gold Coast ...	Coghill and Hänschell	259	56·8	18·0	25·2
Sekondi, Gold Coast ...	Coghill and Hänschell	211	72·5	11·1	16·4
Accra, Gold Coast ...	Laboratory records ...	250	87·6	5·2	7·2

(Coghill and Hänschell) show that at Sekondi from 1st May to 30th September, 1913, sub-tertian parasites were found in 189 persons (56·8 per cent.), benign tertian in 60 (18·0 per cent.), and quartan in 84 (25·2 per cent.), and that from 1st October, 1913, to 30th April, 1914, sub-tertian parasites were found in 177 (72·5 per cent.), benign tertian in 27 (11·1 per cent.), and quartan in 40 (16·4 per cent.).

At Freetown, Sierra Leone, Butler in 201 cases examined between 1st May and 14th September, 1913, found sub-tertian parasites in 191 (95 per cent.), benign tertian in 1 (0.5 per cent.), and quartan in 9 (4.5 per cent.); but from September, 1913, to March, 1914, Dalziel and Johnson found sub-tertian parasites in 174 (77.7 per cent.), benign tertian in 1 (0.4 per cent.), and quartan in 49 (21.9 per cent.). The five investigators quoted all agree in attributing the majority of infections to the sub-tertian parasite, but they differ considerably in the percentages they assign to the benign tertian and quartan organisms; and whereas at Sekondi the two latter types were found more frequently during the period May to September, at Freetown they were commoner from September to March. There may, of course, have been a natural explanation of these apparent discrepancies, but as crescents are notoriously difficult to find in the peripheral blood in West Africa, a fact which was remarked also by these investigators, most of the identifications must have been made from ring forms alone, and it is more probable that they depend on the personal factor. The same explanation may perhaps account for the fact that Connal (1912) assigned 35.4 per cent. of the malaria cases he examined at Accra to the quartan type, an observation which has not been confirmed by any subsequent worker.

Rogers (1910) has collected some data regarding the prevalence of different varieties of malaria in India, which are of interest in this connexion. In Calcutta sub-tertian cases constituted 54.2, benign tertian 38.6, and quartan 7.2 per cent. of 539 malaria cases; in Bombay the percentages were respectively 46, 52.6, and 1.4; in Madras sub-tertian infections were commonest and quartan rarest; and in Bareilly, in the United Provinces of Agra and Oudh, benign tertians accounted for over 90 per cent. of the cases. So far as these figures go, they seem to prove that sub-tertian infections are very much more common in West Africa than they are in India.

The rarity of crescents in sub-tertian infections in West Africa has been commented on by practically every investigator who has recorded observations on malaria in this region. Statham (1915), as the result of a careful study of 676 adult cases of malaria at Freetown, Sierra Leone, all but ten of which were due to the sub-tertian parasite, has suggested that 'the sub-tertian parasite of

West Africa is somewhat different from that found in Asia.' The reasons he gives in support of this view are (1) that the gametes are more rarely found, (2) the great difficulty occasionally met with in finding parasites in cases which are clinically typical, and (3) the greater amenability of the disease to quinine treatment. In a section which follows, attention is drawn to certain morphological peculiarities which, if they prove to be less commonly met with in other countries, may lend support to Statham's suggestion.

THE SEASONAL INCIDENCE OF MALARIA AT ACCRA

There are not yet sufficient accurate data on which to base a study of the seasonal incidence of malaria in the different parts of the Gold Coast; but during the last two years, since the laboratory was started on its present footing, it has been possible for the Medical Officers at Accra to have the blood of any patient suspected of suffering from malaria examined for parasites, and the results should give some idea of the prevalence of this disease in this town during the different seasons of the year. The total number of cases examined has been small, and it must be admitted that not all the 'clinical' malarias have been investigated, but such as they are the results are suggestive and should perhaps be recorded. It is possible, however, that some modification may have to be made in our views when further statistics are available.

From September, 1914, to August, 1916, two complete years, malaria parasites were found in 195 cases of fever at Accra, and of these 181 were sub-tertians, 8 benign tertians, and 6 quartans (see Table III). The number of benign tertian and quartan infections were too few to indicate any seasonal variation, but there was a great difference in the monthly distribution of the sub-tertians. Cases of this form of malaria occurred throughout the year, but in July the number suddenly increased, reached a maximum in August, and in September fell rapidly towards the mean level. The actual figures, set forth in Table III, show that 62 per cent. of the sub-tertian cases occurred during the third quarter of the year. This very remarkable seasonal variation appeared to be directly dependent on the rainfall; for although Accra is a relatively dry town, what

rain there is falls mostly in June, and, as will be seen by reference to Chart I, the curve formed by plotting the cases of malaria followed closely the curve of the rainfall during the two years under consideration.

It is of some interest to compare the distribution of the cases of sub-tertian malaria at Accra with those for different parts of India summarised by Rogers (1910). In Calcutta sub-tertian infections accounted for 54·2 per cent. of 539 malaria cases, but no less than 61 per cent. of them occurred during the last three months of the year. That is, the season of prevalence of malignant infections was

TABLE III.—The prevalence of malaria at Accra during the two years, September, 1914 to August, 1916.

Type of malaria	Month											
	January	February	March	April	May	June	July	August	September	October	November	December
Sub-tertian	3	6	10	4	12	12	39	57	17	4	9	8
Benign tertian	1	—	1	—	1	1	1	2	—	1	—	—
Quartan	2	—	—	—	—	1	—	2	—	—	—	1
Totals	6	6	11	4	13	14	40	61	17	5	9	9
Rainfall in inches ...	—	0·45	3·93	3·65	7·83	29·89	5·47	1·67	0·56	0·82	2·42	0·07

relatively short and occurred during the drying up at the end of the south-west monsoon. In Bombay, where the temperature is more uniform, sub-tertian cases occurred more regularly throughout the year, and accounted for 46 per cent. of the infections, and in Madras the seasonal incidence was said to be similar. Both in India and at Accra in the Gold Coast the season of greatest prevalence of sub-tertian infections occurs, as might be expected, during the drying up period following the rains; but in Bombay and Madras, as at Accra, this type of malaria prevails all the year round, a fact that should probably be correlated with the uniform temperature.

Not every case of malaria is a fresh infection, but it is nevertheless probable that the majority of the cases occurring during the third quarter of the year at Accra were of this nature. There was no

CHART I.

The rainfall (●- - - - ●- - - -) and the cases of sub-tertian malaria (●—●—●—) occurring at Accra during the two years, September, 1914 to August, 1916.

coincident fall of temperature such as might have induced a number of relapses, but it is possible that there may be a seasonal influence which determines relapses and that in the case of sub-tertian malaria

at Accra this comes into force in the third quarter of the year. The manner in which the curve of malaria cases followed the curve of the rainfall, as well as the interval shown between the curves, suggests, however, that the mosquitos bred in the pools formed by the heavy rains of June were responsible for most of the cases, and as a matter of fact Anopheline mosquitos (*A. costalis* in particular) were more than usually abundant during the months of July and August.

The persistence of the period of prevalence of sub-tertian malaria throughout the year at Accra, as in Bombay, is probably due to the fact that at no season is it sufficiently cold to cause 'an entire cessation of new infections.' It has been shown by Jansco that the malaria parasite develops rapidly in *Anopheles claviger* between the temperatures of 24° C. and 30° C., but that at 16° C. no development takes place. The minimum temperature at Accra averages about 23° C., and practically never falls below 20° C., so that it is probable that the cycle of the malaria parasite in the mosquito can continue unchecked throughout the year.

ABNORMAL FORMS OF PARASITES OF THE SUB-TERTIAN TYPE

In the majority of the blood films submitted for examination at Accra neither schizonts nor gametocytes are present to aid in the diagnosis. The rarity of occurrence of crescents has already been referred to, but a few figures taken from the records of other observers should perhaps be included here. Statham (1915) found crescents in 5 out of 100 malarial children, and states that 'Out of 176 cases of malaria, one of my (his) predecessors found only 6 cases where crescents were present in the blood, although they were specially looked for'; Butler (1915) notes that in 41 children at Freetown found to harbour sub-tertian parasites 'Crescents appeared to be conspicuous by their absence, for they were only found in one of the films'; and Coghill and Hänschell (1915) found gametocytes in only 8 out of 189, and 17 out of 177 sub-tertian infections; that is, in 683 cases of sub-tertian malaria examined by these investigators crescents were found in only 37, or 5·4 per cent. Schizonts are probably even rarer, and have only been detected once during the

last two years in the blood films examined by one of us (J. W. S. M.) at Accra.

The identification of the parasites has therefore to be made in the great majority of cases from the characters of the trophozoites, and this has necessitated a most careful study of their morphological variations. Rogers (1910) considers that when a number of small rings occur without any larger forms 'the infection is practically always a malignant tertian, this being, indeed, the most distinguishing feature of the blood in this form of malaria.' Powell has pointed out that the chromatin dots of the sub-tertian parasites are situated at the edge of the ring and tend to project slightly, a feature that may sometimes be of assistance. The occurrence of the so-called 'brassy' corpuscles, and the darker-coloured erythrocytes that are their counterpart in stained preparations, although inconstant, may also help, but when they are present we have noticed that they by no means always show parasites. The latter forms would be interpreted by Lawson (1916) as corpuscles that had been abandoned by the parasites. The points which we have found of greatest assistance in recognising the sub-tertian parasites have been the small size of the organisms, the absence of enlargement of the enveloping erythrocytes, the characteristic coarse stippling which can usually be brought out by suitable staining, and especially the precocious division of the chromatin. In a recent publication Lawson (1916) appears to consider that the forms showing precocious division, that is, those containing several masses of chromatin, are in reality two or more parasites superimposed. We are unable to accept this interpretation as a general explanation of the phenomenon, because we have been unable to detect any sign of superimposition in the majority of such parasites. In an exceptionally intense malarial infection recorded by one of us in 1915 a large number of parasites were found free in the plasma, some of which contained more than one chromatin mass, but none showed partially superimposed parasites. If, as Lawson believes, these forms are due to 'multiple infection of corpuscular mounds,' one would hardly expect to find them free in the blood.

The morphology of what we refer to as the sub-tertian parasite is extremely variable, and the 'normal' ring type, although it is certainly the commonest form both in severe and mild cases, is very

frequently departed from. In a few cases parasites without chromatin occurred (Pl. II, figs. 41 and 42), and one such infection was recorded by one of us in the Annual Report of the Accra Laboratory for 1914.

Stephens (1914) recently described what he considered to be a new malaria parasite of man, for which he proposed the name *Plasmodium tenue*, characterised by its extremely amoeboid form and the abundance and irregularity of its nuclear chromatin. This organism was discovered in a blood film taken from a native child in India. The same patient was examined on several subsequent occasions and was found to be infected with quartan parasites, and once 'a single pigmented (presumably simple tertian) parasite was found.'

Considerable discussion has followed the publication of Stephens' paper. Craig (1914) 'is satisfied that *Plasmodium tenue* is an atypical form of *Plasmodium vivax*', but Balfour and Wenyon (1914) consider that Stephens 'has not produced any evidence to prove that he was not dealing with an amoeboid sub-tertian parasite'. The latter observers figured parasites closely resembling *P. tenue* from three cases from the Soudan, West Africa, and the Persian Gulf respectively, in two of which crescents also were found.

At Accra we have frequently found malaria parasites which we believe to be indistinguishable from *P. tenue* (Pl. II, figs. 1-8). In 103 consecutive cases specially examined for these forms they were found in 18. Sometimes all the parasites in the blood films were of this type, but usually only a larger or smaller proportion of them, and in such cases the other forms were with one exception typical sub-tertian rings. The abundance and irregularity of the nuclear matter appeared often to be due to two or more parasites infecting a single red cell and being more or less completely interlaced (Pl. II, fig. 5). In several cases crescents were found, and in many others a coarse stippling was demonstrated by suitable staining. For these reasons we concluded that it was impossible to differentiate between *P. tenue* infections and sub-tertian infections such as occur in West Africa, and accordingly in the Annual Report of the Accra Laboratory for the year 1915 both types were classed under the heading *P. falciparum*. Of the sub-tertian infections thus defined, over 20 per cent. showed *P. tenue* forms.

The one case noted above as being exceptional showed a mixed

infection with *P. tenue* and quartan parasites. The amoeboid parasites occurred in corpuscles which showed a characteristic coarse stippling, and for this reason we incline to the view that they were distinct from the quartan organisms, which in this case had not produced any stippling.

Benign tertian malaria is uncommon at Accra, and could not possibly account for the large number of cases in which *P. tenue* forms were found. One native child with a heavy infection with *P. vivax* was examined in whom the parasites showed an extreme degree of amoeboid irregularity. It was impossible, however, to confound these forms with *P. tenue* owing to the large size of the organism, the distension of the corpuscles, and the characteristic stippling.

Stephens (1914) has described yet another form of malaria parasite, for which, however, he has proposed no name. This organism was found in the blood of a native child in the Gold Coast, and the most characteristic forms were 'chromatin particles or strands without any protoplasm.' In the same blood film normal quartan rings were found, and all stages could be traced between these and the remarkable forms peculiar to this infection. We have met with this form of malaria parasite on four occasions at Accra (Pl. II, figs. 10-19). We have not found it associated with the quartan organism, however, but we have observed a coarse stippling of the infected erythrocytes which led us to suspect that this form should also be referred to the sub-tertian type.

Stephens states that three views are possible as to the nature of these forms, namely (1) that they are new species of parasite, (2) that they are degenerative, and (3) that they are artificial; and he considers that the fact that forms are found in which chromatin alone occurs is in favour of one of the latter two views. The fact recorded by one of us (1914) that in blackwater fever parasites without visible cytoplasm may occur is also perhaps in favour of these views.

The frequency with which we have found malaria parasites resembling *P. tenue* associated with typical sub-tertian parasites and sometimes crescents, or enclosed in red corpuscles exhibiting the characteristic coarse stippling (Stephens' and Christophers' dots),*

* This coarse stippling was first described by Stephens and Christophers (1900), and subsequently by Maurer (1902). It is therefore incorrect to call it 'Maurer's dots' as is sometimes done.

convinces us that these forms are in many cases at any rate abnormal forms of the sub-tertian organism; and for similar reasons we believe that the second new form described by Stephens must be interpreted in the same manner. The cases examined by Stephens appeared to be associated with quartan parasites, and it is possible that these abnormal forms may also occur in infections with this organism, but on this point we have no evidence from our own experience.

We have already stated that we have found *P. tenue* forms in over 20 per cent. of the cases diagnosed by us as sub-tertian malaria. It cannot but appear a remarkable fact that these forms should not have been repeatedly noted if they occur with similar frequency elsewhere. In West Africa it is only comparatively recently that microscopical examinations have become possible as a matter of routine, and it is not surprising that the occurrence of such forms has not previously been recorded; but this cannot be said of other tropical countries. It has been suggested that the sub-tertian malaria in West Africa is different from the Asiatic variety, a theory that would receive some support if it proves to be the fact that *P. tenue* forms are more frequently met with in this part of the world.

If, then, *P. tenue* and the second form of malaria parasite described by Stephens are in reality abnormal forms of the sub-tertian and perhaps the quartan parasites, on what does their occurrence depend? Balfour and Wenyon state that such 'amoeboid forms . . . are occasionally found, more especially in the late stages of those cases which have very large infections and which often terminate fatally', but it must be admitted that in exceptionally intense infections and in fatal cases these forms are not always found. The same authors suggest 'some mechanical explanation' without, however, clearly defining it. Lawson (1916) has recently supported the view that *P. tenue* forms are due to distortion by technique, and has denied that they represent either a new species or an amoeboid parasite. Some of the forms she figures as examples of *P. tenue* which particularly favour this view can hardly be considered as identical with those described by Stephens, and it is difficult to believe that the more amoeboid forms we have repeatedly observed could have been produced in the manner suggested. But even if it were the fact that these forms were produced by distortion the

difficulty is only put back one step, since it still remains to be explained why it is that these forms are found in some patients but not in others, when the same technique is employed in making the films in every case.

It has been suggested that *P. tenue* forms might result from spreading the blood on a slide which had been raised to an unusually high temperature by exposure to sunshine or some such condition. All the blood films examined by us were taken on slides at the ordinary atmospheric temperature, so that this explanation could not have been the correct one. By actual experiment, spreading films from a single drop of blood on slides at various temperatures we failed to produce, in a case of benign tertian malaria, highly amoeboid forms such as we had seen in a previous patient. When the slide on which the blood was spread was sufficiently hot most of the red corpuscles broke up into small globules, but those that were parasitised remained intact, and the parasites themselves were just as compact as those in the control slides (Pl. II, figs. 20 and 21). An abnormally high degree of fever had also to be abandoned as an explanation, as many of the patients in whom abnormal parasites were most numerous had little or no fever.

Most of the patients in whom we have found the abnormal forms of malaria parasites have been native children with greatly enlarged spleens and a history of repeated attacks of 'fever.' Out of 28 cases examined by us up to the present, 16 (equal to 57·1 per cent.) were children under two years of age, and only 8 (equal to 28·6 per cent.) were adults. The children were usually greatly debilitated and highly anaemic, and nucleated red corpuscles (normoblasts) were abnormally numerous in some cases. The adults in whom abnormal parasites were found were also anaemic and debilitated, and the constitutional disturbances associated with an attack of malaria were unusually severe. It appeared to us that the occurrence of the atypical parasites was definitely associated with the debilitated condition of the patient. As a rule, quinine treatment immediately banished the malaria parasites from the peripheral blood, but in two cases they persisted for a day or two. The one case, a child aged $3\frac{1}{2}$ years, when first examined showed *P. tenue* forms and crescents in the blood, but two days later the atypical parasites had all vanished and only crescents and typical sub-tertian parasites in

corpuscles showing coarse stippling were found. The second case was an adult European man in a very critical condition and with a heavy malaria infection. When first seen *P. tenue* forms were numerous, but there were also some typical sub-tertian rings and crescents. Three days later, after vigorous treatment with quinine, a few crescents and a few normal sub-tertian rings were all that could be found.

The suggestion of Balfour and Wenyon that the presence of *P. tenue* forms implies some diminished resistance on the part of the patient is supported by these observations, the quinine assisting the patients in combating the infection. But as in fatal cases of malaria only typical parasites may be found, it must be concluded that the anaemia is an important factor, either through some chemical change in the plasma or a physical action on the corpuscles.

THE ASSOCIATION OF MALARIA AND OEDEMA

Although it is generally admitted that nephritis may occur in malaria infections, but little attention appears to have been paid to this complication, and great differences of opinion exist as to its frequency. Castellani and Chalmers (1913) state briefly that 'Nephritis may be found in tertian and sub-tertian fevers, being directly due to the irritation of the kidney by the malarial toxins'; Rogers (1910) considers that the urine 'very rarely shows albumen or other marked changes in uncomplicated cases', but Osler (1914) records that a moderate albuminuria is of frequent occurrence, having been observed in 46·4 per cent. of the cases treated in his wards, that acute nephritis occurred in over 4·5 per cent. of his cases of aestivo-autumnal malaria, and that chronic nephritis occasionally follows long-continued or frequently repeated infections; and according to Henson (1913) nephritis is 'a very common complication,' and he attributes to malaria the high mortality rate from this affection, which he affirms is 'so common in all tropical and sub-tropical countries.'*

So far as we are able to ascertain, the occurrence of nephritis in

* For further references to the occurrence of albuminuria in malaria, see the Fourth and Final Report of the Yellow Fever Commission (West Africa), which has been issued since the above was written.

malaria has most frequently been in imperfectly treated cases, or in patients who have suffered from repeated attacks, and it has more often been associated with sub-tertian infections than with either benign tertian or quartan. Acute nephritis in the active stages of malarial infections appears to be relatively seldom recorded, and it may therefore be of interest to describe briefly a series of cases observed by us which suggested that in the Gold Coast the condition may be commoner than is generally supposed.

Between the 17th February and the 30th August, 1916, nine native children brought for treatment to the dispensaries at Koforidua and Nsawam showed oedema of the face, hands and feet, and in three of them that were in a more advanced condition ascites was also present. The children were all under ten years of age, the youngest being about five and the oldest nine. Seven were boys and two girls. In some of the cases a history of gradual onset of the swelling following upon repeated attacks of fever was obtained from the parents or persons in charge of the patients.

The general appearance of the patients closely resembled that of a case of acute nephritis, indeed the first two were looked upon and treated as cases of this disease, and it was only after this treatment had been carried on for some time with but little improvement that quinine was tried in increased doses, with the result that the oedema began to resolve rapidly.

It is difficult in dispensary practice to induce patients, especially those coming in from out-lying villages, to take the trouble to bring with them specimens of urine or faeces for examination, so that the urine was examined in five cases only and the faeces in four. None of the specimens of urine was 'smoky,' but no microscopical examination could be made for blood or tube-casts; all five, however, contained albumen. Three of the four specimens of faeces contained ova of *Ascaris lumbricoides*, but no hookworm ova were seen, and no ova of other helminths. None of the patients showed any involvement of the peripheral nerves. Two of them had slight fever when they attended for the first time, namely, 99·6° F. and 100·8° F. respectively.

Dried films of blood were made from all the cases, and were stained by Romanowsky's stain. Quartan parasites were found in every case, both ring forms, half-grown forms occasionally, and

sporulating forms; but in no case were they numerous. In one case there was a double infection with quartan and sub-tertian parasites (crescents). In these films the pigment appeared to be more finely divided and of a browner colour than is usually seen in *Plasmodium malariae*.

As already stated, the first two patients were considered to be suffering from acute nephritis, and they were therefore ordered a milk diet, given saline purges and a diuretic mixture together with two grains of quinine daily. This treatment was found to produce but little improvement, and accordingly the quinine was increased to nine grains daily, with the result that the oedema began to resolve at once and had practically disappeared within ten days of the alteration in dosage. After this experience the other cases, when they presented themselves, were given a saline purge and from six to nine grains of quinine daily, the diuretic being dispensed with. It is no easy matter to keep in touch with dispensary patients living at a distance, but most of these cases were seen three or four times at intervals of four days, and they invariably improved under the treatment with quinine alone. Once the improvement was marked they ceased to attend, contenting themselves with sending in for medicine at intervals. It is thus not possible to state whether any of them relapsed or not, but two cases resident in Koforidua which could be kept under observation had not relapsed four months after the disappearance of the oedema. The dosage of quinine in these two cases was gradually reduced to two grains daily.

Subsequently another case, probably of the same nature as those described above, was met with at Accra. The patient was a little girl about four years of age who was brought to the hospital because she had been 'swelling' for some weeks. The general appearance of the child is sufficiently shown in the photograph (Pl. I), which indicates clearly the oedema of the face, the legs and the hands, and the enormous distension of the abdomen which was due to free fluid. The blood was pale and watery, and in the red cells numerous malaria parasites were found. The urine was pale yellow in colour, acid in reaction, with a specific gravity of only 1005, and contained a fair amount of albumen and a number of hyaline casts. The faeces did not contain anything of pathological importance, and no ova of helminths could be found. The child was treated

with quinine, 2 grs. thrice daily, and rapidly began to improve; but unfortunately about a week later the parents insisted on taking her away, so that the final result was not observed.

This child had a mixed malaria infection. There were in the blood a few crescents and a few small sub-tertian rings, but the majority of the parasites were of an unusual type (PL II, figs. 22-35). They were compact organisms which appeared not to have been actively amoeboid; they were rich in chromatin, which in pre-sporulating forms was divided into six or eight pieces; they showed pigment of a brown colour at an early stage of their development; and the parasitised erythrocytes were not enlarged, but were heavily stippled with Schüffner's granules and occasionally with coarser particles more closely resembling Stephens' and Christophers' dots. The parasites themselves resembled quartan organisms more nearly than either of the other two types, and this is perhaps what they were, because on a subsequent occasion when the blood was examined similar forms were found, but without the stippling of the erythrocytes. It has been pointed out by Lawson that both Schüffner's granules and coarse stippling may be found in quartan infections, and, admitting this, there was no great reason to hesitate as to the identification of these parasites, although their general appearance was not quite like that of *P. malariae*.

The organism appeared to us to resemble *P. malariae* and to differ from *P. vivax* in the following respects:—The young trophozoites were smaller than those of *P. vivax* and their pseudopodia were not long, the pigment appeared early and was often arranged peripherally, the schizonts were about the size of red corpuscles, the merozoites numbered about eight, and the infected erythrocytes were about normal in size and colour. Unlike *P. malariae* the pigment was rather fine and brown, and Schuffner's granules were observed on the first day the blood was examined.

Ahmed Emin (1914) has described a malaria parasite, for which he proposed the name *Plasmodium vivax* var. *minuta*, which in many respects closely resembled that described above. It is not quite easy to distinguish in his figures chromatin from cytoplasm, and pigment granules from Schuffner's dots, but the young ring forms, five of which were often found in a single erythrocyte, resembled young trophozoites of *P. falciparum*. The youngest

forms of the parasite we have described were more compact and coarser structures, and were unlike the delicate rings described by Ahmed Emin. It is possible that had our case been examined at some other stage such forms might have been found, although it is not probable, or perhaps some of Ahmed Emin's patients may have had a concurrent infection with *P. falciparum*, and admitting this, the two parasites (*P. vivax* var. *minuta* and the one found at Accra) would appear to have been indistinguishable. No mention is made by Ahmed Emin of any association with oedema in his cases.

The parasites found in the other cases of malaria associated with oedema have been referred to above as quartan organisms (*P. malariae*). The organisms found after the first day in the case just described, that is when no stippling of the red corpuscles was observed, were more like *P. malariae* than either *P. vivax* or *P. falciparum*. The occurrence of the stippling seemed to be uncertain, so that little reliance can be placed on it. It is possible, therefore, that the parasite in all these cases may have been the same species.

It may be of interest in connexion with this action of quinine in these cases of oedema which were in all probability of malarial origin, to give the history of a case showing extensive oedema with much albumen in the urine which appeared to react to adequate doses of this drug, although no malaria parasites were found in the blood.

Mrs. B., a native aged 20 years, a primipara, was seen for the first time on the 29th April 1916, when she stated that she was five and a half months' pregnant. Her condition was serious, the whole of her lower extremities were markedly oedematous, as were also her hands and face; she was unable to lie down in bed, she was dyspnoeic on the slightest exertion, her pulse rate was 120 per minute, and there was dullness on percussion over the bases of both lungs posteriorly. The urine was scanty in amount and loaded with albumen. The patient had had no fits, and her mental condition appeared quite clear.

Treatment was begun by giving saline purgatives and a diuretic mixture containing digitalis, but at the end of a week, the condition of the patient being but slightly improved, she was ordered five grains of quinine three times a day in addition. By the end of another week the patient had greatly improved, her orthopnoea had

gone, the quantity of urine passed had doubled, while the albumen was reduced to a mere trace. The diuretic mixture was then stopped, but the saline purges were continued regularly every second day together with the quinine in diminished quantity, ten grains a day. She continued to improve rapidly, the oedema disappeared, the urine lost all trace of albumen, she was able to get out and about, and eventually during the second week of August she was delivered without assistance of a living full-time child. This patient took ten grains of quinine daily for nearly three months.

It is open to doubt whether this case was due to malaria, as no parasites were found, but it was not until after the patient had had fifteen grains of quinine that the blood was examined.

Albuminuria is probably by no means an uncommon symptom in children suffering from malaria, but the interest of these cases lies in the occurrence of oedema, the association of the condition with quartan-like infections, and the rapid recovery following quinine treatment.

In a popular lecture delivered by Dr. Oswaldo Cruz, and subsequently published in the 'Brazil Medico' (1915), a peculiar type of malarial fever existing in the Amazon Valley was referred to which was characterised by a liability to oedema of the legs. This disease was said to have been studied by Chagas, and to have been due probably to a distinct variety of quartan parasite. We have been unable to trace the work of Chagas referred to by Dr. Cruz, and it is possible that it has not yet been published; but the association of oedema with a quartan organism in the Amazon Valley is of interest in view of the discovery of an apparently somewhat similar type of malaria in the Gold Coast. With this exception we have not been able to find any reference to a malaria of this type in the literature at our disposal.

THE OCCURRENCE OF ANAPLASMA-LIKE BODIES IN THE BLOOD OF PATIENTS SUFFERING FROM MALARIA

Anaplasma-like bodies are frequently met with in examining the blood of animals. At Accra, for example, we observed them without special search in 1914 in the blood of the following healthy animals: monkey, bat, donkey, hedgehog, cat, brown rat, black rat, pouched rat, mouse, guinea-pig, cattle, sheep, and goats, and

in pigs 'they were found, even in this casual way, in 33 per cent. of the animals examined.' They have also been found by other observers in a great many different hosts.

From time to time these bodies have been associated with various parasitic infections such as piroplasmosis, gall-sickness, trypanosomiasis, leishmaniasis, etc., and it has been shown that they can be produced by inoculations of phenylhydrazine and other substances. They are apparently most frequently found in young or anaemic animals, or in blood containing haemolytic substances, but there can be no doubt that they are very far from uncommon in perfectly healthy adult animals.

It is therefore improbable that these *Anaplasma* bodies are organismal, and although as Porter (1915) has pointed out, they 'are probably of diverse origin,' it is perhaps most likely that they are nuclear structures.

Gulland and Goodall (1912) state that the process by which normoblasts give rise to erythrocytes consists in the internal disintegration and absorption of the nucleus, the old view that the nucleus was extruded being now almost entirely given up. In the blood of a young specimen of the wild 'hare' of the Gold Coast recently examined by us, both *Anaplasma* bodies and normoblasts were abundant, and every stage could be traced between the two (see Text-figs. 1-5). In this case it could hardly be doubted that

the *Anaplasma* were the remains of incompletely absorbed nuclei.

Anaplasma-like bodies are also common in human blood, and have been associated with infancy, leishmaniasis, anaemia, etc. Porter (1915) has recorded the occurrence of these bodies in 'the blood of a man returned from the tropics, who had perhaps previously had malaria.'

During the last two years we have repeatedly observed *Anaplasma*-like bodies in human blood at Accra. At first we paid but little attention to them, attributing their occurrence to anaemia,

but eventually our suspicions were aroused and a more careful study of their incidence was begun. It was then found that they were quite common in cases of malaria, and were often present in the blood of patients suffering from conditions diagnosed clinically as malaria and which responded readily to quinine treatment when no parasites could be found. Most of the latter cases were Europeans who took prophylactic doses of quinine with more or less regularity. They were also found in blood films in which crescents or pigmented leucocytes occurred, but no vegetative forms of malaria parasites.

Three possible explanations of the nature of these bodies occurred to us, namely :—

- (1) They might be Anaplasmatas—that is, incompletely absorbed nuclei.
- (2) They might be imperfectly stained plasmodia.
- (3) They might be forms of malaria parasites devoid of cytoplasm.

Anaemia is of course a common condition in the tropics, but the high degree usually associated with the occurrence of Anaplasmatas is not so very frequently met with, and it seemed unlikely that the large number of cases in which these bodies were found could all have been anaemic. Some of the patients, as a matter of fact, were not notably anaemic at all. The bodies we found associated with malaria appeared, moreover, to differ slightly from those found in anaemia.

Anaplasmatas are small, spherical, chromatin-staining bodies. They vary somewhat in size, according to Porter (1915), from 0.3μ to 2μ in diameter, but forms about 0.5μ in diameter are relatively numerous. They almost always are round, but may be oval; and their outline is generally smooth and sharp, very rarely irregular. By Romanowsky methods they stain intensely a deep chromatin colour, but do not show any characteristic structure. The bodies found by us (Pl. II, figs. 36-40) resembled exactly in size, shape, and staining reactions the round chromatin masses seen in a typical sub-tertian ring (*P. falciparum*). They appeared to be rather more uniform in size than Anaplasmatas, and never reached the large sizes to which these bodies may attain. They also appeared to stain less deeply with Leishman's stain, as though their structure were less dense. The distinction, however, was not very marked, and the colour varied

of course with the intensity of the staining, and we were doubtful about it until we examined a case in which a considerable number of normoblasts were present. In the blood of this patient both Anaplasma and the chromatin bodies associated with malaria were found, and on comparing them there was undoubtedly a difference.

Peculiar malaria parasites were observed in two cases of black-water fever by one of us (1914), in which in spite of intense staining the cytoplasm was all but invisible, being indicated only by a paler area or halo beside the chromatin particles. At the time it was suggested that this peculiarity might have been due to the abnormal condition of the blood (haemoglobinaemia) accompanying the haemoglobinuria.' Lawson (1916) has recently stated that in blood films malaria parasites may be found partially stained, for instance, with only the chromatin stained, and she explains this phenomenon as being due to fading, and affirms that it is 'usually possible to re-stain these specimens bringing out the faded cytoplasm.' Malaria parasites may therefore simulate Anaplasma, and the bodies we have observed might be explained in this manner. We have already stated that they exactly resembled the chromatin particles of typical sub-tertian rings, but we do not believe that they were due to irregular staining because they appeared to us to differ from such forms, with which we are familiar; re-staining never resulted in revealing the presence of cytoplasm, and they were nearly always spherical and less variable in shape than the chromatin particles of ordinary malaria parasites. The specimens were always examined immediately after they had been stained, so that 'fading', in the ordinary meaning of that term, could not have taken place.

The third theory is that they might be malaria parasites devoid of cytoplasm, and this we believe to be the true explanation. Their close resemblance to the chromatin masses of malaria rings, their association with typical plasmodia in some cases, and their occurrence in patients suffering from an illness clinically resembling malaria, which was moreover amenable to treatment with quinine, support this view. They differed, however, from the forms described by Stephens in his Gold Coast case in which 'chromatin particles or strands without any protoplasm' occurred, in being rounded and in occurring singly in the erythrocytes.

If, then, they are of this nature, what is their significance? As

we have already stated, they were most frequently found in Europeans accustomed to take prophylactic doses of quinine or who had already taken quinine since their illness began. In such patients it is often extremely difficult or impossible to find parasites, although the physician attending them may be morally certain that they are suffering from malaria. We incline to the view that these Anaplasma-like bodies are due to the action of quinine in the blood, that is, that they are degenerative. In this connexion it is of interest to recall that in blackwater fever, which also eliminates the parasites from the blood, somewhat similar forms were found, but that in this case the degeneration did not appear to have proceeded so far.

The practical importance of the recognition of these forms is that it enables a diagnosis of malaria to be suggested in those cases, by no means uncommon, in which no typical parasites can be discovered.

ACCRA, November, 1916.

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EXPLANATION OF PLATES

PLATE I

A Case of Malaria associated with Oedema.

A CASE OF MALARIA ASSOCIATED WITH OEDEMA

PLATE II

Various forms of malaria parasites. × 2000.

Drawings by Miss Mabel Rhodes.

- Figs. 1-8. Parasites resembling *P. tenue*.
- Fig. 9. A sub-tertian parasite with a faint halo as the only indication of the presence of cytoplasm.
- Figs. 10-19. Various forms of parasites with little or no visible cytoplasm.
- Figs. 20-21. *P. vivax* in blood spread on a slide heated sufficiently to cause most of the red corpuscles to break up.
- Figs. 22-35. Parasites of an unusual type from a case of malaria and oedema.
 Fig. 22. A parasitised cell and three normal red corpuscles to show the relative sizes.
 Figs. 33-35. Red corpuscles showing stippling but no parasites.
- Figs. 36-40. Anaplasma-like bodies associated with malaria infections.
- Figs. 41-42. Parasites (*P. falciparum*) devoid of chromatin.

MALARIA PARASITES FROM THE GOLD COAST.