Watercolour sketches by Brevet Colonel Sir William Leishman of Plasmodium Kochi, and the manuscript draft of his paper on monkey malaria which they illustrate, read to the Pathological Society "probably at their meeting in January 1914"

Publication/Creation

1914

Persistent URL

https://wellcomecollection.org/works/r2g9n5k8

wellcome collection

Wellcome Collection
183 Euston Road
London NW1 2BE UK
T +44 (0)20 7611 8722
E library@wellcomecollection.org
https://wellcomecollection.org

Gentlemen.

The malarial parasite found in the blood of monkeys (in Central Africa) by Koch and named by Laveran the Plasmodium Kochi has not, as far as I am aware, been studied in detail since Kossel first published the results of his work in 1899. Kossel's material was derived from films placed at his disposal by Koch and others which he obtained himself from the examination of the blood of monkeys in the Zoo at Berlin. His description, a figure clearly indicated that the parasite was closely allied to the malarial parasites of man but his observations referred chiefly to the sexual forms of the parasite or "gametes"; younger forms he found but rarely and the complete cycle of development in the blood of the monkey could not be determined from the material at his disposal. Since that time (nothing has appeared) beyond an occasional reference to his work.

I have therefore thought it might be of interest to the Society if I laid before them the result of my own observations which, although very far from clearing up the whole story may serve, I think, to throw a little additional light upon it.

The material which I have studied was derived chiefly in part from 8 monkeys brought back from Uganda by Col Bruce after his investigations in sleeping sickness and placed in my laboratory; all of them harboured the Plas. Kochi in their blood. Subsequently, I obtained films from Uganda of the blood & organs of other monkeys from Capt Fung & the late Lieut Tillock of the Aruwimi.

The regards the clinical manifestations of this form of Malaria, such as its influence on temp., and its amenability to drugs &c I have nothing to say, since Bruce's monkeys had all been experimentally and were under observation for Trypanosomiasis infected with Tryp. Gambiense and till eventually died from which they eventually died of Trypanosomiasis

1'.30"

My observations, then, are confined to the appearances met with on examination of either fresh or stained films from the blood or organs of infected monkeys.

One of the most striking features noted was the persistence of the parasites in the blood. All of the 3 monkeys lived for several months and one of them over a year and during this time malarial parasites were never absent from their blood, which was examined frequently & regularly in connection with the subject of Trypanosomiasis. As regards numbers they showed, however, great variations, at times only a few & at another very numerous parasites were seen; no regular periodicity was observed and, as a general rule, the forms noted were those recorded by Ross & — namely free gametes, of both sexes but, chiefly, medium gametes. In addition to these however, at irregular intervals, I found large numbers of young intracapsular parasites of which Ross had met with only a few rare examples.

I do not propose to occupy your time with a detailed description of the various forms exhibited by the parasite at the different stages of its development but will ask you instead to examine the sketches which I have made of them from time to time and which I have cut out of my sketch book & tried to place together in a more or less connected fashion.

Speaking generally, the Plasmodium Vivax shows a great similarity in its early intracorpuscular stages to the corresponding stages of human malaria. I however am unable to agree with Ross in thinking it most closely allied to Bengo Tertian and appears to me in its to be general features more like the Quartan parasite of man. From the youngest forms observed — to which I shall return in a moment — it develops through the usual ring form to a large fragmented intracorpuscular parasite which, in the case of the sexual forms, completely fills

the red corpuscles. The amoeboid movements are moderately active and the melanin granules are extremely fine & pale brown or yellowish in colour. The staining reactions are the same as in other forms of malaria while the relations of chromatin to protoplasm may be judged from the sketches. The infected R.B.C. is not enlarged and retains its normal staining reaction — tho' I have, in only one instance observed Schüffners dots in an infected red cell.

The Gametes or sexual forms, which abound in most specimens and frequently are the only forms to be found in the peripheral blood, conform to the usual points of sexual difference as regards staining reaction of the protoplasm and character and quantity of chromatin. The female or macrogametes far outnumber the microgametocytes. They are spherical parasites and often most often present themselves to view as free gametes i.e. having escaped from the R.B.C. within which they developed. Ross has observed exflagellation of the male gamete in vitro but I have not myself been successful in spite of numerous attempts.

You may notice, perhaps, in this brief account and on examination of the sketches a conspicuous blank inasmuch as I have neither figured nor described rosette formation — the completion of the asexual cycles of development or schizogony and I may say at once that I have never observed a rosette in any of my specimens. Ross. met with similar failure and suggested that such forms were perhaps best sought in the case of young monkeys, presumably freshly infected, Bearing this in mind

4.

I obtained (& examined) films from the blood and organs of such young monkeys, made on the spot at Uganda, but once more with compatibly negative results as regards finding the later stages of schizogony. On the death of each of the monkeys under my own observation I made a most careful search in their internal organs but could find no forms in any way suggestive of rosette formation although all had numerous gametes and young intracorpuscular parasites at the time of death and, in one of them, these were abundant.

I do not for a moment suggest that schizogony or rosette formation does not occur in Monkey Malaria but it is at least remarkable that in spite of the appearance of crop after crop of young parasites in the blood no evidence of such a stage should have been observed (either in the peripheral blood or the internal organs) in the course of what I think I may fairly describe as an arduous search (for the missing rosettes). This search 5.45 = I believe, recently renewed at intervals of other work and, although but without success as regards finding evidence of schizogony, I have been struck with the unusual appearance of many of the "free gametes" and (on a careful examination of my old films and sketches, I) have been led to hazard the conjecture that the maintainance of the constant supply of fresh parasites in these monkeys depended upon an alternative method of reproduction originating in the gametes, chiefly, if not altogether, in the macrogametes.

This will not permit of a detailed account of the stages by which I arrived at this conclusion and I must again refer any of you who may be interested in the subject to the sketches in explanation of the process which I conceive to occur and of which I may now give you an outline.

The mature macrogametes, free in the plasma, appears to me to have the faculty of extruding from its substance the

(as it is variously called)
small chromatin mass, 'nucleus' or 'karyosome' which is almost always a compact, brightly staining body of an average diameter of 1 μ. This free karyosome (may, at the time of extrusion, be either) imbedded in the badly named 'achromatic zone', which usually takes a faint eosin tinge with Chromatin staining, but, sooner or later, it appears to become completely freed and in this condition it may settle on another R.B.C & become the starting point of a fresh parasite. I am quite aware that such behaviour on the part of a gamete is unorthodox, to say the least of it, but I have found it hard to avoid the conclusion that this is what actually takes place. The various stages of this process may be followed in the sketches the majority of which I may say, in self defence, were drawn before this idea presented itself to me. The fallacious nature of this (of the) The most obvious objection to such a procedure would be that, even if it did occur, it would not account for (such an) increase in the number of parasites (as) was undoubtedly present from time to time in the animals under observation, but I have seen many gametes, some of which are figured, in which two chromatin masses are present, each lying in its own achromatic zone, and others in which one is in act of being extruded while another usually of smaller dimensions is to be seen in the substance of the protoplasm. At various times large numbers of gametes were to be seen with a vacuole close to the margin (and others) with a deep indentation or bay breaking the otherwise smooth contour of the parasite and as a matter of fact it was the frequency (of such an appearance) with which this appearance occurred (first) which suggested to me the possibility of such a process. The further objection that such forms and such an extrusion of the Chromatin might be no more than

evidences of degeneration was not born out by the appearances & staining reactions of the gametes concerned and was in no way similar to the forms met with 'post mortem' in the spleen, some of which are figured; the fact, also, of the replacement of the chromatin which has been extruded is against such an explanation. Coming now to the extruded chromatin I have in a few specimens found little "chromatin bodies free in the plasma which from their staining reactions, size and shape could not be confused with cocci and which were absolutely identical in appearance with the chromatin of the macrogametes on the one hand and with the small chromatin bodies found now often in or on the red cells on the other. Next With regard to the youngest forms of intra corpuscular parasites these, I find to be, once more, small, deeply staining chromatin masses indistinguishable in appearance from those occurring in and extruded from the macrogametes, they possess no visible trace of blue staining protoplasm but I have seen every intermediate form between such a naked mass of chromatin and a fully complete but minute 'ring form', in many of these it was only possible to detect the minute tag of blue staining protoplasm with a 1.5 mm lens and the least possible illumination.

The danger of forming erroneous conclusions from the study of stained specimens alone is fully appreciated by me and ~~I do not wish to say more than th~~ I will only say that my observations leave me with the strong impression that the constant supply of young parasites in these monkeys was maintained by the gametes in some such manner as I have indicated. Actual proof could only be obtained by the

continuous observation of fresh blood films in a thermostat, a test which I have not had the opportunity of applying.

In conclusion I may refer to the facts familiar to all workers with human malaria, that the gametes and especially the macrogametes are by far the most resistant and long lived of all forms of these parasites and that they have long been under suspicion as the cause of relapses of malarial fever occurring long after removal (of the individual) from all possible source of fresh infection. Schaudinn, in 1903, described and figured in connection with the Benign Tertian parasite a process of what he termed "Reifebildung" in which the macrogametes underwent a complicated series of changes resulting in the formation of a number of young merozoits by a process of schizogony presenting no essential difference to ordinary rosette formation. Such a process is in no way similar to that which I have suggested to you in the case of Monkey Malaria but you will note that in each case it is the lady - the macrogamete - who is indicated as the root of the evil.

Monkey Malaria

Path Soc meeting

(4 plates)

627

Water-colour sketches of *Plasmodium kochi*, drawn by Brevet-Colonel Sir William Leishman, F.R.S., R.A.M.C., to illustrate a paper on "Monkey Malaria", read to the Pathological Society probably at their meeting in January, 1914. Sir William afterwards became Lieutenant-General, K.C.B., K.C.M.G., and Director-General of Army Medical Services.

Monkey Malaria.

No I.

Young intra-corpuscular forms, of various types.

Young intra-corpuscular amoeboid forms.

W.B.L.

No: II.

Monkey Malaria.

C. 1-9

Young intra-corpuscular forms, mostly gametes.

D (1-11 not 9)

Intra-corpuscular parasites showing segmentation or irregular distribution of Chromatin.
Fig 38 represents the nearest approach to rosette formation.

Lond.

Monkey Malaria.

No: III.

Free Gametocytes.

Free Gametocytes, showing extrusion of Chromatin mass or Karyosome.

Free Gametocytes, showing indentations or vacuoles in the protoplasm.

Free Gametocytes with deeply indented contours & extruded chromatin

W.B.L.

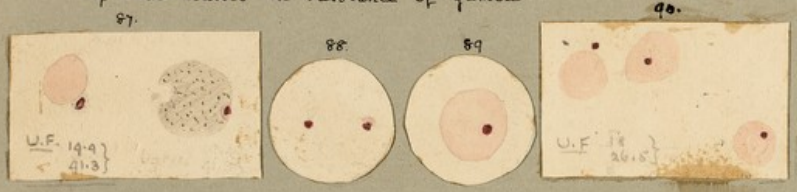
RAMC 627 No IV.

Monkey Malaria.

Free Gametocytes with two Chromatin masses.

Extrusion of Chromatin mass, with reproduction of other masses in substance of Gamete.

Gametes with "achromatic zones" destitute of Chromatin.



Free chromatin masses in contact with red cells.

Gametes without Chromatin - Dead?

"Post-mortem" forms, from Bone-marrow.

Small gametes in contact
98 - with a red cell
99 - with a microgametocyte

Unusual forms of Gametocytes.

W.B.L.