

Original Articles.

NOTE ON THE PHAGOCYTOSIS OF RED BLOOD CORPUSCLES IN THE SPLEEN OF A CASE OF BLACK-WATER FEVER.

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THE critical examination of the splenic blood taken during life in black-water fever has not, so far as we are aware, been previously undertaken. The microscopical appearances seen in splenic blood from a case of black-water fever, in which we obtained splenic puncture at an early stage in the attack, seems therefore of sufficient interest to merit a brief description.

The patient, a Bengali, had been resident in the Dooars for five years, and for the past ten months had been living under intensely malarious conditions in the immediate neighbourhood of coolie lines and within a stone's throw of a small perennial swamp. On January 13th, 1908, he had what he describes as an attack of ordinary malarial fever for which on the 14th he took quinine. He took quinine also on the 15th and the morning of the 16th. At about 10 A.M. on the 16th he had a rigor followed at about 2 P.M. by the passage of hæmoglobinous urine. The hæmoglobinuria then continued uninterruptedly until noon on the 18th, after which the urine contained a large quantity of urobilin but no hæmoglobin. The patient was seen by us at 7 P.M. on the 16th, and as at this time the spleen was easily palpable, we performed splenic puncture obtaining a small quantity of splenic blood very rich in cells.

Since hæmoglobinuria continued for forty-one hours after we had obtained our specimens, this case enabled us to examine the visceral blood at a time when blood destruction was presumably in active progress. In the splenic blood films a few pigmented cells were seen showing that there had been a recent but apparently not at all a severe infection with the malignant tertian parasite; neither in the splenic nor the peripheral blood were actual malarial parasites found. The closest scrutiny of the films failed to disclose any structures that could possibly be considered as of the nature of a special parasite. There were certainly no organisms at all resembling either the ordinary or the minute forms of piroplasma with a number of types of which we are very familiar.

Apart from these facts the chief interest of the result of our examination lay in the existence in the spleen of a considerable amount of led cell phagocytosis involving in many instances red blood corpuscles retaining their full hæmoglobin content, and therefore not merely the

stromata of cells that had undergone partial or complete hæmolysis prior to engulfment. Two distinct types of cell were seen enclosing red blood corpuscles:—

(1) Large macrophages such as have frequently been noted in connection with phagocytosis of this kind; and

(2) Small cells, each containing a single blood corpuscle only.

This latter type of cell possesses only just sufficient protoplasm to form a thin layer around the engulfed red cell and a nucleus which, owing to the presence of this body, is crescentic in shape. (The exact nature of these small phagocytes is not yet clear to us, but that they are an important factor in the engulfment of red cells under the conditions present at the time of puncture is shown by the following differential count of 2,200 splenic cells.) It will be seen that cells of this type containing red blood corpuscles were nearly as numerous as macrophages similarly laden—

| | | | |
|---|-----|-----|--------------------|
| Large macrophages | ... | ... | 55 % |
| Small mononuclear cells of various types | ... | ... | 49 8 % |
| Large mononuclear leucocytes | ... | ... | 4 4 % |
| Polymorphonuclear leucocytes | ... | ... | 13·7 % |
| Eosinophile leucocytes | ... | ... | 7 % |
| Large cells with basophilic protoplasm | ... | ... | 1 8 % |
| Cells of doubtful nature, free nuclei, etc. | ... | ... | 24 0 % |
| | | | <hr/> 99 9 % <hr/> |

| | | | |
|--|-----|-----|-------|
| Large macrophages containing red cells | ... | ... | 1·7 % |
| Small mononuclear cells containing red cells | ... | ... | 1·3 % |

In both types of cell were seen—

(1) Blood corpuscles shewing no recognisable alteration from the normal either in size or in hæmoglobin content.

(2) Corpuscles more or less decolorized, often showing the periphery still coloured when the centre was free from hæmoglobin.

(3) Clear vacuoles about the size of blood corpuscles, which from a study of the films seem to be due to still later changes in engulfed red cells.

In the macrophages altered cells and vacuoles were in excess of unaltered cells, but the reverse held good in the case of the smaller type of phagocyte which contained in most cases unaltered corpuscles, as is shown by the following list of cells counted in a portion of a film:—

| | | | | | |
|---|-----|---|------------------------------|-----|----|
| Unaltered cells | ... | { | Large macrophages | ... | 3 |
| | | | Small mononuclear phagocytes | ... | 37 |
| Partially altered cells | ... | { | Large macrophages | ... | 10 |
| | | | Small mononuclear phagocytes | ... | 9 |
| Vacuoles derived from engulfed red cells. | ... | { | Large macrophages | ... | 22 |
| | | | Small mononuclear phagocytes | ... | 5 |

In the peripheral blood the phagocytosis of red cells was not very conspicuous, and most of the engulfed cells met with were in the form

of the clear vacuoles referred to above, whose origin might have been overlooked had the conditions seen in the spleen not been at hand to guide one in arriving at a knowledge of their true significance. In this case the cells concerned were all of large mononuclear or macrophage type, none of the small type being at any time found in the peripheral blood.

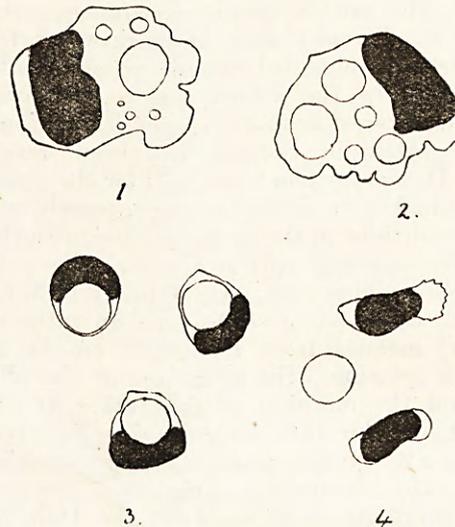
The existence in black-water fever of an extensive engulfment of apparently normal blood corpuscles is evidently of importance in relation to the study of the causation of this disease. In canine piroplasmiasis, a condition which one of us has studied closely, there occurs at certain crises in the infection an extensive engulfment of red cells. But in the great majority of these engulfed cells it is easy to see that they contain one or more parasites; the same condition is seen in malaria. The closest scrutiny of the included cells in our specimens with a Zeiss oil immersion apochromat N. A. 1.30 Fc. 1.5 mm. and compensating eyepieces up to No. 12 failed to reveal within any of them either malarial parasites or any other appearance of parasitic invasion. This absence of contained parasites was the more convincing since, though the specimens were very intensely stained with Giemsa's stain, the included red cells remained beautifully translucent and free from all deposit. We are, therefore led, so far as we may judge from the present case, to regard the process of red cell destruction as not being directly parasitic in nature.

That black-water fever is related in some very definite way to malarial infection is, we think, borne out not only by the weight of existing evidence but by the trend of our own recent researches, for it is evident that mere residence in a tropical climate is not sufficient in itself to predispose to black-water fever, a disease which is practically localised in India to certain areas, the most striking features of which, from an ætiological point of view, is their intensely malarious character. If there are strong reasons for disbelieving in the existence of any special form of parasite, and the present case brings still further evidence against such a view, there is, with the evidence accumulated, scarcely any alternative, but to regard the disease as a result of malarial infection.

That malaria acts either alone, or in association with quinine sulphate by causing very marked alterations in the isotonic point or in the hæmosozic value of the plasma is not borne out by our observations, which seem to negative any such view. Quinine, even, if a necessary factor, can be considered only as the match that fires a train already laid, for there is no evidence to show that quinine alone can bring about hæmoglobinuria.

Phagocytosis of red cells is observed *in vitro* as a result of the action of specific sera upon

blood corpuscles, and in the body as a result of injection into a given species of animal (dog) of the serum of an animal (rabbit) immunized against the blood of this species, as well as in certain pathological conditions such as pernicious anæmia, jaundice and malaria, in most of which it seems likely that bodies toxic to the red cells are present. The most probable significance of the condition described, if we take the phagocytosis of apparently normal red cells in conjunction with the generally recognised fact that exposure for a certain time to malarious conditions is necessary before black-water fever can be contracted, is that under certain conditions at some stage in the process of malarial immunization, a process which is



known in some degree to occur, there results a liberation of specific poisons for the red cells causing the extensive destruction of these elements which is the essential feature of the disease.

REMARKS ON THE VACCINE TREATMENT OF COLICYSTITIS AND SOME ERRORS WHICH MAY ARISE IN THE DETERMINATION OF THE OPSONIC INDEX WITH BACILLUS COLI.

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THE presence of *B. coli* in the urine of both males and females is a phenomenon which has long been recognised and the condition has been known occasionally to persist for years without apparent harm. Spontaneous cure after months or years is said to occur in some instances, in others staphylococci gain an entrance to the bladder and the combined action of the two organisms sets up a purulent cystitis which may extend to the kidneys with the usual serious results.

Colicystitis, therefore, is not an affection which the sufferer can afford to neglect. How it arises cannot always be decided. The organism may reach the bladder on a catheter or by