

detected. At the outer margin of the nodules the cells of neoplasm extended by direct intercellular spread between the surrounding liver cells, the majority of which showed very advanced fatty infiltration and degeneration.

A microscopical examination of the other organs showed nothing especially noteworthy except in the case of the kidney, where the convoluted tubules and the ascending limbs of Henle showed cloudy swelling of their parenchyma. The glomeruli were swollen and contained a recent fibrinous exudate. Swelling of the endothelial lining of Bowman's capsule and an increase in the number of nuclei of the glomerular tuft were also apparent. The microscopical examination of the minute pea-like nodule in the diploë showed it to consist of cells which from their structure and arrangement indicated a chronic inflammatory focus with commencing caseation in its centre, such as would be explained by the effect of tuberculous disease. The microscopical examination of the liver confirmed the diagnosis made at the post-mortem examination of primary sarcoma.

The extreme rapidity of the growth of the neoplasm had been responsible for the retention of many of the interlobular septa and the formation of the stroma described thereby. The hæmorrhage present in the majority of these alveolar spaces is readily capable of explanation on the same ground. It is of interest that, despite the extreme rapidity of growth and the presence of many tumour cells inside blood capillaries in the liver, no secondary metastatic foci could be detected on careful examination by the naked eye and microscope. Whether the changes present in the kidneys indicative of a recent acute toxic absorption are to be explained merely as the result of a terminal infection or are due directly to the products of the neoplasm we do not at present intend to discuss. The appearance of the cells forming the tumour suggested that they were derived from connective tissue and their point of origin had been intra-lobular, the tumour being thus a true sarcoma and not, as de Haan has suggested, an endothelioma.

The points of interest in this case deserving special note are as follows. The occurrence of a primary round-celled sarcoma of the liver in a child aged four months. The rapid enlargement of the organ, as shown by an increase in the abdominal circumference at the umbilicus—an increase of $4\frac{1}{2}$ centimetres taking place in three days. No associated emaciation, diarrhoea, or vomiting. A marked degree of infiltration of the whole organ by the neoplasm, the few liver cells which remained being in an extreme degree of degeneration. Jaundice and ascites were entirely absent. The late appearance of the clinical symptoms with such gross pathological changes is of interest.

So far as we have been able to ascertain only two recorded cases exist of this condition in children younger than the patient in the present case—namely, those of Heaton and Hewlett, whose patients were aged eight weeks and 14 weeks respectively. The clinical characteristics of these correspond very largely with the present case—namely, rapid enlargement of the liver associated with no other signs or symptoms. Necropsy in both cases revealed diffuse infiltrating sarcoma of the organ. Another case has been recorded by Lendrop, in which the child was four months old. It was also characterised by rapid development of abdominal swelling due to enlargement of the liver, which post mortem was found to have the appearance and structure very similar to that recorded by us. In his case, like the present one, the abdominal enlargement took place with special rapidity in the last two weeks of life.

Another case has been recorded with great accuracy and detail by de Haan. The age of the child was, like that recorded by us, four months. The clinical signs and symptoms were almost identical with those of the present case, the child being admitted with marked abdominal swelling. The liver could be palpated with ease, the lower border extending to the umbilicus. Extreme rapidity of growth took place after the child's admission to hospital so that the enlargement extended into the right iliac fossa in a fortnight. During this period, also, pressure symptoms on the diaphragm and thoracic viscera supervened. Exploration of the liver was carried out as in our own case, in the supposition that the enlargement might be due to the presence of an acute inflammatory condition. The child died four days after operation, the post-mortem examination revealing a diffuse neoplasm of the liver with no secondary deposits throughout the body. Microscopical examination showed numerous hæmorrhages, large thin-walled blood-vessels supported by connective tissue forming spaces filled by tumour

cells, which he believed to be of endothelial or connective tissue origin.

The other cases, recorded by Bossowski, Tooth, Pert, Dudgeon, and others, occurred in older patients. The clinical characteristics of these correspond closely with those already referred to in the rapid increase in the size of the growth. Ascites, however, was present in one case, while a trace of jaundice was present in another. In only five of these recorded cases was, as far as can be ascertained from the literature, the lesion entirely confined to the liver.

The investigation of this case seems to show that from the clinical standpoint primary sarcoma of the liver in children, although of rare occurrence, presents definite characteristics, which, although simulating an acute infective condition of that organ, are sufficiently distinctive to warrant a diagnosis of a malignant condition being made.

Our thanks are due to Dr. Burn-Murdoch, senior physician to the hospital, for permission to publish this case, also to Dr. R. J. Mackessack, resident physician, for the photograph taken at the post-mortem examination.

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Edinburgh.

NOTE ON THE LIFE CYCLE OF THE PARASITE OF SLEEPING SICKNESS.

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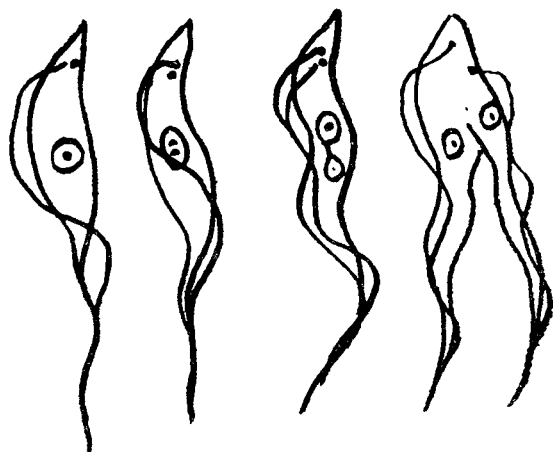
THE observations upon the life-history of trypanosomes to which we desire to call attention in this preliminary note relate chiefly to *Trypanosoma gambiense*. But in order to bring them into their true perspective it is desirable to refer briefly to certain facts already more or less familiar in relation to several other forms. In the case of dourine it is known that the disease can be transmitted directly from animal to animal, contact in this case being the normal mode of transmission. It is clear, therefore, that the life-history of any particular trypanosome need not be necessarily complicated by any transmission through two or more different hosts. The observations of Bruce seem to show that in the case of *Trypanosoma brucei* infected flies cease to be able to infect after 48 hours and it consequently follows that in this instance it is at least possible that transmission is only effected directly as in an ordinary inoculation experiment. *Trypanosoma gambiense* can be transferred directly from animal to animal for many years, the strain utilised in the present work having been propagated artificially for two and a half years. Consequently, if the sexual stage exists in the body of some other host, this stage can be altogether dispensed with for a countless number of generations.

In rats infected with *Trypanosoma gambiense* the disease runs a fluctuating course with respect to the number of parasites to be found upon examination of the peripheral blood. During its course there are a succession of periods when no trypanosomes are to be found in the blood at all. If the blood of rats infected with *Trypanosoma lewisi* be filtered through a Berkefeld filter it has been found to be capable of infecting other rats into which it is injected; though not conclusive in itself, this last observation directly suggests the presence in the infected animals of some minute form of the parasite not hitherto elucidated. During the phases of the infection of rats with *Trypanosoma gambiense* when the number of the parasites is rising in the peripheral blood we have encountered only amitotic division of the macro- and micro-nuclei, this process being accompanied by longitudinal fission of the animals. The double and unequal individuals produced, although often at

first sight suggesting conjugation, we find to be much more readily explained as stages in the simple process of bipartition, no nuclear changes being seen at all suggesting conjugation as it appears in other protozoa.

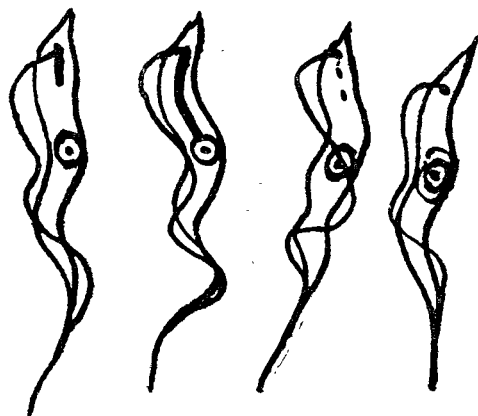
In the case of *Trypanosoma gambiense* we are unable to distinguish any marked dimorphism—the so-called males and females of many authors, Prowazik, Minchin, and others, appearing to be arbitrarily chosen extremes in a continuous series of dimensions. As the increase in the number of trypanosomes in the blood proceeds towards any particular maximum we have encountered no other phenomena than that of fission worth recording. At the height of the

FIG. 1.

Stages in the growth and division of *Trypanosoma gambiense*.

maximum, on the other hand, numbers (from 5 to 20 per cent.) of trypanosomes may be found wherein a thick stainable band may be seen growing out from the micro-nucleus and extending through the animal's body towards the nucleus. It is at least twice as thick as, and quite distinct from, the stainable margin of the undulating membrane. This band extends backwards until it reaches or even passes beyond the nucleus. In some cases it enters directly into contact with the nucleus. In other cases it reaches the nucleus only indirectly, after passing round one or other side of this body. At this stage of the

FIG. 2.



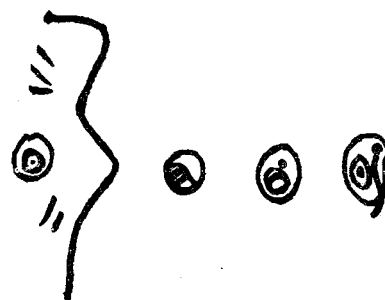
Stages in the formation of the "black line" and the "resistant body."

increase of the parasites in the peripheral blood the nucleus and the micro-nucleus thus become connected; at a subsequent period the connecting band disappears.

At the time the number of parasites in the blood is falling rapidly another series of phenomena may be encountered in the lungs, spleen, and bone marrow. Here we find trypanosomes in which the nuclei are surrounded by a clear space with a distinct margin encircling the nucleus. Along with these we find in the bone marrow and the spleen numbers of forms in which the body of the trypanosome has disintegrated and the flagellum, together with the remains of the micro-nucleus, is detached. The nucleus in these stages, together with the surrounding hyaline substance, however, remains intact. During the absence of the trypanosomes in the blood these bodies, which we term "resistant forms," undergo no further change. They undoubtedly correspond to the bodies figured by Plimmer and Bradford and erroneously regarded by them as the nuclei of a plasmodium. So, also, they equally unquestionably represent

the so-called "free nuclei" described by Holmes¹ and apparently correctly regarded by him as a stage in the development of *Trypanosoma evansi*. During the negative period of the infection they appear to decrease in size, but at the time of the reappearance of the trypanosomes in the blood they are seen, however, to have grown considerably. At this

FIG. 3.



Development of the "resistant body."

period the nucleus of each resistant form buds off a small, micro-nuclear granule and from this at a later stage there grows out a flagellum.

It appears, then, that from the spore-like resistant bodies, produced after the connexion of the macro- and micro-nuclei, small trypanosomes are formed directly and thus the life cycle begins over again. Starting from the resistant form the micro-nucleus originates from the macro-nucleus, and in the subsequent division (whereby both kinds of nuclei are indefinitely multiplied) there is a process which may be analogous to the separation of two kinds of nuclei destined to conjugate. A pair of such differentiated nuclei is retained in each trypanosome and unites during the period when the number of parasites in the blood is at a maximum. Viewed in this way the formation of the stainable band and the ensuing union of the substance of the macro- and micro-nuclei may correspond to a sexual act. In the parasite of sleeping sickness we have a life cycle which appears to be complete within the body of one animal just as in the instance of dourine. In this way it appears to be suggested that contagion may be only effected by a mechanical transference of blood in accordance with the results of Bruce in relation to *Trypanosoma brucei*.

Finally, we find when rats infected with *Trypanosoma gambiense* are treated with atoxyl that although large numbers of the parasites are rapidly killed, some become rounded, form a distinct membrane, throw off the flagellum, and apparently remain unchanged for a prolonged period.

It will be observed that the present observations upon *Trypanosoma gambiense* open up a wide field for further inquiry; but it should be pointed out that for these studies we have found it necessary to depart from the usual method of making dry preparations, and to utilise a mode of procedure whereby blood films, or "organ-smears," are fixed wet and afterwards stained and mounted in the usual manner.

The figures are from specimens fixed in Flemming's fluid and stained with a modification of the ordinary iron-alum hæmatoxylin, or with a combination of two basic stains.

ON THE EFFECT OF THE EXPOSURE TO TOBACCO SMOKE ON THE GROWTH OF PATHOGENIC MICRO-ORGANISMS.

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THE belief that smoking decreases the risk of contracting the infectious diseases is so widely held that all whose work provides opportunity for meeting men exposed to the danger must have noted the hurried lighting of a pipe or cigar immediately after any such exposure. One is appealed to frequently to give an opinion as to the efficiency of the procedure and as some references in medical literature gave vague support to the belief, I began a series of experiments

¹ Journal of Comparative Pathology and Therapeutics, 1904, p. 213.