INTESTINAL SCHISTOSOMIASIS IN THE SUDAN.

WITH NOTES ON THE TREATMENT OF TWO CASES BY
MEANS OF AUTOGENOUS VACCINES OF
COLI-LIKE ORGANISMS.

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SCHISTOSOMIASIS exists as a common parasitic infection among the inhabitants of Egypt, and it is mainly due to the excellent researches that have been carried out by different observers in that country that our knowledge of the disease has been obtained. There are, however, particular aspects of it as met with in the Sudan that merit a certain amount of attention, inasmuch as the disease is responsible for a clinical picture that often presents some difficulties to the diagnostician.

The cases described in this paper represent the intestinal type of schistosomiasis. It has been considered worth while recording them, as they are undoubtedly examples of some of the so-called pyrexias of uncertain origin met with in the Sudan. The patients affected have usually been well-nourished adults admitted to hospital with fever, headache, furred tongue, and frequently enlarged spleen. As will be seen from the clinical histories of a few of the cases, neither diarrhoea nor tenesmus form constant symptoms; indeed they are fre-

giving in some cases a slight group reaction, afford negative evidence as regards a systemic infection with organisms of the *B. typhosus* group. Blood cultures give further negative proofs, while spleen and liver punctures eliminate a leishmanial or chronic malarial condition. The examination of urine does not always assist the diagnosis, and as a *dernier ressort* the faeces are investigated; even then one may be at a loss in finding the etiological factor, for in the light of recent experience it is not always a simple matter to locate the lateral-spined ova of *Schistosomum mansoni* in the excreta. The clinical histories of some of these cases might conveniently be considered here.

CASE I.

An Egyptian soldier, admitted to hospital in a weak condition with fever and an enlarged liver and spleen. Diarrhoea was not present. Six months previously, while in an out-station, the patient had suffered from an attack of diarrhoea, with blood and mucus in his stools, but since then had been free from similar symptoms. The peripheral blood was examined, and, apart from a leucocytosis, nothing abnormal was noted. The spleen was enlarged to a point about 3 in. below the ribs, and on palpation was of a doughy consistence. The liver increased in size, and in view of the leucocytosis present an exploratory operation

was carried out, but no sign of an abscess could be found. Quinine injections failed to influence the temperature. No examination of the faeces was carried out owing to the absence

Case 1.

Case II.

of intestinal symptoms. The patient became weaker, and died on the seventh day after admission.

Post-mortem examination showed that there was extensive ulceration of the large intestine. Smear preparations from the base of the ulcers revealed the lateral-spined ova of *Schistosomum mansoni*. Adult worms were present in the iliac and portal veins. The liver was fatty and cirrhotic and the spleen congested and enlarged.

CASE II.

A powerful-looking Egyptian soldier was admitted to hospital suffering from pyrexia. His blood was examined for malarial parasites, but with negative results. The temperature fell to normal on the third day after admission, and he was discharged from hospital at the end of a week. Five days later he was readmitted with high fever, and looked very ill. He complained of headache and rigors. The tongue was thickly furred and the spleen slightly enlarged. The abdomen was distended but not rigid. No diarrhoeic symptoms were present. Blood examination proved negative for malarial or other parasites. The patient became steadily worse, his condition closely simulating a case of enteric fever; the faeces were rather fluid in character and of a pea-soup colour. Two days later he was passing almost pure blood per rectum. A rapid enlargement of the liver was observed, but no jaundice was noted. Examination of the faeces was carried out. Neither the ova of intestinal parasites nor amoebae were found. A daily increased enlargement of the spleen was then observed, and the organ eventually reached a point level with the umbilicus. The patient appeared to be in a state of acute toxæmia, and died on the seventh day after admission to hospital.

Post mortem examination showed very extensive ulceration throughout the large intestine as high up as the ileo-caecal valve. In this area there was a small intussusception, with ulcers present in that portion of the gut forming the intussusceptum. Smear preparations taken from the base of the ulcers showed the existence of lateral-spined ova of *Schistosomum mansoni*.

CASE III.

Case III. An Egyptian soldier was admitted to hospital suffering from fever and diarrhoea. He was somewhat anaemic, and the spleen was slightly enlarged. Blood examination for malarial

Case III.

parasites proved negative. After admission the patient's condition quickly became worse. He lost flesh rapidly, and his whole appearance was one of extreme lassitude, suggesting a toxæmic condition likely to be attended with fatal results.

The diarrhoea was a feature of the case from the onset. The faeces were examined, and the lateral-spined ova of *Schistosomum mansoni* were found.

The observations made *post mortem* on the previous cases suggested the possibility of good results accruing if vaccine therapy was employed. A sample of the patient's stools was obtained and plated out on suitable media. The plates were carefully examined, and contained for the most part two different types of *B. coli* colonies. Their cultural characters were worked out, and a bivalent autogenous vaccine prepared. The patient received a first dose of 0.5 c.cm., representing 250 million organisms, followed five days later by a dose representing 500 million. The result obtained was striking. After the first injection the patient stated he felt much better. A marked and rapid improvement in his condition set in. The diarrhoea ceased, the temperature fell, and a week after the second dose he was discharged fit from the hospital.

CASE IV.

It will only be necessary to refer to the salient points in this very interesting case. A full account of it is being published elsewhere.

The patient was a woman of about 24 years of age, who had never been out of Khartoum. She was admitted to hospital with fever, anaemia, and debility, and a very enlarged spleen extending to the umbilicus. Examination of the peripheral blood was negative for malarial parasites, and a careful search for evidence of malarial pigment was attended with negative results. The red blood corpuscles showed a certain degree of poikilocytosis and microcytes, and a few normoblasts were present. In addition, there were found oval and circular cells about 3.5μ in diameter, whose cytoplasm stained a delicate blue with Leishman stain. Some of these cells contained a few granules showing a chromatin tint. Myelocytes were not in evidence, nor did the blood films suggest lymphatic leukaemia. The red blood cells numbered 2,250,000 per c.cm., and the white blood cells 8,000 per c.cm. Blood culture was carried out, but yielded no results as regards the presence of a septicaemia. Puncture of the spleen was then resorted to. This organ was very firm, and resisted considerably the entrance of a fine hypodermic needle. Several smears were carefully examined, but neither Leishman-Donovan bodies nor malarial parasites were ever found.

As the spleen continued to enlarge and the patient's condition showed no improvement, the operation of splenectomy was decided upon, and successfully carried out by Dr. Atkey, of the Sudan Medical Department. The operation wound healed satisfactorily, but the patient's temperature continued to rise steadily and was in no way influenced by quinine administered hypodermically. An examination of the faeces was then carried out after a purge had been given; it may be mentioned that since her admission the patient had not shown any signs of intestinal irritation. After a prolonged search the ova of *Schistosomum mansoni* were found.

The patient's physical condition did not improve, and it was noticed that the liver was now commencing to enlarge rapidly. As a possible line of treatment vaccine-therapy was suggested. A sample of the faeces was obtained and suitably plated out, and a bivalent vaccine prepared from two different types of *coli* organisms isolated. An injection of 250 million was given as an initial dose, followed four days later by an injection of twice the

number of micro-organisms, and a similar number a week following the last dose.

The patient's temperature after the third injection became consistently lower. Another sample of faeces was obtained, and almost a pure culture of a *proteus*-like organism obtained. A fresh vaccine from this was prepared, two injections were given, and at the end of a week the patient had improved considerably, and a week later was discharged from hospital with practically a normal temperature. Her liver, which had previously extended to a position almost level with the umbilicus, had now retracted to a point 1 in. below the costal margin.

One has only to study the clinical histories of these cases to understand that the diagnosis of intestinal schistosomiasis is not always easy. The clinical signs and symptoms may be very misleading, particularly in those cases in which positive evidence is not furnished by a single examination of the faeces.

The failure to find the ova in some of the cases was due neither to faulty technique nor to a cursory inspection of the specimens sent for examination. In Cases I and II several samples of the faeces taken from the vicinity of the ulcers in the lower gut failed to show evidence of the ova of *Schistosomum mansoni*; even portions of the faecal matter and mucus taken from the surface of the ulcer were devoid of ova, and it was only possible to find the latter by scraping the walls and base of the ulcer. In Case IV no fewer than thirty-five specimens were examined from two different samples of faeces before the ova were detected.

As regards the pathology of the disease little need be said, for the lesions produced resemble those so well described by pathologists in Egypt. It may be mentioned, however, that the papillary type of growth mentioned as occurring in viscera lined by mucous membrane and in the vicinity of the anus is exceedingly rare in the Sudan.

Enlargements of the liver and spleen appear to be fairly constant features. In the former a cirrhotic condition is usually seen; in the latter a chronic hyperaemia, associated with a certain degree of fibrosis, is observed. Ova have, so far, not been found in these organs. In Case II the enlargement of the spleen was extremely rapid, and at the *post-mortem* examination its gross macroscopical appearance closely simulated the spleen met with in typhoid and allied conditions, so much so that it was deemed advisable to make cultures from its substance. A bacillus was isolated which in cultural and other characters resembled an organism previously isolated by me from the faeces of a case of intestinal schistosomiasis. Its presence in the spleen might be explained by the fact that it had gained access to the circulation by way of the ulcers in the intestine.

If this was so, it was not beyond the pale of supposition to suggest that the enlargement of the liver and spleen in intestinal schistosomiasis might be dependent not only on the absorption of the toxins of the causal helminth, but also on the absorption of intestinal micro-organisms and their toxic products from the abraded surfaces of the intestine. If these micro-organisms play a prominent part then vaccine therapy would appear to be a feasible line of treatment, particularly in the acute toxic types of the disease. The beneficial results obtained in the two cases treated appear to justify a further trial, and it has occurred to me that the employment of autogenous vaccines of intestinal organisms might also be extended to cases of splenomegaly in which no apparent cause can be found. Richards and Day¹ have recently described such cases of splenomegaly in Egypt, and it is of interest to note that a certain percentage of them showed a helminth infection.

Maxwell² records similar cases of splenomegaly of obscure origin occurring in China, and Wooley,³ from his observations of splenomegaly in the Philippines, is inclined to consider that some cases are dependent on a chronic infection originating in the intestinal tract, and that various organisms are associated with the clinical picture.

How far vaccine therapy may be serviceable in ankylostome fever remains to be determined. Definite proof is still lacking as to whether this fever is dependent on the toxins of the helminth or upon intestinal bacteria. Castellani⁴ noted that ankylostome fever was represented by three different types of pyrexia—a clinical fact which appears to support the view that different intestinal organisms and their toxins play a certain part in its production. It may be added that I have recently had very favourable results from the use of a *coli* vaccine in a serious case of ankylostomiasis.

Among other interesting points in intestinal schistosomiasis may be mentioned the frequent absence of eosinophilia. In the cases seen in the Sudan not one of them showed this blood change—a negative sign somewhat misleading, for it is generally understood that a helminth infection raises the number of eosinophiles in the blood. Low,⁵ however, in a recent paper states that chronic helminthiasis need not be productive of an eosinophilia. His experience was based on the examination of a number of natives in Uganda. Absence of eosinophilia must, therefore, not be taken as a contraindication to the examination of the urine or faeces. In urinary schistosomiasis one has found that an eosinophilia is invariably present, even up to 40 per cent.—a fact which may favour the theory of duality of the species of schistosomum.

Another point observed in the blood of these cases of intestinal schistosomiasis is the constant increase of large lymphocytes and a certain degree of leucocytosis affecting the polymorphonuclear leucocytes; indeed, the total number of leucocytes appears to be made up almost entirely of these two types of cells. The red blood cells show a certain amount of poikilocytosis, and one may obtain all the changes observed in secondary anaemias.

The difficulties associated with diagnosis have already been referred to. It is dependent on the finding of the spined ova in the faeces. The similarity to enteric and other fevers must be remembered. If complicated with malaria or tuberculosis it is easily understood what a clinical puzzle might be produced. The method of complement fixation may be useful on the lines adopted for the diagnosis of echinococcosis.

CONCLUSIONS.

The main points referred to in this paper may be briefly summarized.

1. There exists a specific fever in the Sudan, acute or chronic in type, dependent on an infection with *Schistosomum mansoni*.

2. This fever is usually accompanied by an enlargement of the spleen, a varying degree of anaemia, a polymorphonuclear leucocytosis, a large lymphocytosis, and an absence of eosinophilia. In the more chronic cases the liver becomes enlarged.

3. Intestinal symptoms may or may not be present.

4. The importance of a careful examination of the faeces in all cases of pyrexia of uncertain origin.

5. The possible value of treatment by autogenous vaccines of intestinal organisms, particularly in the acute toxic types of intestinal schistosomiasis, and in cases of splenomegaly due to no apparent cause.

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THE ETIOLOGY OF BERI-BERI.

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IN view of the widespread tendency to accept as proved that beri-beri is due to the eating of acorticated rice, it behoves those whose experience contradicts this theory to express their opinions. The leading exponents of the rice-eating doctrine, Drs. Fraser and Stanton, writing in the *JOURNAL* of October 25th, 1913, state: "It is now beyond dispute that the etiology of beri-beri in the Federated Malay States and Straits Settlements have been demonstrated." They are careful to speak only for the Malay States and the Straits Settlements. There is no doubt, however, in the minds of many competent observers that beri-beri occurs in many other parts of the world, and on board ships, amongst persons who do not eat rice and whose diet is in no material way deficient. Dr. MacGilchrist, writing from Bengal, has quite recently given an instance of its occurrence on board ship where diet was not at fault, but everything pointed, in his opinion, to an infectious origin.¹ Dr. Stanley, writing of fifteen years' experience of Shanghai and other places, is convinced that beri-beri is infectious, and probably conveyed by parasites.²

The epidemic which occurred on this island in 1901 amongst the Boer prisoners of war was certainly not attributable to diet. Rice formed no part of the diet, which was in every particular a liberal one. Prior to the appearance of the disease there had been much overcrowding in the Boer encampment. Groups of the prisoners, linked by ties of kindred or friendship, had built for themselves small huts made from old biscuit tins, the floors and bunks being of wood. Into these they packed themselves like sardines in a box. The Boers were the reverse of cleanly. Here, therefore, were two factors usually associated with outbreaks of beri-beri. The disease is not unknown in South Africa, and was probably imported with the prisoners of war.

I have long been impressed with the probably infectious nature of the disease. In such a case as the following it is difficult to avoid this conclusion.

In July, 1903, an American whaling brig, 411 tons burthen, put into Jamestown for medical aid. The captain reported that seven men had died of some illness during the past three weeks, and that many of the men on board were apparently suffering from the same disease. He did not know what it was, but thought it must be beri-beri from what he had heard of it in other ships. The deaths of the men had taken place suddenly while they were at work on deck.

On examining the ship's company I found eleven men in varying stages of beri-beri. Several were in a serious condition, and one man was in the last phase of heart failure. He died the following day in hospital.

This vessel had a crew of thirty all told. Nineteen men slept in the small fore-castle, ventilated only by the companion way, and lighted by a small glass oblong let into the deck. The cubic space available for these nineteen men involved gross overcrowding, and there was a lack of even average cleanliness. I did not find that the diet varied substantially from that found on board most sailing vessels. No doubt salt beef and pork as the staple article of diet is not ideal, but fresh bread was served every day, and preserved vegetables and lime-juice were issued at regular intervals. Rice was not eaten. A monotonous fare