Progress report

Intestinal schistosomiasis

Geographical Distribution

Intestinal schistosomiasis, caused by the trematodes Schistosoma mansoni and S. japonicum, is found over a wide area of Africa, the Middle East, in the Orient, South America, and parts of the Caribbean. It has been estimated\(^1\) that in the Americas and the Far East 40 million people are infected; in Africa where intestinal schistosomiasis coexists with the urinary form of the disease, the figure is 74 millions but probably less than half of these are infected with S. mansoni. It is therefore likely that about 80 million people have intestinal schistosomiasis and the number is increasing, largely due to the greater use of irrigation, a result seen in Egypt following the building of the Aswan dam and of the Volta dam in Ghana.

Diagnosis

Although the finding of ova in the stools or in snips of rectal mucosa or other biopsy material remains the only satisfactory means of diagnosis in the individual patient, the skin test and serological tests are of value. In the individual a positive result indicates that a search for ova should be made; in a community they are of value for survey purposes. A comprehensive review of such tests was published by Kagan and Pellegrino\(^2\) in 1961 and since then others have been added\(^3\). The complement-fixation test remains the most reliable and should give about 95% sensitivity; false positives are few but are seen in persons infected by animal schistosomes.

Hepatic Disease

Ova deposited by the female schistosome in the smaller tributaries of the portal vein around the gut may (1) be voided in the stools; these produce no ill-effects in the patient but as a link in the life cycle of the parasite are of great public health importance; (2) be retained in the wall of the bowel where they may produce lesions but these are seen in only a small proportion of infected persons; (3) be carried embolically to the liver. In fact they may also be found in the lung and in almost every organ and tissue of the body (Gelfand)\(^24\); it is difficult to understand how this wide dissemination is achieved.

Ova found in the liver may be those of S. haematobium, S. mansoni, or S. japonicum and they may or may not provoke a reaction; that the hepatic lesions result from the presence of eggs rather than being the effect of a 'toxin' or a reaction to adult worms is strongly supported by the work of Bogliolo\(^4\) in Brazil; livers from patients with hepatosplenic schistosomiasis, cirrhosis, and infectious hepatitis were examined microscopically and by injection of coloured gelatine or vinyl acetate. It was concluded that impacted ova produce a granulomatous periphlebitis, later followed by fibrosis,
the distribution of which is strictly that of the portal tracts, the lobules being spared and there being no distortion of architecture or regeneration. The concomitant formation of new vessels is characteristic, a network surrounding the branches of the portal vein but not invading the lobules; no lacunae are formed or portal vessels amputated as may be seen in cirrhosis, and in the series reported by Bogliolo portal thrombosis was not seen; the findings in this 'pipe-stem' fibrosis, first described by Symmers in 1904, are therefore characteristic of schistosomiasis and quite different from those of cirrhosis; similar portal fibrosis of unknown aetiology does occur, however, in different parts of the world, including India where schistosomiasis is hardly known.

That ova provoke the reaction was suggested by Symmers in his original description and is supported by the study of von Lichtenburg on the vascular lesions; Andrade, however, favours a delayed hypersensitivity reaction to schistosomal antigens as the cause of the inflammatory lesions rather than the presence of ova. In experimental schistosomiasis in the mouse, Warren has shown that the egg is the factor determining the development of disease.

Clinical Features

Patients present with a haematemesis, swelling of the abdomen, or a dragging pain on the left side; they may or may not be malnourished, and ascites, oedema, or other evidence of chronic liver disease is often absent. The liver may be enlarged but splenomegaly is the rule and may be massive. Tests of liver function are usually normal or only slightly disturbed, but a barium swallow shows oesophageal varices. An extensive study of the haemodynamic changes has been carried out by Coutinho in Recife, Brazil. One hundred and twenty patients whose chronic liver disease was considered to be primarily of schistosomal origin were investigated. The main findings were: (1) raised intrasplenic pressure (mean 412 mm water); (2) raised portal venous pressure (mean 327 mm water); (3) normal or only slightly raised sinusoidal pressure as measured by the occluded hepatic venous pressure (less than 20 mg Hg); (4) normal or only slightly raised intrahepatic pressure (less than 200 mm water); (5) splenoportography showed lengthening and widening of splenic and portal veins, the formation of collateral vessels and oesophageal varices but not portal thrombosis. It was concluded that these results indicate a presinusoidal obstruction and that together with the biochemical and histological findings and the age incidence in Brazil (10 to 30 years) constitute an entity quite different from cirrhosis; haemorrhage from varices in these patients carries a low mortality and surgery is well tolerated, again in distinction from cirrhosis. Despite the prehepatic anastomotic vessels which may be very large in schistosomiasis, the hepatic blood flow may be normal and attributable to increased arterial flow.

Haematological Changes

Patients suffering from intestinal schistosomiasis are frequently anaemic. In Puerto Rico Ramos-Morales found that 58% of 1,547 untreated patients had a haemoglobin concentration of less than 13 g/100 ml with 4% less than 10g/100 ml. Seventy-six per cent of these patients were aged 15 years or less and some had hookworm infection which could have contributed to blood loss. The relative importance of hookworm and schistosomal infections in
causing blood loss has been well demonstrated by Farid et al. In eight Egyptian farmers heavily infected with *A. duodenale* but without schistosomiasis, the main daily blood loss was 65 ml and mean iron loss 18 mg/day, but, using a double isotope, $^{51}$Cr and $^{59}$Fe, technique they showed that 8 mg of iron so lost was reabsorbed daily. On the other hand in eight similar patients with severe intestinal polyposis (biopsy showed polypi full of *S. mansoni* ova) but no hookworm infection, the mean blood and iron losses were 13 ml and 4 mg/day; very little of this iron was reabsorbed.

Evidence regarding the part played by haemolysis in the production of anaemia in those suffering severe intestinal schistosomiasis is conflicting. Farid et al. studied four patients with marked hepatosplenomegaly in Cairo; all were anaemic (Hb concentration 7.4-12 g/100 ml) with low serum iron concentrations and high iron-binding capacity. Serum bilirubin and reticulocyte counts were not raised and the $^{51}$Cr half-life was not shortened; an initial high uptake of isotope by the spleen did not subsequently increase. The white cell count was less than 2,500/c mm and the platelet count was reduced: the response to oral iron was good. On the other hand Woodruff et al., working in Alexandria, found a somewhat reduced red cell life span with an increased initial splenic uptake which continued to rise; the estimates of the blood volumes of these patients varied from 4.3 to 7.2 litres (mean 105 ml/kg). This greatly increased plasma volume was also noted in a further study by Farid and his colleagues on two patients with very big spleens. Both were anaemic with evidence of iron deficiency and a reticulocytosis up to 5%. In one the red cell life span was reduced but in the other it was normal. Although both showed an increased plasma volume and an initially high splenic uptake of isotope, in only the first did this continue to rise; splenectomy was followed by rise in Hb concentration to 10 g/100 ml without the administration of haematinics, and an increase in the life span of the red cells. Sabour et al., also working in Egypt, found a markedly reduced life span, moderate anaemia in the absence of hookworm infection, hypervolaemia, and intestinal blood loss; splenectomy was followed by considerable reduction in blood volume and a rise in Hb concentration but in only two patients was there an increase in the red cell life span; they were the two whose splenic activity continued to rise following the administration of isotope.

It would therefore seem that gross splenomegaly may be associated with a dilution anaemia and with pooling of red cells and on occasion with increased destruction of red cells in the spleen; a similar dilution anaemia in patients with splenomegaly and suffering from leukaemia, thalassaemia, and Gaucher's disease has been noted by Prankerd. In schistosomiasis iron deficiency commonly contributes to the anaemia and this may partly be due to blood loss from the gut.

**Treatment**

For more than 50 years the mainstay of treatment has been the antimony compounds and when carefully given they may be expected to produce almost 100% cure despite the unpleasant side effects. The orally administered lucanthone hydrochloride (Miracil D, Nilodin), although giving quite good results, produced a high incidence of side effects which put it into disrepute. Niridazole (Ambilhar, Ciba 32, 644), also taken by mouth, is moderately effective (see references by Jordan). In a high proportion of patients its
side effects, although very common, are not severe. In those patients with marked liver involvement the position is different. Eighty-eight patients suffering from hepatic schistosomiasis were studied by Coutinho and Barreto in Recife, Brazil; in 52 the involvement was severe and in these patients there was a higher incidence of marked toxic effects, notably psychotic disturbance and convulsions, than in those with less severe liver involvement. The incidence was 36% and 8% for those with more advanced disease compared with 7% and 0% in those whose liver was less severely affected. EEG tracings normal before treatment became abnormal in 86% and 15% of the two types of patient during therapy; tests of liver function, however, did not differ in the two groups. Splenoportography suggested a greater diversion of portal blood through collaterals in those patients suffering marked side effects in the nervous system. Faigle and Keberle found a blood concentration of niridazole three times higher in patients with hepatosplenic schistosomiasis than in those with an intestinal infection only. It is concluded that the severe side effects in the central nervous system are attributable to a diversion of portal blood in those with advanced liver involvement so that non-metabolized drug reaches the systemic circulation in greater concentration.

Hycanthone is a hydroxymethyl derivative of lucanthone, and the effect of this substance is being investigated. In Egypt results are encouraging, egg excretion being interrupted for several months following a single intramuscular dose given to children (A. H. Mousa, personal communication).

**Conclusion**

Schistosomiasis is probably the only important parasitic disease which is increasing in incidence despite the expenditure of large sums of money and effort. In its intestinal form it gives rise to a great deal of morbidity and substantial mortality as a result of liver involvement. A cheap, safe, orally administered drug which is effective and not toxic is not yet available despite an enormous amount of research by pharmaceutical companies.

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**References**

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