Functional and Structural Changes in the Small Intestine in Children with Hookworm Infection

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Hookworm infection is prevalent in tropical countries, and much attention has been paid to the various aspects of anaemia associated with it (World Health Organization, 1959). Gastro-intestinal disturbances, such as anorexia, diarrhoea, abdominal pain, and flatulence, are also often noted in patients with hookworm infection. Advances in methods for studying the functional and structural status of the small bowel have enabled study of the pathogenesis of these clinical manifestations. Rotter (1931) first suggested that intestinal absorption might be impaired in this condition, and recently several authors have reported structural abnormalities in the small intestine in adults with hookworm infection (Sheehy et al., 1962; Salem and Truelove, 1964; Chaudhuri and Saha, 1964; Tandon et al., 1966). The present communication reports our observations on 14 children with hookworm infection.

Material and Methods

Studies were made of 14 children between the ages of 4 and 12 years, who were suffering from hookworm infection in association with microcytic hypochromic anaemia; in addition 14 children with no evidence of anaemia, gastro-intestinal or renal disease, served as controls. The following investigations were carried out.

Stools were examined by the saline-iodine preparation and/or the concentration method; haemoglobin was estimated by the cyanmethaemoglobin method (Williams and Zak, 1957); and haematocrit, reticulocyte count, haemogram, and bone-marrow examination by standard methods (Dacie, 1956); bone-marrow was stained for haemosiderin by Douglas and Dacie's method (1953); serum iron was estimated by the method of Ramsay (1958), unbound iron-binding capacity by the method of Ressler and Zak (1958), and serum protein by the biuret method of King and Wooton (1956). Occult blood in stool was determined by the benzidine test.

A fat balance study was carried out over a 6-day period on a diet containing 50 g. fat (van de Kamer, ten Bokkel Huinink, and Weyers, 1949). A 5 g. D-xylose absorption test was done (Butterworth et al., 1959). The 5-hour urinary D-xylose excretion was estimated by the method of Roe and Rice (1948). Jejunal biopsy (Rubin's multipurpose biopsy tube) was performed in 12 children, and the histopathological changes were graded without the knowledge of the clinical data.

After completion of the above investigations, patients were treated with a single dose of 5 g. bephenum. Iron dextran complex was administered intramuscularly in all patients with evidence of iron deficiency. The total dose of imferon was calculated according to the formula of Smith (1960). 8 to 24 weeks after initiation of therapy, 12 children were investigated a second time.

Results

The haematological and other data are summarized in the Table. The mean D-xylose and faecal fat excretion in controls were 1·481 g./5 hr. urine/5 g. dose, and 3·1 g./day, respectively.

The 5-hour D-xylose excretion was found to be less than 1 g. in 7 patients (range 510–877 mg.). The daily fat excretion was noted to be increased in 8 patients. Most patients had a mild steatorrhoea (maximum excretion 12 g./day). Histological abnormalities were detected in the small intestine in 5 of the 12 jejunal biopsies. Grade I changes in 3 children consisted of some blunting and fusion of villi and increased cellular infiltration in the lamina propria. The villous crypt ratio was more or less normal. The villous epithelial cells were properly oriented and showed no abnormalities. Grade II abnormality was observed in 2 cases: these changes were characterized by moderate reduction in the villous: crypt ratio, to 1:1 or 2:1. The villi showed varying degrees of fusion and blunting (Fig. 1). A moderate amount of cellular infiltration was detected in the lamina propria. Goblet cells were increased, but the epithelial cells

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TABLE
Summary of Cases

<table>
<thead>
<tr>
<th>Case No., Sex, and Age (yr.)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>Hb (g./100 ml)</th>
<th>Haematocrit (%)</th>
<th>Serum Iron-binding Capacity (ug./100 ml)</th>
<th>Unbound Serum Iron (ug./100 ml)</th>
<th>D-xylene Excretion (g./5 hr. urine)</th>
<th>Faecal Fat (g./day)</th>
<th>Occult Blood in Stool</th>
<th>Intestinal Biopsy</th>
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<tbody>
<tr>
<td>1 M 8</td>
<td>118</td>
<td>19.7</td>
<td>6.8</td>
<td>26</td>
<td>32</td>
<td>452</td>
<td>0.811</td>
<td>9.5</td>
<td>-</td>
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<tr>
<td>2 F 11</td>
<td>119</td>
<td>23.1</td>
<td>13</td>
<td>41</td>
<td>138</td>
<td>288</td>
<td>0.850</td>
<td>10.0</td>
<td>-</td>
<td>Normal</td>
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<tr>
<td>3 F 12</td>
<td>154</td>
<td>26.3</td>
<td>6.0</td>
<td>22</td>
<td>26</td>
<td>449</td>
<td>2.7</td>
<td>0.850</td>
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<td>4.0</td>
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<td>444</td>
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<td>2.120</td>
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<tr>
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<td>13</td>
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<td>400</td>
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<tr>
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<td>22.2</td>
<td>7</td>
<td>27</td>
<td>31</td>
<td>386</td>
<td>3.3</td>
<td>1.069</td>
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a, b, first and second investigation, which was done in Cases 1–12.

did not show any significant changes. None of the patients showed advanced villous atrophy amounting to grade III and grade IV. The investigations were repeated in 12 children 8 to 24 weeks after de-worming and correction of the iron deficiency. All of them showed clinical improvement, Hb rising above 12 g./100 ml., and serum iron above 70 ug. Only 2 patients were still

**FIG. 1.—Case 3. Jejunal biopsy before therapy, showing partial villous atrophy (Grade II changes).** The villi are significantly shortened, blunted, and occasionally fused. (**H. and E.** × 100.)
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harbouring hookworm. The D-xylose excretion and the fat excretion returned to normal in all the patients. Jejunal biopsy was repeated in all the 5 children who were initially abnormal, and all showed a return towards normal (Fig. 2), despite the fact that 2 of them were still harbouring hookworms. Another group of 5 children whose jejunal mucosa was normal at the time of jejunal biopsy was observed to return towards normal (Fig. 2), despite the fact that 2 of them were still harbouring hookworms. Another group of 5 children whose jejunal mucosa was normal at the time of jejunal biopsy was observed to return towards normal (Fig. 2), despite the fact that 2 of them were still harbouring hookworm infection. Reversal of these changes after treatment is also significant in this respect.

The pathogenesis of this enteropathy in patients in the present series is speculative. Malnutrition, with its impact on small bowel function and structures, may be one factor, as it is not uncommon for these children to have low or marginal nutrition. Iron-deficiency anaemia due to hookworm infection may set up a vicious circle of intestinal damage; it is worth mentioning here that iron-deficiency anaemia can lead to epithelial abnormalities (Badenoch, Evans, and Richards, 1957; Beveridge et al., 1965; Rawson and Rosenthal, 1960; Witts, 1931), and intestinal changes have been observed in patients with iron-deficiency anaemia without hookworm infection (Naiman et al., 1964; Saha, Chatterjea, and Chaudhuri, 1965; Guha et al., 1968). Finally, parasites themselves may have a direct and damaging effect on the intestinal mucosa because of their habit of biting, or because of the production of yet undetected toxins.

The association of intestinal changes and hookworm infection makes this problem more important in tropical countries.

Summary

The structural and functional changes in the small intestine in 14 children between 4 and 12 years of age, with hookworm infection and iron-deficiency

Fig. 2.—Jejunal biopsy after therapy, showing normal histological pictures. (H. and E. ×100.)
anaemia were studied both before and after therapy. Increased faecal fat excretion was found in 8 children, and d-xylose absorption was poor in 7. Mild histopathological changes in the small intestine were found in 3 children, and moderate (grade II) changes in 2. Following treatment with intramuscular iron dextran complex and bephenium, all the abnormalities reverted to normal. The possible pathogenesis and practical implications are discussed.

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