There was no increased incidence of reflux in the transplanted ureter in those patients with preoperative reflux. Of the 10 with reflux four had a persistent urinary tract infection, whereas only one out of the seven without reflux had infection. Though the numbers are small it would seem that a patient without reflux of his own or the transplant ureter is least likely to suffer urinary infection. If reflux occurs in both the patient's own ureters and the transplanted ureter the risk of infection is considerable. If a tunnel has not been fashioned there is also a high risk of reflux and infection. Ureteric necrosis occurred in two patients (Cases 1 and 18). In both nearly the whole ureter was necrotic, not only the segment buried in the tunnel, and therefore the method of implantation was not incriminated. The ureteric fistulae were repaired by anastomosing infrapelvic ureter to the vault of the bladder. At the time of this second anastomosis the urine was infected in both cases, but despite protracted antibiotic therapy it remained impossible to sterilize the urine.

There does not seem to be any risk of producing serious urinary infection by catheterizing patients for a micturating cystogram, and prophylactic antibiotics are not essential, but a

specimen of urine should be cultured one week after the examination. Intravenous pyelography in the seven patients with ureteric reflux showed some dilatation of the ureter and calices in two (Cases 1 and 5), though at the time of examination there was no evidence of urinary infection. Of the six with competent ureterovesical junctions there was no evidence of obstruction due to the anastomosis.

Micturating cystography is regarded as a worthwhile and safe investigation after renal transplantation, as those with infected reflux possibly need long-term antibiotics and regular bacteriological examination of the urine to reduce probable renal damage. Those with sterile reflux should also have close bacteriological control of their urine as they may be more prone to urinary infection.

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Small-intestinal Cell Turnover in Patients with Parasitic Infections

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Summary

Small-intestinal deoxyribonucleic acid (DNA) loss rates were measured in six patients with *Strongyloides stercoralis* hyperinfestation, in four patients with hookworm disease, and in eight normal controls. In the four patients with strongyloidiasis having weight loss, hypoproteinaemia, and oedema the mean DNA loss rates were 73.9, 51.6, 58.0, and 62.2 ng atoms DNA-P/min respectively, which was significantly higher than that of patients with hookworm disease (mean 17.3, S.D. 6.6) or in eight control subjects (mean 14.5, S.D. 7.5). In two of three patients with strongyloidiasis the high DNA loss rates fell to normal after treatment, and in two others investigated only after treatment the rates were normal. It is suggested that the high epithelial cell turnover in these patients may result in excessive loss of endogenous substances and that this may be an important mechanism in causing malnutrition and hypoproteinaemia in patients with *S. stercoralis* hyperinfestation.

Introduction

Strongyloides stercoralis has been found to be a cause of malabsorption in man (Stemmerman and Nakasone, 1960; Milner et al., 1965). In this parasitic infection the small-

intestinal villi become flattened or convoluted with a dense inflammatory infiltrate in the lamina propria. Adult worms and larvae are found in the crypts. Sheehy et al. (1962) described malabsorption in patients with hookworm disease. They showed steatorrhoea, malabsorption of vitamin A and fat, a deficiency pattern on barium series, and flattening and clubbing of the intestinal villi. Salem and Truelove (1964) reported two cases of hookworm disease with steatorrhoea. Presumably in these parasitic disorders the flattening of intestinal villi represent a substantial loss of absorptive surface area which could account for most of the alterations in absorptive function. It is also possible that endogenous substances may be lost into the lumen of the gut in excessive amounts and that this may be an additional mechanism leading to malnutrition in these patients. The small-intestinal mucosa is dynamically the most active epithelial surface of the body in man, losing some 20-50 million cells per minute (Croft et al., 1968b). This cell loss can be estimated by measuring the deoxyribonucleic acid (DNA) content of the intestinal lumen. The rate of cell loss from the small intestine of patients with parasitic infestations is unknown. In this study small-intestinal DNA loss rates have been used to estimate the rate of cell loss in patients with *S. stercoralis* and hookworm infection.

Patients and Methods

Small-intestinal DNA loss rates were measured on nine occasions in six patients with *S. stercoralis* infection. All were males, and their average age was 25 years (Table I). The following case is typical of patients with malabsorption due to *S. stercoralis* infection.

Case Report.—A 15-year-old boy presented with a three-month history of nausea, anorexia, vomiting, and weight loss. He also noted increasing diarrhoea and, one week before admission, oedema of his legs. On examination he was seen to be a thin, malnourished

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TABLE I—DNA Loss Rate in Six Patients with *Strongyloides Infestation*

Case No.	Sex	Age	Dissecting Microscopical Appearances of Mucosa	DNA Loss Rate (ng Atoms DNA-P/Min)	
				Before Treatment	After Treatment
1	M	25	Flat mucosa	81.1 69.2 71.6 77.6 } 73.9	34.5 19.8 } 27.1
2	M	17	Flat mucosa	75.7 64.5 51.5 } 51.6	10.7 13.4 6.1 } 12.0
3	M	28	Flat mucosa	85.6 61.2 40.0 } 58.0	7.5 } 6.8
4	M	26	Flat mucosa	—	—
5	M	30	Leaves and ridges	—	16.5 17.2 } 16.7
6	M	24	Mainly leaves	—	16.2 11.1 } 13.6
Average				61.4	15.2
S.D.				21.5	7.8

teenager with anaemia, ascites, oedema of his legs, and crazy-pavement skin pattern over his legs. Investigation showed a haemoglobin of 11.4 g/100 ml, serum iron 31 µg/100 ml, total iron-binding capacity 289 µg/100 ml, saturation 11%, serum folate 1.5 pg/ml, serum proteins 5.5 g/100 ml (albumin 1.9 g, globulin 3.6 g), stools and jejunal aspirate contained strongyloides larvae. Faecal fats were 10 g/24 hours. Folic acid absorption was flat, xylose absorption was abnormal. Barium follow-through examination showed a malabsorption pattern. Examination of a small-bowel biopsy specimen under the dissecting microscope showed a flat mucosa. Histologically, there was subtotal villous atrophy. Treatment was instituted with thiabendazole (Mintezol). The patient's recovery was rapid and uneventful.

Three patients were studied before and two weeks after treatment. One patient was studied before treatment only, and the two were too ill to be studied before treatment but were investigated two weeks after treatment. Before treatment they showed gross evidence of malabsorption with severe electrolyte disturbances. At the time of investigation they were no longer having diarrhoea and were rapidly regaining weight.

Small-bowel DNA loss rates were also measured in four male patients with hookworm disease; their average age was 49.5 years (Table II). None of these patients had any evidence of malabsorption. Their presenting features were those of severe anaemia.

Eight normal Jamaicans (average age 44 years) were studied as controls. They had no evidence of malabsorption, their stools were negative for ova and parasites, and biopsy of the small bowel showed nothing abnormal. The purpose of the test was explained to each of the 10 patients and the eight controls and their permission obtained.

Small-Intestinal Washings

The details of the technique of measuring small-intestinal cell loss has been described (Croft *et al.*, 1968a). The method measures the loss of substances from a 5-cm segment of

TABLE II—DNA Loss Rate in Four Patients with Hookworm Disease

Case No.	Age	Dissecting Microscopical Appearance of Mucosa	DNA Loss Rate (ng Atoms DNA-P/Min)
1	60	Fingers and leaves	10.1
2	45	Fingers and leaves	7.5 26.7 } 17.1
3	17	Fingers and leaves	18.7 10.2 } 14.4
4	76	Mainly leaves	22.8 32.4 } 27.6
Average			17.3
S.D.			6.6

duodenal mucosa without significant contamination by gastric, biliary, and pancreatic secretion. A special four-lumen tube was constructed with an infusion tube (internal diameter 2 mm) opening midway between the ends of the two collecting tubes (proximal and distal—internal diameter 2.5 mm) which were 10 cm apart. The fourth tube (internal diameter 1.5 mm) was used to obtain small-bowel biopsy specimens, with a Crosby capsule, at the end of the washing experiment. Tests were performed after an overnight fast of 12 hours. The tube was guided under fluoroscopy into the duodenum so that the tip was at the level of the duodenal jejunal flexure. An initial priming with 300 ml of warm normal saline containing the nonabsorbable marker polyethylene glycol 0.8 mg/ml was done. Flow was initiated by gentle suction of the proximal and distal tubes. One to three washings were made, 500 ml of warm normal saline containing polyethylene glycol 0.8 mg/ml being used. The infusion rate was 16 ml/min. Specimens were collected from the proximal and the distal collecting tubes and stored immediately at -14°C for up to two weeks.

D.N.A. was measured by a modified diphenylamine technique (Croft and Lubran, 1965). After correction for the loss of the non-absorbable marker polyethylene glycol, DNA loss rates were calculated by dividing the DNA content of the washings by the time of infusion, the values being expressed as ng atoms DNA-P/min. Bilirubin seems to act as a marker for DNA coming from above the washing site (Croft *et al.*, 1968a), and when the bilirubin content is less than 0.5 mg/100 ml, contamination from gastric, biliary, and pancreatic secretions is insignificant. Bilirubin concentration was 0.5 mg/100 ml or less in all the distal specimens. Polyethylene glycol was measured by the method of Hyden (1956) and bilirubin by the method of King and Coxon (1950).

Results

Small-intestinal DNA loss rates were measured on four patients with *S. stercoralis* before treatment. All were anorexic, losing weight, hypoproteinaemic, and oedematous. A small-bowel biopsy specimen taken before treatment showed a flat mucosa. The mean DNA loss rates were 73.9, 51.6, 58.0, and 62.2 ng atoms DNA-P/min respectively (range 27.6–85.6 ng atoms DNA-P/min). These were well above the normal range when compared with eight control subjects (range 4.8–34.0 ng atoms DNA-P/min, mean 14.5) (see Chart).

Three of these patients were again studied two weeks after treatment with thiabendazole. All now had good appetites, were gaining weight, and had lost their oedema. Small-bowel biopsy specimens showed much improvement. The mean DNA loss rate was 27.1, 12.0, and 6.8 ng atoms DNA-P/min

Comparison of the rates of DNA loss in a group of normal subjects, patients with strongyloidiasis before and after treatment, and patients with hookworm disease.

respectively (range 6.1 to 34.5, mean 15.3). In two of these patients the DNA loss rate was well within the normal range. In the third it was raised but the trend was toward a return to normal. In two patients who had been studied only after treatment the mean DNA loss rates were 16.7 and 13.6 ng atoms DNA-P/min, again well within the normal range.

Four patients with hookworm anaemia were studied for a total of seven specimens (Table II). Their mean small-bowel DNA loss rate was 17.3 ng atoms DNA-P/min, which was not significantly different from the mean value for the control group. There was no evidence of malabsorption in these patients, and the intestinal biopsy specimens showed nothing abnormal.

Cells and cellular material were present in the washings. Microscopically, the debris from the washings consisted mainly of epithelial cells and nuclear debris with less than 5% inflammatory cells. Bacteria, another possible source of DNA, were microscopically few in number. After the initial priming with 300 ml of saline, there were very few parasites visible in the first washings or in smears of the debris, and usually there were no parasites in the final washing. It was thought that they were not contributing significantly to the total DNA content of the specimens. If they were, then the earlier washings, containing more parasites, should have a higher DNA content. There was no consistently significant difference in the DNA content of the first or third specimens. Finally, all specimens were tested for blood with the Hemocombostix and were found to be negative. It is suggested that the increased DNA loss in the patients with strongyloidiasis was not due to inflammatory cells, bacteria, or parasites and reflected a true increase in the rate of cell loss and, therefore, of cell turnover in these patients.

Discussion

The association between *S. stercoralis* infection in man and malabsorption is well established. The infection results in abnormal small-intestinal mucosal changes not unlike those seen in patients with the coeliac syndrome. The mucosa is flattened or convoluted, and there is an increase in crypt length and in the number of cells in mitosis. These findings are suggestive of a high turnover state (Creamer, 1967). In the coeliac syndrome the turnover of epithelial cells is abnormal (Creamer, 1962), and Croft *et al.* (1968a) showed that the rate of small-bowel cell loss is increased in patients with active coeliac disease and weight loss. Symons (1965) showed that the small-intestinal mucosa of rats infested with the nematode, *Nippostrongylus braziliensis*, is characterized by anatomical and kinetic changes of a similar nature to that found in the jejunum of patients with the coeliac syndrome. Loehry *et al.* (1969) estimated cell loss by the DNA technique in rats infested with *N. braziliensis*. They found flattening of the mucosa and a considerably increased rate of cell loss, suggesting an increased turnover state. It therefore seems highly possible that in patients with *S. stercoralis* infection the small-bowel mucosal cell loss might also be increased. So far no one has

attempted to measure the rate of small-intestinal cell loss in patients with this disease.

These results show that patients with strongyloidiasis and malabsorption have a significantly higher than normal rate of DNA and cell loss into the lumen of the small intestine. Following treatment, when the patients were rapidly gaining weight and the mucosa was reverting to normal, the rate of cell loss was normal in four patients and was near normal in another. It has been suggested that cell loss and weight loss are related in the coeliac syndrome; the higher the rate of cell loss, the greater the weight loss (Croft *et al.*, 1968a). It has also been shown that other substances such as iron (Loehry *et al.*, 1969) and protein (Da Costa *et al.*, 1971) may be lost by this mechanism. In the healthy individual the small-intestinal epithelial cells are exfoliated from the tips of the villi into the lumen of the gut. Here the cells are rapidly digested and their various constituents are reabsorbed, only a small proportion being lost into the faeces. In conditions with an increased epithelial cell turnover there is, therefore, an increased loss of important endogenous substances into the gut. In addition, in strongyloidiasis there is a loss of absorptive surface due to the abnormal mucosa, thereby permitting an increased loss of endogenous substances into the faeces. Increased cell loss combined with loss of absorptive surface may thus be an important mechanism in the production of malnutrition in *S. stercoralis* infection in man.

Sheehy *et al.* (1962) described a malabsorption state in association with hookworm anaemia, and this was confirmed by Salem and Truelove (1964). This has not been the experience in Jamaica. Only four patients with hookworm anaemia were studied, so conclusions cannot be drawn from the results. In all four patients the mucosal pattern was normal. There was no clinical evidence of malabsorption, and there was no significant difference in the rate of DNA loss when compared with eight normal controls.

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