Effects of ileal and caecal resection on the colon of the rat

J. H. B. SCARPELLO,* B. A. CARY AND G. E. SLADEN†

Academic Division of Medicine, Royal Hospital, Sheffield, U.K.

(Received 23 March 1977; accepted 2 September 1977)

Summary

1. Rats were subjected to resection of either the distal 50 cm of small bowel, the caecum or a combined ileocaecal operation. The effects on stool production and growth were observed over the following 8 weeks. Subsequently measurements were made at various levels in the remaining gut of intestinal weight, mucosal thickness, mucosal adenosine 3':5'-phosphate (cyclic AMP) concentration and the water and bile acid content of luminal material.

2. Rapid adaptation, in terms of growth and the production of formed stools, was seen after ileectomy or caecectomy. This was slower and less complete after ileocaecectomy. Changes in water content indicated that colonic absorption of water was normal after ileectomy but impaired after ileocaecectomy.

3. After ileectomy there was growth of the caecum but not colon, whereas after ileocaecectomy there was growth of the remaining colon.

4. The intraluminal bile acid concentration in the small-gut remnant was markedly decreased at 2 weeks with little further change at 8 weeks after ileal resection. The colonic intraluminal bile acid concentration was only modestly increased after ileectomy or ileocaecectomy.

5. When studied by a perfusion technique in vivo, deoxycholate (2.5 mmol/l) in intact rats induced a net secretion of water into the colon; by contrast the colon of 8 week ileectomyed rats absorbed water, although this was at a reduced rate compared with control rats. Deoxycholate increased mucosal cyclic AMP concentrations in the intact rats but not in the ileectomized rats.

6. Sodium ricinoleate (5.0 mmol/l) inhibited colonic water absorption and when mixed with deoxycholate (2.5 mmol/l) the effect on water transport was summatory. However, ricinoleate either alone or with deoxycholate did not alter mucosal cyclic AMP concentrations.

7. These results demonstrate that the colon can absorb water effectively after ileectomy in spite of being exposed to increased concentrations of luminal bile acids. This may result in part from an altered mucosal response to secretagogues. If so this represents a form of functional adaptation by the colon to ileal resection.

Key words: adenosine 3':5'-phosphate, bile acids, colonic adaptation, fatty acids, intestinal resection.

Abbreviation: cyclic AMP, adenosine 3':5'-phosphate.

Introduction

After small-bowel resection in the rat rapid functional adaptation takes place accompanied by morphological change (Loran & Althausen, 1958; Nygaard, 1967; Dowling & Booth, 1967). The degree of adaptation varies with the site and extent of resection. Nygaard (1966) found that functional adaptation was more rapid and complete after proximal small-bowel resection than comparable resection of the distal ileum. Hypertrophy of the small-bowel remnant was greater after proximal resection although after distal operation there was also some hypertrophy of the large bowel.

In man, distal ileal resection is commonly associated with watery diarrhoea, which may persist for long periods. This is largely attributed to the colonic secretion of water and electrolytes as a
result of bile acid malabsorption (Hofmann & Poley, 1972). By contrast, Cummings, James & Wiggins (1973) showed that the severity of the diarrhoea was more related to the extent of associated proximal colonic resection. If impaired colonic absorption is important then the colon must be capable of absorbing water even if exposed to malabsorbed bile acids. We have shown that the colon can absorb water effectively even when the luminal bile acid concentration is moderately increased. Two possible reasons for this have been examined in separate colon-perfusion studies.

There is evidence that the secretogenic effect of bile acids on the small intestine is significantly reduced when they are present together with fatty acids as mixed micelles (Lamabadusuriya, Guiraldes & Harries, 1975), although this has not been investigated in the colon. It is also possible that the colonic mucosa of the resected animal responds differently, since all experimental studies have hitherto involved testing the effects of secretogenic agents upon the normal colon. Current evidence has implicated mucosal adenosine 3':5'-phosphate (cyclic AMP) as the mediator of bile acid-induced secretion of fluid (Binder & Rawlins, 1973; Binder, Filburn & Volpe, 1975).

We have used a single-pass perfusion technique to test the effects, singly or combined, of sodium deoxycholate and sodium ricinoleate, a secretogenic hydroxy fatty acid (Binder & Bright-Asare, 1973), upon water and electrolyte transport in the rat colon. In addition we have tested the effect of sodium deoxycholate upon the colon of the rat 8 weeks after ileal resection. In both cases the role of cyclic AMP was investigated by measuring mucosal concentrations in the colon after perfusion.

Methods

Animals

Male albino rats (Sheffield strain) were used for all experiments. They weighed initially between 200 and 250 g. They were fed on a standard chow (Burnhill’s diet 86) with tap water to drink and maintained on a 12 h light/12 h dark photoperiod.

Intestinal resections

Surgery was performed via a mid-line abdominal incision under methoxyflurane anaesthesia (Penthrane; Abbott Laboratories, Kent, U.K.).

Four operations were used:

Ile-ectomy. The distal 50 cm of small intestine (half the total small intestine) was resected by counting 5 cm segments proximally from the ileocaecal junction. The ileocaecal valve was preserved with, in addition, the terminal 2–3 cm of ileum.

Caecectomy. The whole of the caecum was resected, together with the terminal 2–3 cm of ileum in order to preserve a good blood supply.

Ileocaecectomy. Resection of both the caecum and the distal 50 cm of small bowel.

Sham operation. The small bowel was transected at a point 2–3 cm proximal to the ileocaecal junction and then anastomosed. These animals formed the control group.

For all animals care was taken to preserve a good blood supply and intestinal continuity was re-established by end-to-end anastomosis with atraumatic 5/0 silk. After surgery the animals were fed with glucose solution (5 g/l) for 48 h. Subsequently they received the standard rat chow and water ad libitum.

During the postoperative period the animals were weighed each week and the appearance of a fresh faecal specimen was observed. This was obtained by handling the animal in order to stimulate defaecation.

Terminal procedures

Terminal experiments were performed under the same experimental conditions as the initial operation, with methoxyflurane anaesthesia. The animals were killed either at 8 weeks, at which time they were mostly producing formed stools, or after 2 weeks when many still had diarrhoea.

Full patency of the anastomosis was examined by passing a standard probe, and any animals with a stricture or apparent obstruction were rejected. Observations were made on approximately 10 cm lengths of bowel from particular sites along the intestinal tract:

(1) Proximal jejunum: starting point 5 cm distal to the ligament of Treitz.

(2) Distal jejunum: starting at 5 cm proximal to the anastomosis in resected animals and 50 cm proximal to the ileocaecal junction in control rats.

(3) Distal ileum: 5 cm proximal to the ileocaecal junction in control and caecectomized animals.

(4) Caecum.

(5) Proximal colon: 1 cm from the caecal–colonic junction.
Colon after intestinal resection

(6) Distal colon: the distal 5 cm of colon above the rectum.

Weight per unit length ratio. The segments of bowel were excised, cleared of residual fat, and the lumen was washed with sodium chloride solution (9 g/l; physiological saline). The segments were blotted dry and weighed. Length was measured by vertical suspension with a standard weight (5 g).

Morphology. Smaller lengths (5 cm) of intestine were then fixed mucosal surface upwards on blotting paper and immersed in 10% formalin solution. Perpendicular sections were cut in the longitudinal axis and stained with haematoxylin and eosin.

Mucosal thickness was measured under light-microscopy by means of an eye micrometer lens. Only true perpendicular sections were measured where the whole crypt base was visible, and the mean of six measurements was recorded.

Mucosal cyclic AMP. Other segments (5 cm) of intestine, from the distal jejunum, caecum and proximal colon, were rinsed in ice—saline and opened out on a cold plate (0-5 °C). The mucosa was scraped off and assayed for cyclic AMP as described below.

Luminal water and bile acid content. Portions of intestinal contents were removed (where available) from the distal jejunum, caecum, proximal and distal colon, weighed and frozen. The gut segments were opened longitudinally and surface mucosa was not included.

One portion was later heated to dryness in an oven and the water content per gram of luminal material calculated. A second portion (0.2 g) was analysed for total bile acid concentration by an enzymic assay using 3α-hydroxysteroid dehydrogenase obtained from Pseudomonas testosteronii (Sigma Chemical Co., Surbiton, Surrey, U.K.) as described by Sheltawy & Losowsky (1975).

Colonic perfusions

Colonic perfusions were carried out in normal intact rats and in 8 week ile-ectomized (50% small intestine) and sham-transected rats.

Under pentobarbitone anaesthesia (Nembutal, 60 mg/kg body weight) the abdomen was opened and the colon was isolated from the caecum by an encircling ligature at the caecocolonic junction. The colon was cleaned by retrograde flushing with warmed saline infused with a syringe via the anus, the luminal contents being delivered via an incision made in the proximal end of the colon. Tubes were inserted into the anus (15 cm long, 4.5 mm o.d.) and into the proximal colonic incision (3 m long, 2 mm o.d.) for collecting and delivering the perfusate respectively.

The perfusate consisted of: NaCl, 105 mmol/l; KCl, 5 mmol/l; NaHCO₃, 25 mmol/l; Na₂SO₄, 7.5 mmol/l; [¹⁴C]polyethylene glycol, 1 μCi/l; unlabelled polyethylene glycol, 3 g/l; gas phase, O₂/CO₂ (95:5); pH 7.4. In test solutions sodium deoxycholate (2.5 mmol/l) and/or sodium ricinoleate (5 mmol/l) was added at the expense of NaCl.

After flushing the colon free from any residual saline or air the perfusate was passed through the colon at a rate of 0.23 ml/min. The temperature was maintained at 37°C by passing the tubing through a thermostatically controlled water bath at this temperature. After an equilibration period of 40 min three samples of perfusate were collected, each for 10 min. After this the colon was excised and the length perfused was measured, whilst suspending it vertically with a standard weight attached. It was then transferred to a cold plate maintained between 0° and −5°C [custom-made, Grant Instruments (Cambridge) Ltd], where the mucosa was scraped off for the estimation of cyclic AMP.

Portions (0.5 ml) of the perfusate before and after perfusion were counted for ¹⁴C radioactivity by using a toluene-based cocktail in a liquid-scintillation spectrometer (Intertechnique S.L. 30). Sodium potassium concentrations were measured by flame-emission spectrometry.

Net absorption rates of water and electrolytes were calculated, relative to changes in concentration of polyethylene glycol, with standard formulae. The rates of absorption were expressed as μl or μmol min⁻¹ 20 cm⁻¹ of colon (20 cm being the approximate length of the whole colon).

Cyclic AMP estimations

Mucosa, which had been scraped off with a spatula, was immediately homogenized in iced 80% ethanol. The time elapsed from removal of the colon was less than 90 s. The precipitate was centrifuged down and analysed for protein (Lowry, Rosebrough, Farr & Randall, 1951) and the ethanolic extracts were evaporated to dryness and taken up in 10 ml of distilled water. Portions (100 μl) in duplicate were assayed for cyclic AMP after the method of Brown, Albano, Elkins & Sgherzi (1971).

The system was tested by comparing the cyclic
AMP content of mucosa from isolated ileal loops (approximately 10 cm long) exposed to physiological saline and crude cholera toxin (Burroughs Wellcome Laboratories) in saline (5 μg/ml) for 3 h. One control loop and one cholera toxin-treated loop was studied in each of six animals. In all rats the control loops were almost empty after 3 h, whereas the toxin-treated loops were swollen. Mucosal cyclic AMP concentrations (+SEM) were 2.02 ± 0.64 pmol/mg of protein in the untreated loops and 3.35 ± 0.59 pmol/mg of protein in the treated loops. This 66% increase was significant (P < 0.01; paired t-test).

**Statistical analysis**

Values were expressed as the mean ± SEM. Significance values shown were derived from the paired or unpaired t-test, where appropriate.

**Results**

The mortality of the ileocectomized series was approximately twice that of the other groups, with only 11 of 24 animals surviving 8 weeks compared with 18 of 23 ile-ectomized animals. All the sham-operated and caecetomized animals survived.

**Weight gain, stool appearance (Fig. 1)**

After a small initial weight loss the caecetomized animals gained weight at similar rates to the control rats. By contrast, the ile-ectomized and ileocectomized animals lost considerable weight during the first 2 weeks. Weight gain by the ileocectomized animals was slower than the ile-ectomized series over the first month. At 8 weeks both these groups of animals weighed the same and considerably less than the control and caecetomized series.

All the control animals produced normal faecal pellets after surgery whereas the caecetomized and ile-ectomized animals had watery diarrhoea for up to 3 weeks. By contrast, the ileocectomized series had more severe diarrhoea for a minimum of 4 weeks and in two animals this persisted for the whole 8 weeks.

**Morphometric measurements**

**Gut weight** (Table 1). At 8 weeks the caecal weight of the ile-ectomized animals was significantly greater than that of control rats (P < 0.001). Similarly both the ile-ectomized and ileocectomized groups had significantly increased weight per unit length ratios at both the jejunal sites compared with control rats (for P values see Table 1). In the ileocectomized animals weight per unit length of the proximal colon was also significantly increased.

By comparison no significant change from control values was found in the jejunum or large bowel of the caecetomized series although there was a significant increase (P < 0.01) at the distal ileum.

**Mucosal thickness** (Table 1). (a) Small intestine.

After either ile-ectomy or ileocectomy the mucosal thickness (combined villous and crypt depth) was increased significantly compared with the control values. No significant change occurred in the caecetomized series. (b) Large intestine.

Mucosal (crypt) depth after ile-ectomy increased significantly in the caecum compared with control values (P < 0.02) but no significant increase was found in the colon. The ileocectomized series had significantly increased mucosal thickness at both colonic sites (for P values see Table 1). After caecetomy no significant change in mucosal depth was found.

**Mucosal cyclic AMP** (Table 2)

No significant differences were found in the values for cyclic AMP between resected and control animals apart from the distal jejunum after 2 weeks (P < 0.05). After ileocectomy colonic cyclic AMP was significantly increased compared with the ile-ectomized animals (P < 0.05), but was not significantly different from control values.
Colon after intestinal resection

Values are mean ± SEM (number of rats). P values represent significance compared with control values: *P < 0.05; **P < 0.02; ***P < 0.002. Small intestinal mucosal thickness is the sum of villous height and crypt depth.

<table>
<thead>
<tr>
<th>Site</th>
<th>Control</th>
<th>Ile-ectomy</th>
<th>Caecectomy</th>
<th>Ileocaecectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal jejunum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (g/cm)</td>
<td>0.07 ± 0.01 (12)</td>
<td>0.09 ± 0.01** (11)</td>
<td>0.07 ± 0.01 (11)</td>
<td>0.09 ± 0.01** (11)</td>
</tr>
<tr>
<td>Mucosal thickness (µm)</td>
<td>597.4 ± 9.0 (11)</td>
<td>756.3 ± 27.5*** (10)</td>
<td>615.0 ± 20.3 (11)</td>
<td>967.0 ± 70.1*** (5)</td>
</tr>
<tr>
<td>Distal jejunum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (g/cm)</td>
<td>0.08 ± 0.03 (12)</td>
<td>0.20 ± 0.20**** (11)</td>
<td>0.07 ± 0.03 (11)</td>
<td>0.36 ± 0.68**** (11)</td>
</tr>
<tr>
<td>Mucosal thickness (µm)</td>
<td>540.2 ± 24.8 (11)</td>
<td>663.8 ± 46.6* (10)</td>
<td>512.2 ± 20.4 (11)</td>
<td>1011.7 ± 134.2** (5)</td>
</tr>
<tr>
<td>Distal ileum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (g/cm)</td>
<td>0.10 ± 0.01 (12)</td>
<td>—</td>
<td>0.16 ± 0.01** (11)</td>
<td>—</td>
</tr>
<tr>
<td>Mucosal thickness (µm)</td>
<td>679.4 ± 50.6 (11)</td>
<td>—</td>
<td>731.0 ± 44.3 (11)</td>
<td>—</td>
</tr>
<tr>
<td>Caecum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (g)</td>
<td>1.3 ± 0.1 (12)</td>
<td>1.9 ± 0.1*** (11)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Mucosal thickness (µm)</td>
<td>195.2 ± 7.4 (18)</td>
<td>227.8 ± 10.3 (18)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Proximal colon</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (g/cm)</td>
<td>0.11 ± 0.03 (12)</td>
<td>0.12 ± 0.06 (11)</td>
<td>0.11 ± 0.03 (11)</td>
<td>0.14 ± 0.11** (11)</td>
</tr>
<tr>
<td>Mucosal thickness (µm)</td>
<td>235.9 ± 14.5 (18)</td>
<td>269.0 ± 18.7 (18)</td>
<td>246.8 ± 11.2 (11)</td>
<td>334.5 ± 28.4** (10)</td>
</tr>
<tr>
<td>Distal colon</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (g/cm)</td>
<td>0.26 ± 0.9-7 (18)</td>
<td>268.4 ± 9.7 (18)</td>
<td>235.1 ± 11.7 (11)</td>
<td>327.3 ± 45.8** (10)</td>
</tr>
<tr>
<td>Mucosal thickness (µm)</td>
<td></td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

In both control and resected animals the cyclic AMP concentrations were lower at all sites after 8 weeks compared with the 2 weeks series. In addition, small-intestinal concentrations were consistently less than in the caecum for both ile-ectomized and control animals at both 2 and 8 weeks. The caecal concentrations tended to be higher than in the colon.

**Luminal water content (Table 2)**

No significant differences were found from the control values at any site in the caecectomized or ile-ectomized animals. By contrast, after ileocaecectomy the water content was significantly greater at both the proximal (P < 0.01) and distal (P < 0.01) colon. In this group the water content in
TABLE 3. Net water and electrolyte transport and mucosal cyclic AMP concentration in the perfused rat colon

Values are mean ± SEM (number of rats). The concentration of deoxycholate and ricinoleate were 2-5 mmol/l and 5 mmol/l respectively. A minus sign indicates secretion. Significance compared with group I (n.s. = not significant): * P < 0·01; ** P < 0·001. (*** P < 0·001 in comparison with group V.)

<table>
<thead>
<tr>
<th>Group</th>
<th>Water transport (μl min⁻¹ 20 cm⁻¹)</th>
<th>Sodium transport (μmol min⁻¹ 20 cm⁻¹)</th>
<th>Potassium transport (μmol min⁻¹ 20 cm⁻¹)</th>
<th>Cyclic AMP (pmol/mg of protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Intact + control solution</td>
<td>33-5 ± 7 (13)</td>
<td>5-4 ± 1-5 (13)</td>
<td>-0-18 ± 0-09 (13)</td>
<td>3-9 ± 0-6 (13)</td>
</tr>
<tr>
<td>II Intact + deoxycholate</td>
<td>-17-5 ± 7** (8)</td>
<td>—</td>
<td>—</td>
<td>6-6 ± 0-9* (9)</td>
</tr>
<tr>
<td>III Intact + ricinoleate</td>
<td>-2-4 ± 6-2* (7)</td>
<td>—</td>
<td>—</td>
<td>4-3 ± 0-2 (7)</td>
</tr>
<tr>
<td>IV Intact + deoxycholate + ricinoleate</td>
<td>-36-8 ± 8-9** (8)</td>
<td>—</td>
<td>—</td>
<td>n.s.</td>
</tr>
<tr>
<td>V Sham + deoxycholate</td>
<td>-7-7 ± 2** (7)</td>
<td>-1-9 ± 0-4** (7)</td>
<td>-0-71 ± 0-03** (7)</td>
<td>7-1 ± 0-9* (8)</td>
</tr>
<tr>
<td>VI Resected + control solution</td>
<td>43-1 ± 4** (7)</td>
<td>7-5 ± 0-6** (7)</td>
<td>-0-14 ± 0-03** (7)</td>
<td>7-6 ± 1-1* (6)</td>
</tr>
<tr>
<td>VII Resected + deoxycholate</td>
<td>7-1 ± 2*** (10)</td>
<td>1-3 ± 0-5*** (10)</td>
<td>-0-68 ± 0-10** (10)</td>
<td>7-0 ± 1-0* (5)</td>
</tr>
</tbody>
</table>

the distal colon was less than that in the proximal colon, but the mean fall in water content was less than in the other three groups.

Luminal bile acid concentrations (Table 2)

After ile-ectomy or ileo-caecectomy the total bile acid concentration in the small intestine was markedly reduced. This was apparent after 2 weeks and no further change had occurred by 8 weeks.

The caecal bile acid concentration was not significantly different from control values at either 2 or 8 weeks. By contrast, the concentrations in the colon were significantly increased at both 2 and 8 weeks (P < 0·05) in the ile-ectomized group but the similar increase found after ileocectomy did not reach statistical significance.

Perfusion studies

Water transport (Table 3). Normal intact rats absorbed water from the control solution at a rate similar to intact rats. By contrast to non-resected rats, however, when perfused with deoxycholate, the colon of ile-ectomized rats absorbed water (P < 0·001). Absorption was still markedly impaired, however, and significantly lower than that from the control solution (P < 0·001).

Electrolyte transport (Table 3). Sodium transport followed a pattern similar to that described for water. Potassium was always secreted into the lumen (net transport); the rate of secretion was increased by deoxycholate (P < 0·001); there was no statistical difference between control and resected animals in this case.

Mucosal cyclic AMP (Table 3). In the 8-week ile-ectomized rats the colonic mucosal cyclic AMP concentration after perfusion with control solution was significantly greater than that observed in the intact animals (P < 0·01).

In the intact normal or sham-operated rats, perfusion of the colon with deoxycholate increased the mucosal cyclic AMP concentration significantly (P < 0·02 and P < 0·01 respectively); by contrast, no further increase was produced by deoxycholate in resected animals.

A linear regression analysis for water transport and cyclic AMP concentrations in the colonic mucosa of intact rats perfused with control and deoxycholate solutions showed a significant negative correlation between water absorption and cyclic AMP (r = 0·6; P < 0·01).

No changes in cyclic AMP concentrations were seen in association with ricinoleate, either alone or when it was combined with deoxycholate.
The results of resection were different in each group of animals. Caecectomy alone had only a minor effect, with some initial slowing of growth and the production of watery faeces during the first 2 weeks. The ile-ectomized animals also adapted rapidly, although weight loss and diarrhoea were more severe. Adaptation after ileocaecectomy was slower and less complete but by 8 weeks there was no difference in weight compared with the ile-ectomized series.

The morphological changes after caecectomy were slight. The small-bowel growth after ileectomy was similar to previous reports (Dowling & Booth, 1967; Nygaard, 1967). Hypertrophy of the large bowel was restricted to the caecum, which contrasts with the study of Nygaard (1967), in which colonic hypertrophy was reported. However, after ileocaecectomy there was significant hypertrophy of both the small- and large-bowel remnants. Caecal and colonic hypertrophy probably results, in part, from the increased bulk or nutritional content of food residue consequent upon ileal resection. It is of interest that the magnitude of the hypertrophy was strikingly less than that observed in the small bowel, suggesting that the colon has a relatively limited capacity to respond to increased luminal bulk at least in the short term. Moreover, in the perfusion studies, although colonic water and sodium absorption rates were greater after ile-ectomy than in control rats, these differences were not statistically significant, confirming the findings of Perry (1975).

The percentage of water in the gut lumen at 8 weeks reflected the observations of stool appearance. The only significant difference from control rats was found in the ileocaecectomized group, where the water content in both proximal and distal colon was increased. However, colonic water absorption was still taking place in these animals since the content in the distal colon was much lower than that found proximally. This indirect evidence suggests that effective water absorption occurred in the colon after ile-ectomy but to a lesser extent after ileocaecectomy.

The bile acid concentration in the distal small-gut remnant of both ile-ectomized and ileocaecectomized animals was very much lower than in the control series. These changes were seen by 2 weeks and there was little additional change after 8 weeks. This could be due either to a decreased pool size, as a result of excessive faecal loss, or to increased bile salt absorption by the remaining small intestine (Perry, White & Dowling, 1972). Faecal wastage of bile salts will lead to a compensatory increase in hepatic synthesis (Austad, Lack & Tyor, 1967). However, the capacity to increase synthesis is limited, and in monkeys it has been shown that an interruption of the enterohepatic circulation of more than 33% will result in a diminished bile salt pool size (Dowling, Mack & Small, 1970). Even if the bile acid pool is reduced the quantity of bile acids passing through the colon should be increased after ile-ectomy.

However, there was only a modest increase in the bile acid concentration in the colon of these animals and throughput could not be estimated because complete faecal collections were not made. Although the increase in concentration is small it is almost double that found in the control animals. The values are similar to the concentrations of deconjugated bile salts known to affect water absorption in the perfused human colon (Mekhjian, Phillips & Hofmann, 1971), and also the rat (Saunders, Hedges, Sillery, Esther, Matsumura & Rubin, 1975) and confirmed in the present study. Most of the bile acids in the colon will be deconjugged by bacteria (Danielsson, Kallner & Sjövall, 1963) and yet, after an initial period of fluid diarrhoea, the rat is able to adapt in such a way as to produce normal stools. This suggests that some form of colonic adaptation takes place whereby the usual cathartic effect of malabsorbed bile acids is reduced.

The alteration of colonic water and electrolyte transport produced by bile acids has already been described in man (Mekhjian et al., 1971) and in the rat (Forth, Rummel & Glasner, 1966; Saunders et al., 1975). In the present study the acute effect in intact rats was associated with an increase in mucosal cyclic AMP concentration, and cyclic AMP concentrations were correlated significantly with the rate of water transport in colons perfused with control and deoxycholate solutions. This is consistent with the observations of Binder et al. (1975) on rat caecum and of Conley, Coyne, Chung, Bonorris & Schoenfield (1976) and Taub, Bonorris, Chung, Coyne & Schoenfield (1977) on rabbit colon.

However, in the ile-ectomized rats, deoxycholate produced a less-striking alteration of fluid transport and no change in mucosal cyclic AMP was detected. Nevertheless, water absorption was inhibited to a considerable extent, suggesting that this effect is produced by mechanisms not involving mucosal cyclic AMP. It is possible that the reduced effect of deoxycholate on fluid transport by the
colon after ile-ectomy is related to enhanced absorption of the bile acids (Perry et al., 1972) and therefore reduced luminal concentrations. It will be necessary in future studies to measure bile acid absorption and to assess the effects of different concentrations of the bile acid on the transport of fluid by the colon of ile-ectomized rats. However, in the chronic studies, increased luminal concentrations of bile acids were not accompanied by increased mucosal concentrations of cyclic AMP when ile-ectomized rats were compared with control rats. It is difficult to compare the acute and chronic experiments and there are discrepancies between the control values for cyclic AMP (Tables 2 and 3). This discrepancy may be related to the very different environments of the mucosa before sampling for cyclic AMP assay in the two studies. Further evidence for non-cyclic AMP-mediated secretion is derived from the studies involving ricinoleic acid. Fatty acid inhibition of water transport is in keeping with previous reports (Binder & Bright-Asare, 1973), but we could detect no difference in cyclic AMP concentration. This is in contrast to a report that ricinoleic acid increases cyclic AMP in colonic mucosa in vitro (Binder, 1974); the difference may relate to whether or not the fatty acid has access to the serosal as well as the mucosal side of the epithelium. Also the addition of ricinoleate to deoxycholate in the perfusion solution abolished the increase in cyclic AMP seen with deoxycholate alone, whereas the secretory effect was further enhanced. The mixture may have formed a micellar complex which does not affect cyclic AMP, yet affects water transport by a different mechanism. A similar discrepancy has been reported by Field, Sheerin, Henderson & Smith (1975) with colera toxin-induced secretion. When adrenaline was added to the system in vitro along with the toxin the increase in cyclic AMP was almost completely abolished despite persistence of the altered electrolyte transport. It seems likely that the component of cyclic AMP related to ion transport is only a small fraction of total mucosal cyclic AMP and changes in this fraction may be difficult to detect.

The enhancing effect of the fatty acid/bile acid mixture on the net secretion of water induced by each separately was of further interest. Lamabadusuriya et al. (1975) have shown that mixed micelles of deoxycholate and oleic acid are significantly less effective in blocking small-intestinal water transport than deoxycholate alone, possibly due to reduced access to the mucosal membrane or a reduction in the active molecular concentration of deoxycholate in the micellar complex. This could be relevant to the effective absorption of water by the colon of ile-ectomized rats, because both bile acids and fatty acids are malabsorbed after extensive ile-ectomy. However, the present evidence suggests that in this respect the colon and small intestine may behave differently, although the explanation for this is not apparent.

In conclusion, this study describes morphological and functional changes in the colon after resection of ileum and caecum and tries to compare the acute and chronic effects of known secretagogues on the colonic mucosa. Effective colonic absorption of water by the colon of ile-ectomized rats cannot be fully explained by the acute experiments, but the evidence suggests that the function of the colonic mucosa is modified by the resection. Other factors must be involved and the physical state of the bile acids and other secretagogues within the colonic lumen may be particularly important.

Acknowledgments
We thank Mr P. Cloke for technical assistance, especially with the bile acid assay, and Mr C. Calladine, who helped with the perfusion studies. J.H.B.S. was supported by a research grant from the Trustees of The Former United Sheffield Hospitals. B.A.C. was supported by The Wellcome Trust.

References
Colon after intestinal resection


