fall-off, however, when the tests were repeated after treatment. The difference between results obtained from in-vivo and in-vitro testing of cellular immunity requires further investigation. In the patients who underwent splenectomy mean serum IgA and IgM levels were significantly depressed after treatment (but not immediately after splenectomy) compared with pretreatment levels. No such change was seen in the other patients after they had been treated. Immunoparesis involving IgM is a contributory factor in the genesis of septicaemia and the spleen is thought to be a major site of IgM synthesis.[7]

The two patients who died with Gram-negative septicaemia showed considerable depression of cellular immunity during their terminal illness; leucocyte counts were low as a result of cytotoxic myelodepression, but neutrophil phagocytosis and killing was enhanced (in case 2). Immunoglobulin levels were normal but were lower than at presentation. Levels of IgM were inappropriately low in response to fulminating septicaemia. In case 3 depressed serum IgM levels and cellular immunity were noted after treatment.

The importance of radiotherapy or chemotherapy, or both, in depressing immunity in patients with Hodgkin's disease who have undergone splenectomy is shown by the patient described by Ammann.[8] This 14-year-old boy received radiotherapy and chemotherapy after splenectomy. He then developed pneumococcal meningitis. After recovery he was immunised with pneumococcal polysaccharides and was unable to respond with antibody formation. Children who have had splenectomy for reasons other than Hodgkin's disease responded normally to immunisation. Ammann[8] suggested that radiotherapy and chemotherapy depress the macrophage processing of antigen and antibody or cellular immunity, or both.

Splenectomy is valuable in staging and managing Hodgkin's disease, but there is evidence that IgA and IgM levels are depressed, and three out of our 17 patients died of septicaemia. More information is required on the morbidity and infective complications of splenectomy so that these may be balanced against the benefits of better initial staging of the patient's disease.

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Sterculia bulk-forming agent with smooth-muscle relaxant versus bran in diverticular disease

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Summary

Sterculia with and without a smooth-muscle relaxant (alverine citrate) had similar beneficial effects on constipation and reduced the transit times in diverticular disease. Intracolonic pressure, however, varied with the preparation used. Though both preparations relieved the symptoms of diverticular disease, the one containing alverine citrate was more effective. Part of the mode of action of bran may be to relax the smooth muscle of the gut, since its actions were more comparable to those of sterculia plus alverine citrate than to those of sterculia alone.

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Introduction

Colonic diverticula are caused by high pressures produced by the segmenting action of the colonic muscle. Segmentation not only propels the colon's contents but halts material moving through the lumen.[1-3] Cineradiography combined with pressure recording shows that natural stimulation or stimulation by drugs produces in the diseased sigmoid an excessive number of waves of high intracolonic pressure. These high pressures favour the progression of established diverticulosis and are almost certainly responsible for the initial herniation of the colonic mucosa. Extreme degrees of segmentation may cause intermittent occlusion of the lumen of the sigmoid and recurrent functional obstruction, which result in episodes of abdominal pain. In about two-thirds of patients this pain is not due to inflammatory diverticulitis,[4] and most clinicians believe that the colic of painful diverticular disease is caused by strong contractions of the colonic muscle.[5] Contractions of the colon have been correlated with episodes of severe abdominal pain in the "irritable bowel syndrome."[6] Hence the behaviour of the colonic muscle probably plays an important part in the genesis of diverticular disease and other colonic disorders.

The intraluminal pressure may be reduced in diverticular disease by adding cereal fibre to the diet in the form of millers' bran,[7] particularly when the fibre is coarsely ground.[8] Not all patients, however, tolerate bran, and as the bulk-forming agent sterculia (Normacol) has been shown to relieve the symptoms of diverticular disease[9] we decided to test two preparations of sterculia—one of sterculia alone and one containing a smooth-muscle relaxant—to see what effect they would have on intra-

colonic pressures and transit times and on the symptoms of proved diverticular disease.

Materials and methods

The two preparations of sterculia—here designated A (sterculia alone) and B (sterculia plus the smooth-muscle relaxant alverine citrate)—were tested in two groups of 10 patients suffering from symptomatic diverticular disease without organic stenosis. The preparations were made similar in taste and appearance and were given in comparable dosage—namely, 10 g daily. Each was given for one month. Their identities were unknown both to the patients and to the consultant who assessed the clinical effects. Colonic motility and transit times were measured and the patients interviewed before and at the end of each month of treatment. After each course the patients were given no medication for one month, partly to see how long the beneficial effects lasted, and partly to estimate the severity of symptoms when these returned. For comparison, all the patients were then given coarse bran[8] for one month.

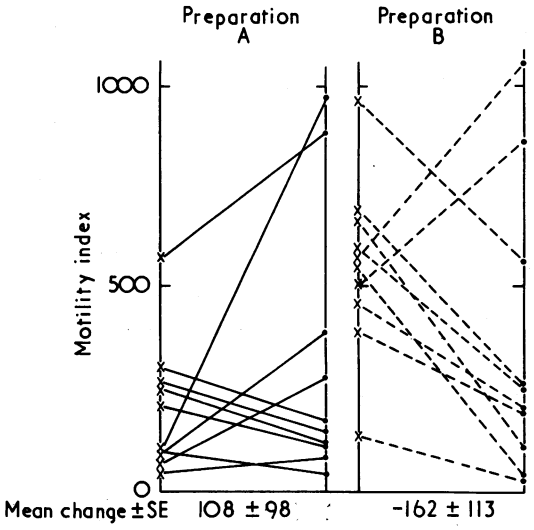

FIG 1—Colonic motor activity in basal period. Motility index is recorded before and after administration of preparations A and B.

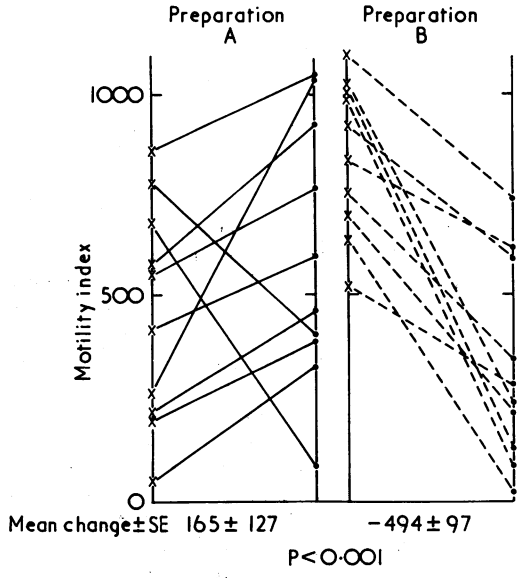

FIG 2—Colonic motor activity after food. Motility index is recorded before and after administration of preparations A and B. Changes produced by the preparations were significantly different.

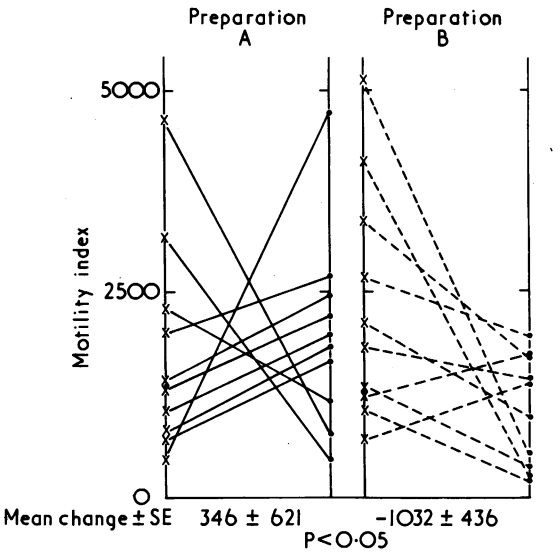

FIG 3—Colonic motor activity after cholinergic stimulation by neostigmine. Motility index is recorded before and after administration of preparations A and B. Changes produced by the preparations were less pronounced than after food.

Pressure measurements—Motility was recorded with the use of a multilumen tube inserted into the distal colon.[10] Pressure was measured before food (basal period), after food, and after intramuscular neostigmine 0·75-1·0 mg The wave forms were given an x and y significance on an analogue-to-digital converter, from which a motility index was calculated. Changes in motility indices with the two preparations were compared by means of Student's *t* test.

Transit times—The patients swallowed 40 barium-impregnated pellets (Portex Limited), the transit time being calculated as the time taken for 32 (80%) of these to be passed.[11]

Clinical assessment of effect on symptoms—Each patient filled in a progress sheet giving the main symptoms before treatment and showing the effects of sterculia at the end of one month. Symptoms were grouped under three main headings—constipation, pain, and other. Severity was graded by calculating a clinical score for each symptom group (table I), the maximum score possible being five for any group and thus 15 for all three. To assess pain or constipation patients were allowed to take medication once if needed and were graded according to their response to it.

Results

INTRACOLONIC PRESSURES

In the basal period the mean motility index (± SE) in the 10 patients given preparation A for one month rose by 108 ± 98, whereas in those given preparation B it fell by 162 ± 113 (fig 1). Because of the wide variations in control values, however, no valid comparisons could be made.

Fig 2 shows the effects of the two preparations on the pressures evoked by food. Preparation A increased the mean motility index by 165 ± 127; by contrast, after preparation B the mean motility index fell by 494 ± 97. This difference was highly significant ($P<0·001$).

TABLE I—*Clinical scores used to grade severity of symptoms*

Constipation	Score	Pain	Score	Other	Score
Nil	0	Nil	0	Nil	0
Occasional	1	Discomfort	1	Flatus	1
Relieved by medication	2	Discomfort plus bearing down	2	Distension	1
Not relieved by medication	3	Intermittent pain	3	Mucus per rectum	1
Alternating with diarrhoea	4	Relieved by medication	4	Urinary symptoms	1
Constipation and bleeding	5	Not relieved by medication	5	Diarrhoea	1

The effects of neostigmine stimulation before and after the two preparations are shown in fig 3. Preparation A increased the mean motility index by 346 ± 621, whereas preparation B reduced the mean motility index by 1032 ± 436. This difference was significant ($P<0.05$). The mean reduction after food (fig 2) was greater than after neostigmine because of the wider distribution of the results in the latter case.

TRANSIT TIMES

Ten patients with untreated diverticular disease were found to have an average transit time of 86 ± SE 26 hours. Findlay *et al*,[7] using the same method, found average transit times of 66·3 ± 18·1 hours in normal people and 93·4 ± 13·8 hours in patients with diverticular disease. In our series preparation A reduced the average transit time to 59·2 ± 16·1 hours, while preparation B reduced the average transit time to 68·4 ± 20·2 hours.

CLINICAL EFFECTS

A clinical score that reflected any change in the severity of the symptoms was derived in the 20 patients, as described above. The clinical score before treatment was halved to adjust it to 10 "notional" patients to compare with the 10 patients each receiving preparations A and B (table II). Before treatment the total clinical score was 121. This fell to 56 after preparation A and to 31 after preparation B. The "pretreatment" scores for constipation and pain were 50 and 46 respectively. These were reduced to 3 and 24 with preparation A, and to 9 and 9 with preparation B. "Other" symptoms—namely, the passage of blood and mucus, diarrhoea, and the excessive passage of flatus, together with sensations of flatulence and distension—accounted for a pretreatment clinical score of 25; this rose to 29 after preparation A but fell to 13 after preparation B. After one month without treatment the total clinical score returned to 112, which was near to the original value. After coarse bran the scores were closer to those obtained with preparation B than to those obtained with preparation A.

The numbers of returns for each score were also listed, as shown in table III. The number of times each compound reduced the symptoms of constipation or pain to a trivial level (less than 2) was compared with the number of times it failed to do so. For constipation, preparations A and B and bran were equally effective in reducing the score; for pain, however, both preparation B and bran were significantly more effective than preparation A (fourfold test: $P<0.005$) in producing, more often, low scores.

Discussion

Preparation A contained 62% sterculia and was a simple bulk former, whereas preparation B contained the same proportion of sterculia with 0·5% alverine citrate, a smooth-muscle relaxant used to relieve "spastic colon" and dysmenorrhoea.[12]

Preparation A raised the mean intraluminal pressure in the resting sigmoid colon after it had been activated by food and neostigmine. By contrast, preparation B reduced the motility index basally, after food, and also after neostigmine. The difference between the effects of the two preparations reached greater statistical significance after food than after neurohumoral stimulation. The changes after preparation B were comparable to those that result from one month's treatment with bran[7] and also to the pressure reduction after the use of coarse bran.[8] Coarse bran was thought by Kirwan *et al*[8] to absorb water more readily; it may dilute or remove an irritant that the antispasmodic in preparation B antagonises.

Two types of diverticular disease have been described. Some colons beset with diverticula are extremely active (spastic colon diverticulosis), and others that are fibrous due to previous inflammatory episodes are less able to contract and generate pressure. Possibly intraluminal pressure studies might enable the two types of diverticular disease to be separated, so that treatment might be given a more logical basis.[1 13] Theoretically, preparation B should be the more effective in lessening the activity of the colonic muscle and hence should reduce the intracolonic pressures, and our results support this contention. The average transit time of 86 hours in 10 patients with diverticular disease was reduced to 59 hours by preparation A and to 68 hours by preparation B. These transit times, however, are still longer than the 45 hours recorded for British vegetarians and patients adding millers' bran to their diets.[14 15] Not surprisingly, preparation B, which reduces the motility of the colon, was slightly less effective in increasing the speed at which the bowel contents were propelled through the intestine.

Both preparations relieved constipation. Our results suggest that sterculia alone (preparation A) should be used in patients with diverticulosis who complain of constipation, while it would be better to give it coupled with a smooth-muscle relaxant (preparation B) to patients with "spastic" diverticulosis or painful diverticular disease. Relaxation of the segmental contraction rings widens the colonic lumen and facilitates the onward passage of the faecal stream, as was shown by cineradiography for pethidine by Painter *et al*.[3]

When the clinical effects of the two preparations on pain, abdominal distension, flatulence, and episodes of diarrhoea were considered, preparation B was found to be the more beneficial and to compare more favourably than preparation A with the actions of coarse bran. This is not surprising if the colic of painful diverticular disease is attributed to contraction of the

TABLE II—*Symptom scores before and after preparations A and B, and, one month later, scores before and after bran in the same patients*

	Sterculia			Bran		
	Before*	After		Before*	After	
		A	B		Formerly given A	Formerly given B
Constipation	50	3	9	56	10	9
Pain	46	24	9	36	12	10
Other	25	29	13	20	8	9
Total	121	56	31	112	30	28

*Adjusted to score of 10 patients.

TABLE III—*Numbers of patients in whom preparations A and B and bran (in the same patients) reduced constipation and pain to trivial levels (scores less than 2)*

Score	Constipation				Pain			
	Sterculia		Bran		Sterculia		Bran	
	A	B	Formerly given A	Formerly given B	A	B	Formerly given A	Formerly given B
0	7	1	6	4		4	1	2
1	3	9	4	3	3	3	6	7
2				3	1	3	3	1
3					5			
4					1			
5								

colonic muscle.[2 5] Flatulence, abdominal fullness, and intermittent diarrhoea may also owe their origin to a disordered intestinal motility caused by a low-residue diet.[9] The addition of alverine citrate to the bulk-forming sterculia was also found to be clinically effective in relieving this group of symptoms. Hence, this preparation may be used in the treatment of diverticular disease in patients who cannot tolerate millers' bran.

We are grateful to Norgine Limited for supplies of preparations A (Normacol Special) and B (Normacol Antispasmodic). This work was done during the tenure of Scottish Hospital Endowments Research Trust grant No 418 to Mr A N Smith. Lieutenant-Colonel G S Srivastava participated in this work while on two years' secondment to the UK from the Indian Army Medical Corps.

Requests for reprints should be sent to Dr A N Smith.

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Metronidazole in prevention and treatment of bacteroides infections after appendicectomy

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Summary

The frequency of non-clostridial anaerobic infection was studied in 95 patients who had undergone acute appendicectomy: 49 received prophylactic metronidazole and 46 received placebo. Anaerobic infection did not develop in any of the metronidazole-treated patients, but infections did develop in nine (19%) of the 46 controls. Metronidazole is conveniently administered by suppository to patients who cannot take oral drugs. Five patients with intra-abdominal infections caused by non-clostridial anaerobes were successfully treated with metronidazole.

Introduction

Acute appendicitis is a common condition that usually requires emergency surgery. The commonest complication of appendicectomy is undoubtedly surgical sepsis, the incidence of which may vary from 4% for normal appendices to 77% for gangrenous or perforated appendices. The average frequency of postoperative infection is probably about 30%.[1-4] Although some of these infections are relatively trivial they often delay discharge from hospital and subsequent return to work, and some are serious or even life-threatening. In an effort to reduce the incidence of sepsis after appendicectomy surgeons have used various topical and systemic prophylactic antibacterial agents. Topical prophylactic agents have included ampicillin, Polybactrin, and tetracycline, while ampicillin, tetracycline, penicillin, lincomycin, and clindamycin have all been used systemically.[3 5-10]

Although none of the prophylactic procedures reported are consistently effective, appropriate systemic antibiotics generally reduce the incidence of intra-abdominal sepsis, while appropriate local treatment reduces the incidence of wound infection.[3 6 8]

Most reports on the chemoprophylaxis of sepsis after appendicectomy have been concerned solely with clinical aspects of infection and have not considered the nature of the infecting agents. This is unfortunate because in this condition the effectiveness of any prophylactic antibiotic clearly depends on its spectrum of antibacterial activity. It is still widely believed that abdominal infections after surgery are usually caused by the Enterobacteraceae and enterococci. As long ago as 1898, however, Veillon and Zuber[11] reported on the common occurrence of non-sporing anaerobes in cases of appendicitis, an observation that was subsequently confirmed and amplified.[12] It was also shown[13] that the foul-smelling pus, which is so commonly associated with these infections, is always due to non-sporing anaerobes, and that true *Escherichia coli* pus is odourless.

Recently there has been an increasing awareness of the importance of non-sporing anaerobes as the major cause of sepsis after surgery of the gastrointestinal tract or female genital tract.[14-16] This matter has been highlighted in relation to appendicitis by Leigh *et al*,[9] who recovered *Bacteroides fragilis* from 90% of wound infections after appendicectomy. Our own experience leaves no room for doubt that most infections that develop after intestinal surgery are caused by non-sporing anaerobes.

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