quantitative analysis of the pressure tracings failed to reveal any preponderance of waves of high intracolonic pressure in diverticulosis. The segments that actually bore diverticula did produce more waves of longer duration than other segments, but such waves represented only a small proportion of the pressure waves recorded and would not appear to be important in the genesis of diverticula.

Despite the approximations inherent in its definition, the colonic motility index is the only measure so far available that allows the motor activity of two groups of colons to be compared with regard to the production of pressures. These indices were calculated and showed a considerable general measure of agreement in each group of leads, while their average values in each group of leads were very similar. This suggests that the total pressures generated or withstood by the colon in health and in diverticulosis are essentially the same under resting conditions.

However, a variety of factors influences the motor behaviour of the human colon, such as eating, drinking, defaecation, and emotion (Chaudhary and Truelove, 1961; Connell, 1961). Therefore the effects of these stimuli on the pressures in the sigmoid colon deserve to be studied as it is possible that they play an important part in the aetiology of the disease by altering the intracolonic pressure patterns.

SUMMARY

The herniation of the colonic mucosa in diverticulosis may be the result of abnormally high intracolonic pressures, of weakness of the muscularis propria, or of a combination of these two factors.

A systematic study has been made of the intraluminal sigmoid pressures in diverticulosis coli and in the healthy sigmoid colon employing open-ended water-filled polythene tubes coupled to a Cambridge multi-channel pressure-recorder.

Under basal conditions no evidence was obtained of any major difference in the intraluminal pressures in diverticulosis and in health when the recordings were analysed in various ways.

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Part II The effect of morphine

Morphine is still the most important analgesic. Much conflicting evidence has accumulated over the past 70 years regarding its effect on the intestine. Vaughan Williams and Streeten (1950, 1951) have pointed out that the opposing views of previous investigators are largely the result of the limitations of the techniques they employed, and that many of the differing conclusions that have been expressed can be reconciled when this fact is appreciated. Nevertheless, even though its mode of action and, in particular, its effect on the human intestine, are so little understood, the drug is very widely used. As it seemed possible that morphine might alter the pattern of the intracolonic pressures, we measured its effect on the pressures in the human colon both in health and in diverticulosis coli.

METHOD

The method of recording the intracolonic pressure has been described in Part I of this study. A large number of the subjects whose resting patterns have been described were given 10 mg. of morphine sulphate, either intravenously or intramuscularly, after their resting patterns had been recorded for one hour. The intracolonic pressures were recorded for a further hour following this injection and the tracing thus obtained was called the 'post-morphine' pattern. Hence it was possible to compare the resting patterns of intrasigmoid pressures with those observed after morphine in both health and diverticulosis.

RESULTS

EFFECT OF MORPHINE ON THE PRESSURE PATTERNS IN THE NORMAL SIGMOID COLON When given intravenously, the effect of morphine became apparent almost at once in almost every patient (Fig. 1). Initially the basal intraluminal pressure nearly always rose one or two millimetres of mercury and, superimposed on this rise, there occurred a succession of waves of high pressure, which continued for several minutes. These dramatic changes were usually followed by a period lasting a few minutes during which the pressure tracing was more or less flat before another series of waves was generated. The height of the waves in the initial complex varied from lead to lead. The height of these initial pressures was seldom exceeded by the waves seen

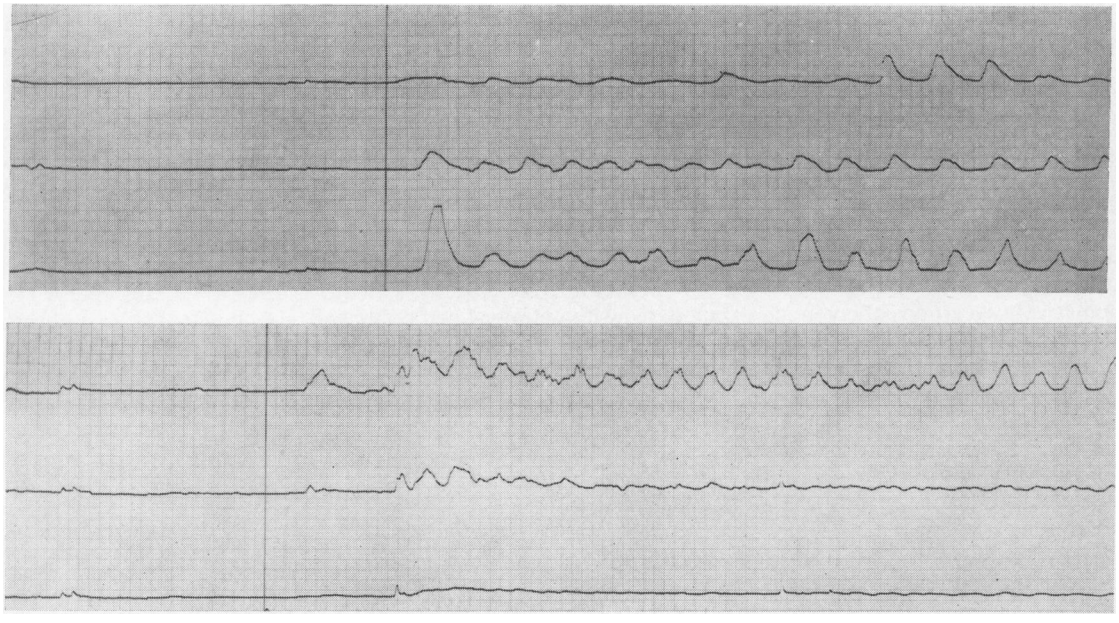

FIG. 1. *The effect of an intravenous injection of morphine on the intrasigmoid pressures. The vertical line indicates the completion of the injection. The upper tracing was obtained from three leads in a normal sigmoid colon, which reacted to the injection within 16 seconds. In the lower tracing, lead 1 was related to diverticula, lead 2 was in the sigmoid below the level of diverticula, and lead 3 was at the recto-sigmoid junction. Lead 1 recorded pressures approaching 50 mm. Hg near the diverticula following morphine.*

in the periods of rhythmic pressure production that occurred later.

Once the initial pressure complex had subsided, the basal pressure was found to have fallen to approximately atmospheric pressure. Morphine was not found to cause any consistent change in the resting basal level of pressure. The pattern of pressure waves that followed administration of the drug was, however, markedly different from the resting pattern and was characterized by the following phenomena.

A rhythmical succession of small pressure waves would occur on one or more leads. They apparently arose independently at each level of the gut, because, when all the pens were active, their movements were not synchronous. Sometimes when all three pens were recording waves, the impression was given that they acted in concert, but careful examination of the tracing did not confirm this, nor was there any definite evidence to suggest that these waves of pressure travelled along the bowel in either direction so as to affect the recording tips in succession (Fig. 2).

Each series of pressure waves would frequently begin with a small wave lasting for less than 10

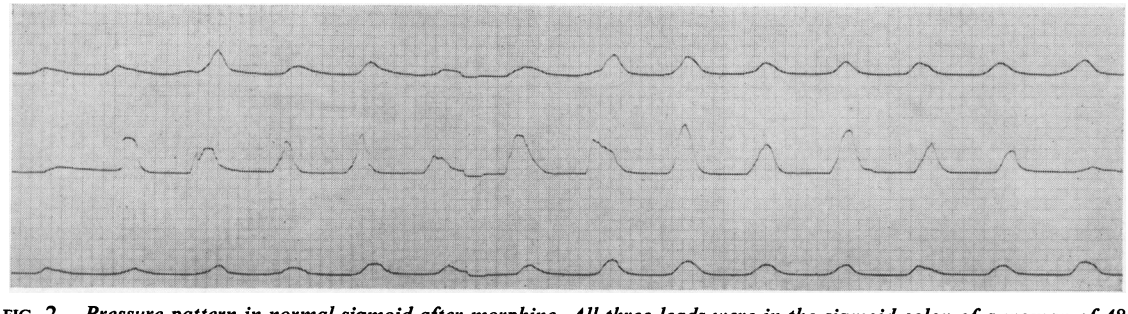

FIG. 2. *Pressure pattern in normal sigmoid after morphine, All three leads were in the sigmoid colon of a woman of 48 who had been given morphine. Waves of pressure occurred rhythmically at all three levels of the sigmoid. The similarity of the form of successive waves suggests that they were produced by a similar mechanism.*

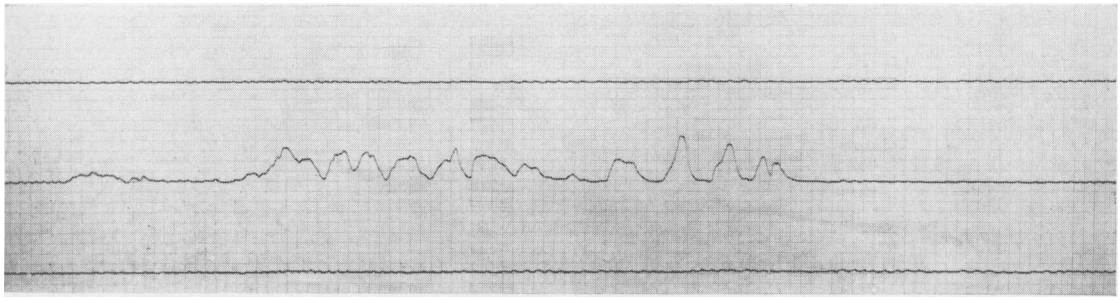

FIG. 3. *Localization of pressure in normal sigmoid colon after morphine. All three leads were in a normal sigmoid colon (the two lower tracings of Figure 1 in Part I were obtained from this subject). Lead 2 recorded pressures of up to 40 mm. Hg, but no change of pressure was registered by leads 1 and 3, whose tips were situated on either side of lead 2 at a distance of 7·5 c.m. Obviously the sigmoid can localize high pressures to a short length of its lumen.*

seconds and reaching a height of a few millimetres Hg, and this would be followed by a succession of waves of similar duration, but of gradually increasing amplitude, sometimes reaching a height of over 40 mm. Hg, but usually being less than 20 mm. Hg. After a few waves of this higher amplitude had occurred, the process was reversed, and, while their duration remained similar, the succeeding waves were of ever-lessening height, until finally the pressure tracing appeared flat. The intervals between the individual waves that constituted such a bout of pressure production were remarkably constant in any one subject, and usually lasted for periods of between 20 and 30 seconds. Following a pressure complex, the tracing would remain almost flat for several minutes, when another pressure complex would occur. This sequence of events was usually repeated several times during the hour. On occasions, one or all the pens would remain almost stationary for long periods of time, but this was exceptional.

When morphine was given intramuscularly, its effects only became apparent after nine to 15 minutes, when a similar series of pressure complexes would occur, but without the dramatic initial complex that followed its administration by the intravenous route.

The sequence of events described above characterized the 'post-morphine' pattern of pressures in the sigmoid colon, and the similarity of the form of these waves strongly suggested that a common mechanism was responsible for them. Moreover, the independent generation of differing levels of pressure in different segments of the sigmoid, separated only by 7·5 cm., suggested that this mechanism and the resultant rises of pressure were local in origin and site. Figure 3 shows a three-channel pressure tracing in which the middle lead recorded waves of up to 40 mm. Hg while the other leads, which were situated in segments of the sigmoid colon on either side of it and only 7·5 cm. distant from it, were completely unaffected by these events. Such observations point to the existence of some mechanism whereby the sigmoid colon can isolate regions of high pressure and they suggest that morphine activates this mechanism.

EFFECT OF MORPHINE ON THE PRESSURE PATTERNS IN DIVERTICULOSIS COLI The 'post-morphine' pattern of pressure waves was studied in the same way in patients with diverticulosis coli. The tracings were divided into two groups as described in Part I of this study, depending on whether the leads were recording pressures from segments that bore diverticula or from apparently normal segments.

The intravenous administration of morphine usually resulted in the same rapid and dramatic change in the tracing that was seen in normal subjects but those leads that were related to diverticula commonly recorded higher waves of pressure than those registered from unaffected segments of the bowel. The intramuscular injection of morphine resulted in the appearance of a similar pattern of recurrent pressure complexes after an initial delay of 10 to 15 minutes.

PRESSURE PATTERNS FROM LEADS NOT IN RELATION TO DIVERTICULA After morphine, the segments that did not actually bear diverticula produced pressure tracings similar to those seen in normal subjects following administration of the drug. There was the same tendency for the pressure waves in any one bout of activity to increase in amplitude up to a peak value and then to decrease until the tracing was flat. The regular recurrence of these pressure complexes was again observed. The intervals between the individual waves of these complexes were again remarkably constant and were similar to those observed in the normal subject. Sometimes the pens would show little movement for long periods, but this was unusual. Examination of these tracings revealed

no obvious difference between them and those of normal subjects after the administration of morphine.

PRESSURE PATTERNS FROM LEADS IN RELATION TO DIVERTICULA It was at once apparent that the form of the pressure complexes differed from those already described (Fig. 4). Although the same rhythmic pressure changes were seen, these were interspersed with waves whose ascending and descending limbs were more precipitous and whose peaks reached to exceptional heights. The amplitude of these waves was frequently greater than that of the initial complex that followed the intravenous injection of morphine. Their peaks often exceeded 50 mm. Hg and pressures of up to 90 mm. Hg were recorded. On several occasions the limits of the pens' excursions were exceeded so that the automatic cut-out operated and the pens had to be reset. These waves of very high pressure sometimes occurred alone, but often several occurred in succession in the course of a single pressure complex. Up to 20 such waves occurring in quick succession have been recorded.

These very high waves were characterized by their abrupt crescendo and the equally rapid fall of their downstroke, but their duration was usually the same as the waves that have been previously described. Consequently they appeared like mountain peaks

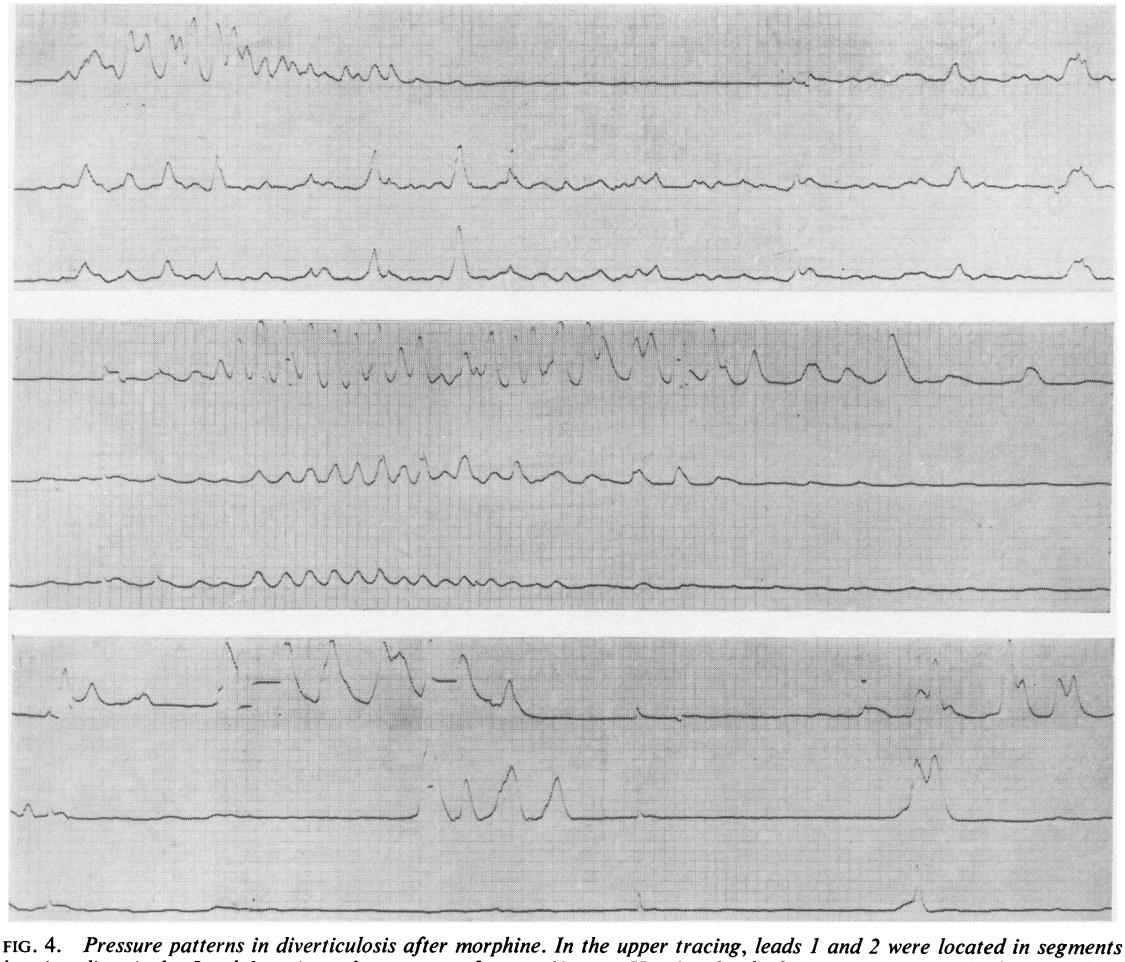

FIG. 4. *Pressure patterns in diverticulosis after morphine. In the upper tracing, leads 1 and 2 were located in segments bearing diverticula. Lead 1 registered pressures of up to 60 mm. Hg. Similar high pressures occurred after morphine in segments that bore diverticula in a patient recovering from acute diverticulitis (lead 1 of middle tracing), while leads 2 and 3, which were below the level of diverticula, registered lower pressures. Leads 1 and 2 of the bottom tracing were related to diverticula and recorded very high pressures of up to 76 mm. Hg. The high pressures registered by lead 1 were not constantly recorded by lead 2, thus demonstrating the ability of the sigmoid to localize pressure.*

among the foothills of the lower waves, whose contours were less steep. The intervals between successive high waves were sometimes similar to those which separated the low waves, but frequently were much shorter, and lasted only a few seconds.

Inspection of the tracings suggested that the number and duration of waves recorded from leads in relation to diverticula were similar to those seen in previous patterns, but that the height they reached was greater. Their different wave form showed that a greater rate of change of pressure occurred after morphine in segments affected by the disease than occurred in unaffected segments. This impression was confirmed when the number of these waves and their dimensions were studied quantitatively.

QUANTITATIVE ASPECTS OF PRESSURE WAVES IN THE SIGMOID COLON IN NORMAL SUBJECTS AND THOSE WITH DIVERTICULOSIS AFTER ADMINISTRATION OF MORPHINE

Table I shows the number of patients studied and the number of observations made. On an average two leads reached the sigmoid in normal patients while

TABLE I

NUMBER OF SUBJECTS STUDIED, OBSERVATIONS MADE, AND LEADS FROM WHICH PRESSURE TRACINGS WERE OBTAINED AFTER MORPHINE

	Number of Subjects	*Number of Observations*	*Number of Leads Analysed*
Normal subjects	21	21	42
Subjects with diverticulosis	25	26	19 (related to diverticula) 26 (not related to diverticula)

the structure and angulation of the bowel in diverticulosis often prevented more than one lead passing beyond the recto-sigmoid junction. Often two leads in the same patient were divided between the two groups 'in relation' and 'not in relation', so

TABLE II

NUMBER OF WAVES BY AMPLITUDE OF WAVE IN SIGMOID COLON AFTER ADMINISTRATION OF MORPHINE[1]

Amplitude of Waves (mm. Hg)	*Normal*	*Diverticulosis*	
		Leads not Related to Diverticula	*Leads Related to Diverticula*
1-9	58·2	70·7	67·7
10-19	10·2	13·9	23·8
20-29	1·9	2·5	8·4
30-39	0·8	1·0	3·9
40-49	0·3	0·2	1·9
50-59	0·05	0·1	1·3
60+	0·0	0·2	1·3
Total	71·4	88·6	108·3

[1]Mean values per lead per 60 minutes' recording time.

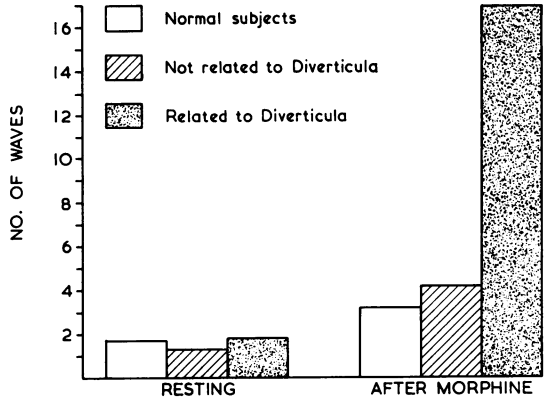

FIG. 5. *Average number of waves exceeding 20 mm. Hg in height (per lead per hour) in the sigmoid colon before and after morphine.*

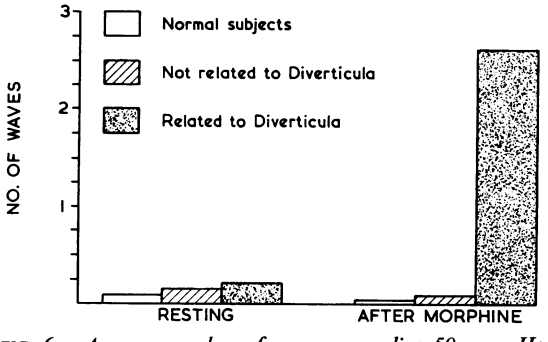

FIG. 6. *Average number of waves exceeding 50 mm. Hg in height (per lead per hour) in the sigmoid colon before and after morphine.*

that to some extent such a patient acted as his own control.

The 'post-morphine' tracings were analysed in the same way as the resting patterns, which were described in Part I of this study. The results are given in Table II, which corresponds in construction to Table II of Part I of this study, so that comparison shows the effect of morphine.

Morphine increased the number of pressure waves in all groups. Small waves of less than 10 mm. Hg were roughly doubled in frequency. Waves of between 10 and 19 mm. Hg were increased considerably in all three groups, being about five times as frequent in the normal colon, and even more common in segments bearing diverticula.

After morphine, waves of moderate height, that is between 20 and 50 mm. Hg, were doubled in frequency in the normal group, quadrupled in the 'not related' group, and became 10 times more frequent in the leads recording pressures from

segments bearing diverticula. High waves of over 50 mm. Hg occurred on average only about once every five hours in the three groups of segments under resting conditions. After morphine such waves occurred in segments of the sigmoid that actually bore diverticula about once in every 24 minutes, but were not increased in frequency in the other two groups of segments.

Figure 5 shows graphically that the number of waves of over 20 mm. Hg were four times as common after morphine in affected segments. This difference in the response of the affected segments to morphine became even more apparent when the high waves of over 50 mm. Hg were similarly represented (Fig. 6).

Such a differential response of the segments that bore diverticula was not seen when the duration of the waves was considered (Table III). The vast majority of waves lasted for less than 30 seconds. Waves of longer duration were more common in diverticulosis than in health, but the difference was not impressive.

TABLE III

NUMBER OF WAVES BY DURATION OF WAVE IN SIGMOID COLON AFTER ADMINISTRATION OF MORPHINE[1]

Duration of waves (sec.)	*Normal*	*Diverticulosis*	
		Leads not Related to Diverticula	*Leads Related to Diverticula*
1-9	14·0	20·2	24·6
10-19	40·0	44·5	60·1
20-29	12·9	14·8	14·6
30-39	2·0	4·9	4·6
40-49	1·4	1·6	2·0
50-59	0·6	1·3	1·3
60+	0·5	1·3	1·1
Total	71·4	88·6	108·3

[1]Mean values per lead per 60 minutes' recording time.

THE EFFECT OF MORPHINE ON THE COLONIC MOTILITY INDEX This index has been discussed in Part I of this study. It is an approximate measure of the 'total pressure' generated or withstood by that part of the colon in the vicinity of a recording lead and may be used to compare the activity of two groups of colons. The value of this index was calculated for each of the leads from which the mean values of the post-morphine pressures that have been given were derived. These indices are shown in Fig. 7 together with the values obtained under basal or resting conditions.

Morphine doubled the average resting value in normal subjects, trebled it in the 'not related' group of leads, and increased it sixfold in those leads that were related to diverticula. It is apparent that those segments that were beset with diverticula reacted excessively when stimulated by the drug.

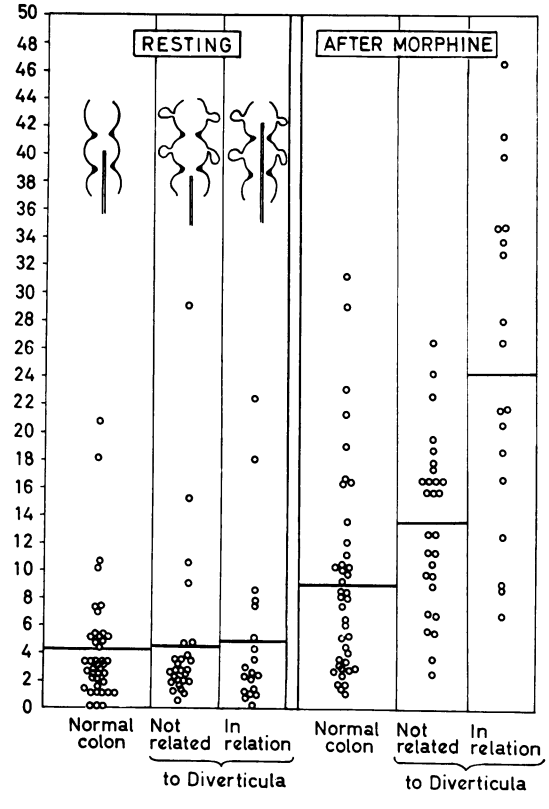

FIG. 7. *Colonic motility index: resting and 'post-morphine' values. The horizontal lines represent the mean values of indices in each column.*

DISCUSSION

The observation that morphine causes those segments of the colon that bear diverticula to react excessively is of great theoretical interest. Whether this differential response precedes the appearance of diverticula or follows upon the structural changes in the bowel wall that accompany diverticulosis is not yet known. The most we can say from the present study is that in one patient, in whom only a single diverticulum was detected, the segment bearing it showed an exaggerated response to morphine. This suggests that the differential motor response is present in an early stage of the disease and at least may be partly responsible for the progressive nature of diverticulosis.

Obviously morphine is not the stimulus which usually activates the sigmoid colon and it would therefore be of great interest to study the effects of other stimuli to discover whether the exaggerated response of the affected segments is peculiar to morphine. If it could be shown that other stimuli

cause a similar differential motor response, such a finding would suggest that naturally occurring stimuli might also elicit a different pattern of intraluminal pressures in the neighbourhood of diverticula.

While the foregoing observations are of theoretical interest, the effect of morphine on the intrasigmoid pressures is of immediate practical importance. Morphine is commonly used as an analgesic and once it is realized that its administration is followed by the generation of very high pressures in those segments that bear diverticula, the wisdom of giving the drug to patients suffering from acute diverticulitis must be questioned. On theoretical grounds it might be argued that morphine might cause the colonic muscle to contract so as to narrow the necks of diverticula and thus protect them from the full force of these pressure waves, but simultaneous cineradiography has shown conclusively that this is not the case (Painter, Truelove, Ardran, and Tuckey, 1964).

Morphine causes high pressures to be generated in the lumen of the sigmoid colon that bears diverticula and as this pressure is transmitted to the diverticula, the drug may have been responsible for some cases of perforated diverticulitis. There is therefore a prima facie case for withholding morphine from patients with acute diverticulitis.

SUMMARY

A therapeutic dose of morphine, given either intravenously or intramuscularly, causes the normal colon to generate an increased number of pressure waves compared with the number generated under resting conditions. In diverticulosis, morphine elicits an essentially similar response from those segments that do not bear diverticula. By contrast, segments bearing diverticula show an excessive response to morphine in that they produce many waves of high pressure.

This differential response of the affected part of the sigmoid is of theoretical interest in relation to the genesis and progression of diverticulosis.

From a practical standpoint, there appears to be a prima facie case against using morphine in acute diverticulitis.

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