INTESTINAL MOTILITY IN MAN.

A STUDY COMBINING THE USE OF INTRALUMINAL PRESSURE RECORDING AND CINE-RADIOGRAPHY WITH SPECIAL REFERENCE TO NORMAL SUBJECTS, PATIENTS FOLLOWING PARTIAL GASTRECTOMY AND PATIENTS WITH THE IRRITABLE COLON SYNDROME

THESIS

SUBMITTED FOR THE

DEGREE OF DOCTOR OF MEDICINE

IN THE

UNIVERSITY OF ADELAIDE, SOUTH AUSTRALIA

BY

ANDERS GUSTAF WANGEL

CONTENTS

ACKNOWLEDGEMENTS

This work was undertaken and completed during the two-year tenure of a Lectureship in the Department of Medicine at the University of Adelaide, South Australia. It is a pleasure to thank Professor H.N. Robson for his interest in the work, and my colleagues in the Department for stimulating discussions. I am particularly grateful to Dr. D.J. Deller, Michell Research Worker, who assisted in the project, for his encouragement and constructive criticism. The Grass Polygraph was kindly made available by Professor R.P. Jepson of the Department of Surgery, University of Adelaide. The Board of the Royal Adelaide Hospital allowed me to use the X-ray Image Intensifier and the cine camera, and I am grateful for the cooperation of the Chief Radiographer, Mr. Jones, and his staff.

I am indebted to the Honorary Physicians and Surgeons of the Royal Adelaide Hospital and Queen Elizabeth Hospital who allowed me access to their patients, and to the many general practitioners who also cooperated in this respect. The patients themselves submitted to investigations without having any assurance that this would be to their benefit. Many of them, who were well, agreed to spend a number of days in hospital for the purpose of this study. Many of the control subjects were volunteers from Yatala Labor Prison, Northfield, and my thanks are due to these men and to Mr. Allen and his staff of H.M. Gaols and Prisons Department.

Miss Heather Martin provided valuable technical assistance and Miss Joan Devaney undertook the onerous task of typing the thesis. I am also indebted to Mr. W. Nolan for photographic reproduction of the tracings and graphs. Miss Becket, Medical Artist, produced the diagrams in Figures 1 and 2.

CHAPTER I

INTRODUCTION

The study of the function of the alimentary tract was particularly intense during the early years of this century. The names of Bayliss, Starling, Cannon and Pavlov first became familiar in connection with their studies of gastro-intestinal physiology. Thus in the first two decades of this century major advances were made in the understanding of intestinal motor function, gastric secretion and the influence of the psyche on the functions of the digestive tract.

However, a change in research interests followed upon Einthoven's discovery of the string galvanometer and the application to medicine of the physical principles of gases and fluids by Haldane, Barcroft and Starling. Physiologists tended to relinquish the gut to the surgeons and to concentrate their efforts on the problems of cardiology, respiratory function and metabolism. This consequently left gastro-enterology one of the least developed specialties in medicine, and little new knowledge of a fundamental nature was acquired for many years.

However, as Sir Thomas Lewis has remarked, the most backward subject is the one ready for the most rapid advance. In recent years, gastro-enterology has acquired a number of valuable techniques which have stimulated renewed interest and accelerated progress in this field. A wealth of information is being provided by radio-isotopes, transistorised telemetering equipment for manometric studies, X-ray image intensification, instruments for the biopsy of the liver and gastro-intestinal mucosa, the electron microscope, histochemical methods and enzyme assays.

The prime functions of the gastro-intestinal tract are digestion and absorption. These processes are wholly dependent on the secretion of digestive juices and on the mixing, distribution, transport and storage of intestinal contents. The motor activity or motility of the alimentary tract is responsible for mixing, distribution, transport and storage and is thus a vital part of gastro-intestinal function.

The motility of the bowel deserves careful study because of the essential part it plays in the over-all function of the gut. Knowledge may be gained of the behaviour of smooth muscle, of the integration and coordination of intestinal motor activity by neural and humoral means, and of the role of substances such as acetylcholine and serotonin in the control of normal motility. Furthermore, aberrations in motility are encountered in many clinical disorders: these include cardiospasm; abdominal pain, constipation and diarrhoea without demonstrable organic cause ("irritable colon" syndrome); diarrhoea and post-prandial distress following gastric operations, jejuno-ileal insufficiency; ulcerative colitis; congenital and acquired megacolon; carcinoid tumour with hyperserotoninaemia; thyroid disorders; and diabetes mellitus.

X-ray image intensification, transistorised telemetering equipment and electronic improvements in transducer design have provided techniques which are more accurate and physiological than those used in the past. The application of these new techniques to the study of motility has already resulted in the acquisition of new knowledge, and it is to be hoped that further progress will dispel the ignorance which still attaches to many aspects of this important part of alimentary function.

CHAPTER II

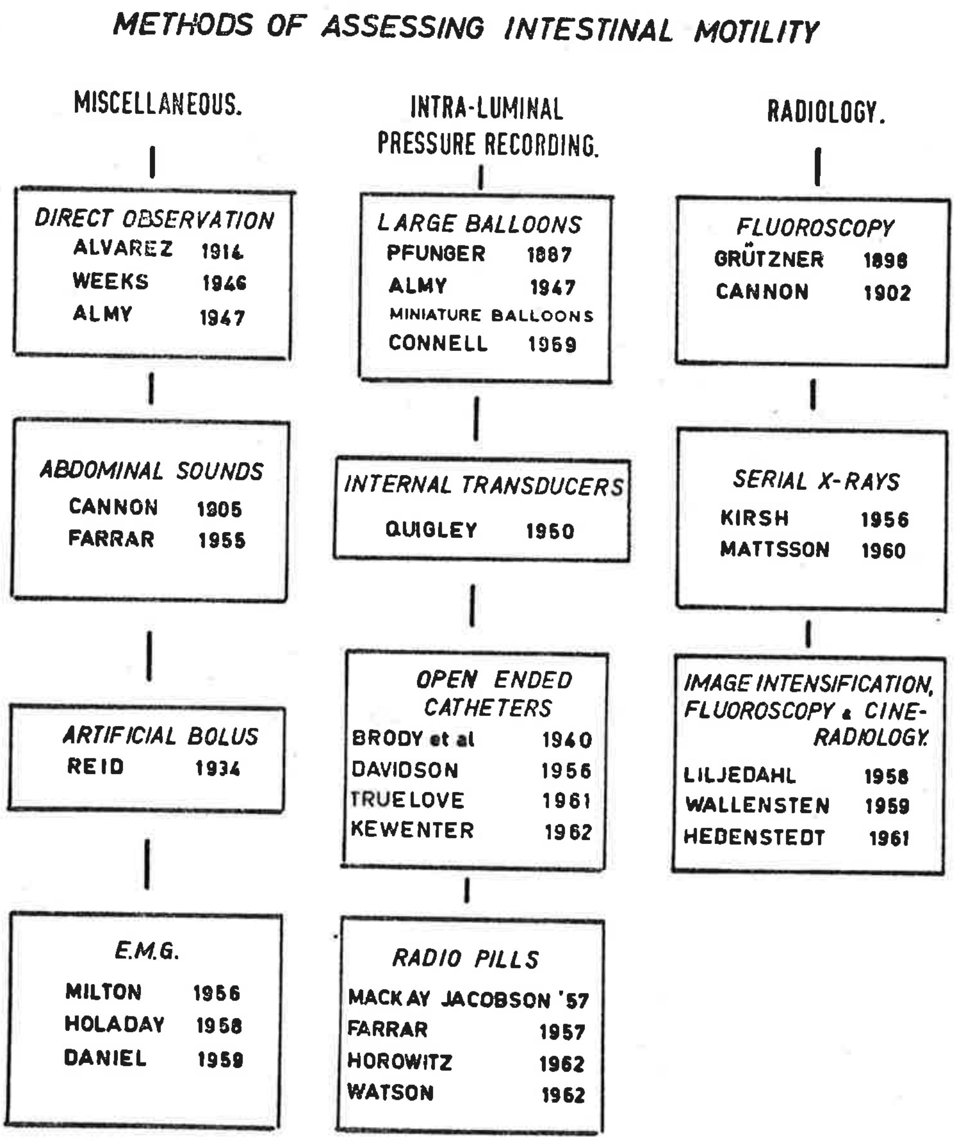


Figure 1: Summary of methods of assessing intestinal motility.

The motor activity of the human intestine in health and disease has been investigated by a number of techniques (Figure 1). These and the results they have provided will be reviewed in this chapter under the following headings:

1. Balloon Studies: introduction
   (a) small bowel
   (b) large bowel
2. Catheter Studies
   (a) small bowel
   (b) large bowel
3. Gastro-intestinal radiotelemetering
4. Radiology
5. Electromyography
6. Miscellaneous
7. Commentary

Balloon Studies: Introduction

As early as 1869, Legros and Onimus used balloons to record fluctuations in intestinal pressure in animals. They described three types of motor activity: peristalsis, antiperistalsis and stationary contractions, and noted that motor activity was more marked in the small bowel than in the large bowel. von Pfungen in 1887 first used the balloon method to study gastric contractions in humans.

For the next 50 years the balloon remained the chief method for recording intestinal pressures, and much of our basic knowledge of motility has been gained through its use. However, it gradually became apparent that the balloon system had considerable physical and physiological disadvantages. These disadvantages have been extensively discussed by Quigley and Brody, 1950, 1952; Code, Hightower and Morlock, 1952; and Chaudhary and Truelove, 1961a. Balloons in the alimentary tract can act as foreign bodies and initiate motor activity by direct stimulation of the intestinal mucosa. If sufficiently large, balloons may interfere with propulsion of the contents of the bowel and thus cause intestinal obstruction. In both instances, induced rather than spontaneous motility will be recorded.

Equally important are the physical characteristics of the balloon: the pressure registered from a large balloon represents the algebraic sum of all the pressures exerted on its surface rather than the pressure at any one particular site.

Apart from the size of a balloon, its shape and degree of filling as well as the outflow resistance in the connecting tubing, influence the accuracy of recording. Finally, the volume-pressure coefficient of the system, that is, the degree of displacement of the conducting medium needed to "drive" the manometer to register one unit of pressure will determine the range and sensitivity of the recording apparatus.

The pressure wave patterns from the bowel were mentioned in purely descriptive terms until Templeton and Lawson (1931) first classified the waves of the dog's colon into types I, II and "tonus changes". This classification was adapted by Adler, Atkinson and Ivy (1941) for the study of colonic motility in man, the waves being referred to as types I, II and III respectively. Later Posey, Dearing, Sauer, Bargen and Code (1948) used this nomenclature in studies of the motility of the small intestine.

The appearance, amplitude and duration of a pressure wave are the criteria which have been used to assign it to a particular category. Whether they occur in the small or large bowel, type I waves are simple and monophasic. In the small bowel their amplitude is from 3 to 30 cm. of water and their duration from 2.6 to 7.5 seconds (Foulk, Code, Morlock and Bargen, 1954), the corresponding figures for the colon being less than 10 cm. of water and 5 to 12 seconds (Spriggs, Code, Bargen, Curtiss and Hightower, 1951).

Type II waves are also usually simple but of a greater amplitude than waves of type I. In the small bowel they have not been recognised by some workers (Foulk et alii, 1954), although others have reported their duration as 30 to 90 seconds. (Posey et alii, 1948). In the colon they are common, lasting from 12 to 60 seconds and reaching amplitudes of up to 50 cm. of water (Spriggs et alii, 1951).

The distinguishing feature of type III waves is a "tonus change" or increase in baseline pressure; upon this waves of type I and II are superimposed. The duration of the tonus change may range from a few seconds to minutes and the amplitude from less than 10 cm. of water in the colon to 30 or 40 cm. of water in the small bowel (Code, Hightower and Morlock, 1952).

In addition to the three types of waves which constitute the "standard nomenclature" type IV waves, presumably peculiar to ulcerative colitis, have been described in motility tracings both from the small bowel (Code, Rogers, Schlegel, Hightower and Bargen, 1957) and the large bowel (Kern, Almy, Abbot and Bogdonoff, 1951). They will be further discussed in connection with studies of motility in this disease (sections 1a and 1b of this Chapter).

Amongst those workers who still conform to the standard nomenclature (Kim and Barbero, 1963) most have added their own modifications, and the criteria for including a wave in a particular category are widely divergent. The differentiation between waves of types I and II on the basis of the supposedly greater amplitude of the latter, has been largely abandoned. In view of the inaccuracy inherent in recording amplitude with balloons, this measure is probably justified (Daniel, Sutherland and Bogoch, 1959).

Balloons still continue to be used in studies of gastrointestinal motility. With the understanding of the physical principles involved came technical improvements leading to better equipment and greater accuracy. Connell (1959, 1961a, b) employing miniature balloons measuring 10 x 7 mm., obtained good records of colonic motility. He showed that virtually identical tracings resulted when miniature balloons and open ended catheters recorded simultaneously from the same segment of the large bowel, and made a plea for retaining miniature balloons as a valuable and inexpensive tool in research. Nevertheless, most workers agree with Chaudhary and Truelove (1961a) that neither the balloon water manometer nor the balloon optical manometer device can produce results accurate enough to merit quantitative analysis.

1a. Balloon Studies of the Small Bowel

Studies of the motility of the small intestine in man by means of balloons are of comparatively recent origin. Ingelfinger and Moss (1943) studied two patients with jejuno-ileal insufficiently; one with tropical sprue and the other with idiopathic steatorrhoea. In both patients the only spontaneous activity was of the "small wave" type, corresponding to type I of the standard nomenclature. No spontaneous "large waves" were seen, but in spite of this, transport of the balloon along the gut was reported to have been only slightly slower than in normal subjects.

Ingelfinger and Moss (1943) also tested the effect of various drugs on the intestinal motility of their patients with sprue, and found that although acetyl beta methylcholine (Mecholyl) caused a temporary return to normal small bowel activity, Prostigmine had only a slight effect. Both of these drugs stimulate structures innervated by cholinergic nerves, so that normally the motility of the gut is enhanced. From this they inferred that in sprue there was an inability of the intestinal autonomic nervous system to liberate acetylcholine. They further stated that although treatment with a multi-vitamin preparation effected no change in motility, the administration of liver extract parenterally caused the return of "large waves". However, it is doubtful that the relationship between treatment with the liver extract and the return of normal bowel motility was a causal one. Furthermore, the authors used only one balloon and made no quantitative analysis of the records they obtained.

Chapman and Palazzo (1949) were the first to attempt a correlation of intraluminal pressure tracings with radiologically observed motility. They used a four-lumen tube with two balloons in the duodenum and two balloons in the upper ileum to register pressure changes. They also attempted to obtain a numerical estimate of motility by polar planimetry of the surface area beneath the waves.

Chapman and Palazzo (1949) described three kinds of wave patterns:

(a) a non-propulsive pattern of repeated single waves (type I of previous authors)

(b) propulsive tall complex waves lasting more than 2 minutes (probably type III of previous authors)

(c) "spasms", defined as baseline elevations with superimposed frequent small contractions. The duration and amplitude of these spasms were not stated.

In 45 observations on 7 subjects, balloon kymography and fluoroscopy were combined. Movement of the barium contrast medium was nearly always associated with a high sustained wave though occasionally no movement occurred. However, these "high, sustained waves" were not described in detail and the reader is left in doubt as to their kymographic appearance. Furthermore, none of the so-called "propulsive waves" with a duration of more than 2 minutes occurred during fluoroscopy, and thus their designation as propulsive lacks radiological confirmation.

Polar planimetry of two to four tracings made simultaneously from the upper small bowel was also used by Chapman and his co-workers in a number of later investigations, most of which were concerned with the action of different drugs and placebos on motility.

In 1950 Chapman, Rowlands, Taylor and Jones found that placebos decreased both propulsive and total small bowel motility, although the effect did not appear for 40 to 210 minutes. It is possible that the mere presence of the balloon system in the intestine might have accounted for this decrease in activity, as no control group was studied.

Rowlands, Chapman, Taylor and Jones (1950a) studied the effect of amprotropine (Syntropan) and adiphenine (Trasentin) in normal persons and were unable to demonstrate any effect on motility. Both of these drugs inhibit structures innervated by post-ganglionic cholinergic nerves. They also showed that morphine decreased propulsive contractions and caused the appearance of repeated sudden spasms of 8 to 60 minutes' duration (Rowlands, Chapman, Taylor and Jones, 1950b). This effect of morphine has been confirmed by many workers, amongst them Andrew (1954a) in Australia. Placebo also caused spasms but these were of shorter duration (Rowlands et alii, 1951b).

Furthermore, Chapman, French, Hoffman and Jones (1952) demonstrated that methantheline (Banthine) and atropine which block the effects of acetylcholine reduced propulsive and non-propulsive motility. Again, placebos had the same effect but to a lesser extent. The validity of these studies can be questioned because of the possible influence of the recording equipment itself on motility, and because of the lack of a control group or phase in the various pharmacological experiments. Nevertheless, quantitative and objective measurements are a prerequisite for statistical analysis, and their introduction by Chapman and his colleagues constituted a significant advance in the field of motility.

Foulk et alii (1954) used single balloons in a study of 21 normal subjects, 5 patients with duodenal ulcer and 5 patients with ulcerative colitis. They found that 75 to 80% of all waves belonged to type I. The rest of the waves were classified as type III waves, and these were reduced in the patients with ulcerative colitis.

Type IV waves were first described in tracings from the small bowel by Code et alii (1957). These investigators introduced tandem balloons through the ileal stomas of two patients with ulcerative colitis. The type IV wave was described as beginning as a type III wave, but being distinguished from it because it had no superimposed type I contractions. The amplitude of type IV waves was between 27 and 30 cm. of water and the duration was approximately 60 seconds. Type IV waves accounted for 6 to 12% of all motor activity. The type IV wave was more frequent after a meal and after Prostigmine, but was abolished by morphine and atropine. It was considered propulsive though not solely responsible for propulsion. However, type IV waves have been considered by some workers to be artefacts (Daniel et alii, 1959) although they have been recognised in later work utilising open ended catheters (Davidson, Sleisenger, Almy and Levine, 1956a; Chaudhary and Truelove, 1961b).

A number of studies with balloons have been made with the purpose of correlating the absorption of various test substances with the degree of motor activity of the small bowel. Cummins and Almy (1953) showed that the absorption of glucose and methionine was enhanced by stimulating the small gut with physostigmine, and Higgins, Code and Orvis (1956) demonstrated that the absorption of labelled sodium and labelled water was impaired by decreasing motility with drugs. In both of these studies the same balloon that was used to occlude the small bowel was used to record its motility, and it is questionable whether an accurate record of motility can be gained with this technique.

Balloons have also been used to assess the effect of surgery on the autonomic nervous system. Bingham, Ingelfinger and Smithwick (1950) found a reduction in the frequency of propulsive waves in 13 of 15 patients studied 3 months after sympathectomy. However, when four of the patients were studied again at a longer interval after the operation, they all had a level of motility which was greater than that observed before surgery. The authors concluded that pre-ganglionic sympathectomy was not followed by a lasting alteration in bowel motility, and they considered that the decrease in motility found in the early post-operative period was not necessarily related to the sympathectomy because a similar decrease was observed following other abdominal operations.

Roth and Beams (1959) found that vagotomy did not significantly affect small bowel motility, though waves of type II were reduced in number.

Other studies in which balloons were used are those of Helm, Kramer, McDonald and Ingelfinger (1948) and Bachrach, Brody and Drury (1951). Helm and his associates (1948) observed that spontaneous sleep was followed by a clear-cut reduction of motility in 12 of the 16 persons studied. The change occurred 1 to 5 minutes after the onset of sleep and on awakening a gradual return to activity took place.

Bachrach et alii (1951) and Bachrach, Rowen, Halsted, Schapiro, Holmström and Price (1954) described a recording system in which tandem balloons were connected to pressure transducers. Other methodological studies are those of Hightower, Code and Maher (1949) and Andrew (1954b).

1b. Balloon Studies of the Large Bowel

In many studies of the motility of the large bowel, balloons have been used to complement direct observation (Almy, Kern and Tulin, 1949a; Almy, Hinkle, Berle and Kern, 1949b; Wener and Polonsky, 1950; Wener, Morton and Polonsky, 1952). Adler, Atkinson and Ivy (1941) were the first to make a systematic study of the motor activity of the human colon. They used balloons connected to a water manometer and, adopting the nomenclature of Templeton and Lawson (1931) separated the waves into types I, II and III. Their initial paper was concerned with the patterns of motility during fasting and after meals. In subsequent work (Adler, Atkinson and Ivy, 1942; Atkinson, Adler and Ivy, 1943) they investigated the action of various drugs such as posterior pituitary extract, prostigmine and ergot, and introduced the concept of dyskinesia of the colon. Dyskinesia or dyssynergia was defined as inco-ordinated activity of adjoining colonic segments. Adler and his colleagues (Adler et alii, 1941, 1942) postulated that no propulsion of gut contents would result if one segment of the bowel exhibited propulsive activity at the time when its distal neighbour was in a state of non-propulsive activity or increased tone. They believed therefore that dyskinesia could cause constipation, and if the pressure gradient were sufficiently high, abdominal pain.

However, Adler et alii (1941, 1942) produced no experimental evidence in support of dyskinesia. They did, however, designate types I and II waves as propulsive waves on the basis of expulsion of faeces or the recording balloons through the colonic stomas during the recording of these wave forms. Because of the obstructing nature of balloons, such conclusions may not be warranted.

It should be noted that considerable doubt still exists as to whether the function of a wave can be inferred from its kymographic appearance (Code et alii, 1952; Connell, 1961a).

Posey, Dearing, Sauer, Bargen and Code (1948) like Adler et alii, (1941, 1942) chose patients with colonic stomas for their experiments, but replaced the water manometer by the more sensitive optical manometer. They supported the propulsive function assigned to type II and type III waves by Adler et alii (1941, 1942) and restated this opinion in a later communication (Posey and Bargen, 1951). According to Posey and Bargen (1951) the motility patterns recorded from closely adjacent levels of the colon were often quite dissimilar; this suggested that the intestine was composed of "functional segments". Each segment worked as a separate unit: generally out of phase, but at times coordinated with its neighbours.

This autonomy of closely adjacent parts of the bowel was observed by earlier investigators (Atkinson et alii, 1943) and has been confirmed in more recent work (Connell, 1959; Chaudhary and Truelove, 1961b). To assess the length of the functional segment, Posey and Bargen (1951) varied the distance between the balloons. They found that when two balloons in the colon were 4 cm. apart the recorded wave patterns were similar in both tracings, whereas an inter-balloon distance of 7 cm. resulted in independent activity. Posey and Bargen (1951) therefore concluded that the functional segment of the large bowel measured between 5 cm. and 7 cm.; the corresponding figure for the ileum was estimated at 4 cm.

Posey and Bargen (1951) did not observe relaxation in one segment of the colon coinciding with waves of a propulsive type in its proximal neighbour, and therefore postulated that transport of intestinal contents required coordinated propulsive activity in two adjacent segments. Complete intersegmental coordination at all times was seen in three patients with ulcerative colitis. If transport was dependent on coordinated activity, it would be expected that these patients would have had diarrhoea at the time of study. However, the authors did not state whether this was the case or not.

It should be pointed out at this stage that in view of the individual variation in the amount and type of motor activity, the use of control groups is important in the investigation of the motility of the intestines. As early as 1929 Hines, Lueth and Ivy included 21 normal subjects in a study of rectal motility in 12 constipated patients. They found that their constipated patients had less rectal motility than the normal persons, but as they used a balloon containing 150 ml. of water, it is likely that induced rather than spontaneous motility was recorded. Hines et alii (1929) also decided to test Alvarez' (1924) theory of "intestinal auto-intoxication" by leaving the balloon in situ for 6 to 12 hours. Although this procedure caused discomfort and "painful urges" it failed to reproduce any of the symptoms regarded as typical of intestinal auto-intoxication.

Spriggs et alii (1951) also included a group of normal subjects for comparison in a study of the motility of the rectum and sigmoid colon in 10 patients with ulcerative colitis. The resting and post-cibal patterns of activity were recorded with tandem balloons connected to optical manometers.

Spriggs and his colleagues (1951) noted the previously recognised waves of types I, II and III. In addition they observed a different type of wave in their patients with ulcerative colitis. This wave did not fit into any of the previously described categories and was therefore separated as type IV. The type IV wave had a higher mean amplitude than any other wave, and although relatively frequent in patients with ulcerative colitis, it was extremely rare in the control group. Spriggs et alii (1951) considered that the type IV wave was propulsive and represented a mass movement of the contents of the colon.

Spriggs et alii (1951) made no attempt to analyse the results in their patients with ulcerative colitis in regard to the duration and severity of the disease, or the presence or absence of diarrhoea at the time of study. However, as a group, the patients with ulcerative colitis showed a markedly decreased proportion of type II waves which accounted for only 9.8% of all waves as compared with 36.3% in the control group. The authors considered that type II waves represented haustral contraction and therefore suggested that haustral activity was reduced in patients with ulcerative colitis.

Spriggs and his associates (1951) attempted a quantitative analysis of their tracings by calculating the percentage activity and mean amplitude for all wave types. This represented an advance in motility work and would be justifiable, as far as the percentage activity is concerned, if all waves could be classified accurately. However, the calculation of mean amplitudes is probably misleading because of the technical shortcomings of large balloons.

Kern et alii (1951) also studied the motility of the distal colon in patients with chronic ulcerative colitis. They investigated 45 patients with this disease and stated that they had used more than 300 normal persons as the control group. They observed type I, II and III waves, and reported the occurrence of type IV waves independently of Spriggs et alii (1951). Waves of type IV were simple waves lasting 2 to 5 minutes and were seen in 9 of the 72 tracings from the group with ulcerative colitis, but never in normal subjects.

Kern et alii (1951) considered that only type IV waves were propulsive. Most of the studies were done with single balloons but when tandem balloons were used the time interval between the appearances of type IV waves in the proximal and distal balloons was constantly 1 minute. The authors proposed that these waves represented caudad progression of mass peristaltic contractions originating in the right half of the colon, but did not present evidence for this view.

Kern and his co-workers (1951) further found that phasic activity (Types I, II and III) was either absent or reduced in 46 of the 72 tracings from patients with ulcerative colitis. Only four tracings showed excess activity and the rest were normal. Type IV waves occurred only when phasic activity was reduced.

Kern and his group (1951) found no correlation between the level of motor activity of the colon and the duration of the disease and the degree of fibrosis of the colon. However, they noted that patients with severe diarrhoea tended to have inactive tracings with type IV waves. Phasic activity returned toward normal when the diarrhoea ceased. Patients with normal bowel habits had normal tracings, and constipated patients showed increased motor activity.

A discussion of emotionally charged topics with the patient with ulcerative colitis resulted in an increase in the frequency and amplitude of the waves in six of seven previously inactive tracings. However, Kern et alii (1951) make no mention of whether a similar response could be elicited in patients with normal patterns of motility.

It should be noted that Kern and his colleagues (1951) used only a single balloon in all but a few of the experiments, and a single recording device may create a false impression of inactivity or hyper-activity because of the variation in motility in different segments of the gut.

Connell (1959) described a more sensitive balloon method. He used three miniature balloons measuring 10 x 7 mm. and 5 cm. apart. The balloons were connected to an optical manometer by narrow bore polythene tubing and the volume of the whole recording system was only slightly greater than 1 ml.

Connell (1959) departed from the time-honoured standard nomenclature and described only two groups of waves. The first, the "principal" waves, were so named in view of their almost universal occurrence in tracings from the sigmoid colon. They correspond to type II of the standard notation. Usually their amplitude was below 20 cm. of water, but they could at times exceed a pressure of 70 cm. of water, and they tended to occur in phases of activity alternating with phases of relative inactivity. In the active periods their frequency was constantly in the range of 2 to 2.7 per minute and inter-segmental incoordination was common. Forward progression of waves was rare but retrogression was more frequent.

The waves of the second group were seen mainly in tracings from the rectum and were of a low amplitude. Their frequency was rapid (3 to 10 per minute) and they sometimes continued for a considerable length of time without interruption. These waves, Connell (1959) considered, corresponded to type I waves of the standard nomenclature.

Connell (1959) reported quantitatively analysed results from more than one hundred patients with disordered bowel function including ulcerative colitis and the "irritable bowel" syndrome. He found normal tracings in slightly more than half the patients. The remainder could be divided into well defined groups:

(a) Most patients with active diarrhoea at the time of study had inactive tracings. With symptomatic improvement of the diarrhoea, the tracings showed a return to normal activity; this had been noted earlier by Almy, Abbott and Hinkle (1950) and Kern et alii (1951). Connell (1959) therefore postulated that in active diarrhoeal states the colon did not act as a pump but "as a rigid drain along which faeces positively trickle to reach the sensory receptors for the defaecation reflex".

(b) Apparently 20% of the patients with the "irritable bowel" syndrome showed a motility pattern characterised by a predominance of rapid frequency waves. The majority of these patients were constipated.

(c) Excessive numbers of high amplitude contractions resembling the effect of Prostigmine occurred in some patients, but Connell did not state whether this type of activity was associated with any particular form of bowel dysfunction.

In later work (Connell, 1961b) the same method was used to study 16 cases of megacolon. The group was not a homogeneous one, Hirschsprung's disease being proven in two cases and suspected in one further patient. The others were grouped together as acquired megacolon.

The commonest motility pattern, observed in 7 of the 16 patients, was one of generalised hypomotility. Whether the hypomotility was the cause or merely an effect of the disease remained unsettled. In addition Connell described segmental hypomotility in three patients, segmental incoordination in three patients, and completely normal records in the remaining three patients.

Connell (1961c) also investigated the motility of the distal large bowel in 14 patients with asymptomatic duodenal ulceration. He found no significant difference in motility between these patients and a control group of 18 normal subjects.

It is interesting to note that Connell had abandoned open ended catheters for miniature balloons because he had found that the catheters he used were blocked by faeces even when a constant infusion technique was used. This has not been the experience of other workers (Davidson, Sleisenger, Almy and Levine, 1956b; Chaudhary and Truelove, 1961b, c, d).

2a. Catheter Studies of the Small Bowel

The earliest study of gastrointestinal motility using open ended catheters was made by Uffelmann in 1877. He studied a child aged seven years who had had a gastrostomy performed for oesophageal stricture, the result of sulphuric acid which had been ingested in mistake for beer. Uffelmann observed periodic fluctuations in pressure which he considered were due partly to respiration and partly to gastric contractions. He estimated the basal gastric pressure to be 2 to 8.5 cm. of water.

Six years later, Schreiber (1883) also described experiments on measurement of gastric and oesophageal pressures through an open ended catheter. He found that while the oesophageal pressure always was negative, the height of the intra-gastric pressure appeared to depend on how much the stomach was stimulated by mechanical contact with the tube. Thus a negative basal pressure could be easily overcome by a contraction resulting from manipulation of the tube. Schreiber did his experimental work both on normal and on anaesthetised subjects.

Forty-five years later, Templeton (1928) recorded the motility of the dog's stomach using a catheter inserted through an external fistula. However, the credit for reviving the interest in open ended catheters in studies of human gastro-intestinal motility belongs to Brody and his colleagues (Brody, Werle, Meschan and Quigley, 1940). Initially they used an air filled lead and rubber tube of 1 mm. bore connected to an optical manometer, and later a tandem system of recording tips connected by 0.75 mm. polythene tubing (Brody and

Quigley, 1947). The equipment was further improved by Quigley, Brody, McKay, Landolina and McAlister (1950) and at that stage consisted of a polythene catheter connected to an electromanometer. The conducting medium in the catheters was helium and a slow flow of this gas prevented the tips from being blocked by intestinal contents. Using these methods Brody and his co-workers investigated the basal pressures and phasic pressure variations of the stomach and small intestine in man and in experimental animals. They were particularly interested in the mechanism of gastric emptying (Brody and Quigley, 1947; Quigley and Brody, 1950).

Rowlands, Honour, Edwards and Corbett (1953) reported a modification of the open ended catheter method and described its performance characteristics. Using an expanded silver recording tip of 3.5 mm. bore on 1 mm. air perfused polythene tubing, they found that no gut contents were forced into the catheter at pressures less than 155 cm. of water. No results of clinical application of the method were reported.

In 1954, Lorber and Shay described the use of fluid filled open ended catheters connected to Statham strain gauges. They found that catheters with an internal diameter of 2 mm. the most satisfactory, because excessive dampening occurred in catheters of narrower bore. From two to four catheters with tips 5 cm. apart were inserted into the stomach and kept patent by a constant slow saline infusion. A Sanborn Poly-Viso recorder traced the intra-gastric pressure changes.

The credit of introducing fluid filled catheters thus belongs to Lorber and Shay (1954) and most subsequent workers have adopted this method.

Thus Fink (1959) recorded intra-luminal pressure fluctuations from the small bowel. He succeeded in making records from the entire small bowel as well as from the sigmoid colon by leaving the single catheter in situ for up to 48 hours.

Fink (1959) studied 60 persons of whom 24 were normal subjects, and the others had duodenal diverticula, duodenal ulcers, sprue or cholelithiasis. The percentage of phasic activity was calculated in two different ways:

(a) by adding the duration of all phasic waves and expressing the sum as a percentage of the recorded time;

(b) by adding the duration of all periods during which phasic waves were seen and expressing this sum as a percentage of the recorded time.

Fink (1959) found that when he calculated phasic activity in the first way there was no clear-cut difference between the patient groups. If, however, the second method was used, patients with duodenal ulcers had increased duodenal and upper jejunal activity, while patients with sprue had reduced motility of the upper small intestine.

Barbero, Kim and Davis (1958) studied the motility of the small bowel in normal children and children with coeliac disease and mucoviscidosis.. The ages of the children varied from less than 6 months to 14 years. They used a double-lumen Miller—Abbott tube in which the proximal opening was in the stomach and the distal opening in the duodenum. The tube was connected to Statham strain gauges and constantly perfused at a slow rate. All waves above 2 cm. of water pressure were analysed and were classified according to Foulk et alii (1954) into types I and III.

Barbero et alii (1958) found that type I waves, which were usually non-rhythmic, accounted for 98.1% of all activity. Waves of type III constituted 3.5% of the total activity which in the normal children was present for 23.3% of the recorded time. There was no difference in total activity between the three groups studied. There was no difference in the response to milk between healthy children and children with mucoviscidosis, both groups showing an increase in non-rhythmic type I waves and type III waves with a decrease in rhythmic type I waves. However, no attempt was made to correlate the degree of motor activity with age. Furthermore, all children were sedated, and this may well have had some effect on motility, as Barbero and her colleagues (1958) showed that there was a significant reduction in motor activity during sleep.

In 1960, Kewenter and Kock in Sweden described another modification of the method of recording intra-luminal pressure changes by means of open ended catheters. Two fluid filled catheters with three terminal holes and a rubber "sail" to facilitate propulsion were connected to pressure receptors and recorded on an Elema-Schönander four-channel mingograph. The recording tips were 20 to 30 cm. apart, one in the duodenum, the other in the jejunum. Kewenter and Kock (1960) studied the motor activity in 30 normal subjects during fasting and following a meal.

During the fasting period waves of unspecified type with a maximum amplitude of 30 cm. of water occurred with a frequency of less than 10 per 5 minutes. Food caused an increase in the frequency of the waves to between 15 and 30 per 5 minutes as well as in their amplitude. Sometimes a distinct time lag was observed in the appearance of a wave in the two tracings and this was taken to indicate propulsion.

Kewenter and Kock (1960) found that Prostigmine augmented motor activity to a slightly larger extent than did food. Morphine caused recurring periods of fast "non-propulsive" waves at a rate of 55 to 60 per 5 minutes superimposed on a rise in basal pressure. These periods lasted for 6 to 10 minutes and could sometimes be seen as late as 24 hours after the administration of the drug.

The same method was used later by Christoffersson, Kewenter and Kock (1962) in a study of small bowel motility in patients after gastric operations. Some patients following partial gastrectomy experience episodes of light-headedness, weakness, sweating and palpitations, borborygmi and diarrhoea. These symptoms occur shortly after eating and are particularly likely to be brought on by sweet, hot and liquid foods. This distressing and not uncommon sequel of gastric resection has come to be known as the post-gastrectomy early dumping syndrome.

Christoffersson et alii (1962) found that instillation of hypertonic glucose into the small bowel was immediately followed by propulsive motor activity - "peristaltic rush". This persisted during the remaining 30 to 50 minutes of recording in those patients who did not develop dumping. In contrast, patients who experienced dumping showed abolition of the initial hypermotility after two to eight minutes, and the small bowel remained completely inactive for the remainder of the recording. In view of these findings Christoffersson et alii (1962) considered that the occurrence of hypermotility of the small bowel in dumping reported by other workers (Wallensten, Garsten, Jonson and Saltzman, 1959; Mattsson, Perman and Lagerlöf, 1960) could have been due to observation of the "peristaltic rush" alone, the subsequent cessation of motility having escaped notice.

The catheter method was further applied to pharmacological studies (Kewenter, Kock, Pompeius and Scheller, 1962) and to an investigation of the immediate effects of gastric surgery on the motility of the small bowel (Kock, 1963; Kewenter and Kock, 1963).

Kock's (1963) aim was to determine how soon after partial gastrectomy oral feeding could be instituted. He assumed that it would not be tolerated until the upper small intestine was capable of propulsion, and therefore investigated the motor response of the small bowel to jejunal feeding. He began the recordings on the first post-operative day and repeated them daily until propulsive activity had returned. This usually took place by the third day after operation, but was delayed until the fifth day in one patient. There was no difference in the time of return between patients with a gastro-duodenal anastomosis and those with a gastro-jejunal one.

Kewenter and Kock (1963) showed that the administration of Prostigmine did not cause a return of propulsive activity if jejunal feeding had failed to do so, and therefore advised against the use of this drug in the treatment of post-operative paralytic ileus.

2b. CATHETER STUDIES OF THE LARGE BOWEL

The use of catheters in studies of large bowel motility was pioneered by Davidson and his group. In 1956, Davidson, Sleisenger, Almy and Levine (1956b) made a study of the motility of the rectum and distal colon in 40 normal children.

The pressure fluctuations were recorded through three constantly perfused polythene catheters with the recording tips six inches apart. The catheters were connected to electromanometers and the tracings made on a Sanborn Poly-Viso recorder. Most of the children were given an enema before the catheters were inserted.

The waves were subdivided on the basis of amplitude and duration. Their pattern of distribution gave no support to the rigid separation of waves into types I, II and III, although examples of all these types could at times be recognised. Later, independent, work has supported this belief (Chaudhary and Truelove, 1961b - d).

Davidson and his colleagues (1956b) found that the motility of the rectum differed from that of the sigmoid colon in so far as the rectal contractions were of longer duration and smaller amplitude than contractions observed at higher levels of the bowel.

The results of this work were used as a basis for comparison in a later study by the same authors (Davidson, Sleisenger, Almy and Levine, 1956a). Seven children with ulcerative colitis, none of whom had diarrhoea, showed motility patterns within the normal range. However, a characteristic pattern was observed in six infants with acute infectious diarrhoea. The distinguishing features of the diarrhoeal pattern was a high degree of coordination at the three levels of the large bowel, although there was often a distinct time lag in the appearance of the wave in the three tracings. This was taken to indicate propulsion.

In addition, the amplitude of the waves was generally much higher than in normal children, and a large part of the activity consisted of 'unique waves' held to be identical with the type IV wave of Spriggs et alii (1951).

In an attempt to reproduce this motility pattern experimentally, 11 normal children were given oral magnesium sulphate. In eight children the motility pattern of diarrhoea was induced with magnesium sulphate. Furthermore, progressive waves of a high amplitude were seen. Davidson and his co-workers (1956a) noticed that these type IV waves were associated with abdominal discomfort only when they occurred simultaneously in adjacent segments of the gut, or when their analward progression from the sigmoid colon did not eventuate. Type IV waves showing progressive delay and resulting in the passage of faeces or flatus did not give rise to abdominal discomfort.

Another paper by Davidson's group (Davidson, Sleisenger, Steinberg and Almy, 1955) described the use of Mecholyl in the diagnosis of congenital megacolon. When this drug was given in a dose sufficient to produce systemic side-effects it was found to inhibit colonic and rectal phasic activity in 9 of 20 normal subjects. Of six children with congenital megacolon, three showed inhibition of motility of the unaffected gut; whereas the aganglionic segment failed to respond. Mecholyl, consequently, failed to relax the aganglionic segment. In two children with megacolon there was lack of response to Mecholyl at all levels of the gut, corresponding to the situation in normal controls. The remaining patient demonstrated a "false positive" result in that the constricted segment alone failed to relax, but at operation the resected gut was not aganglionic. This patient was later described more fully in a separate paper (Davidson and Bauer, 1958).

On the basis of this work, Davidson and his associates (1955) made a plea for the use of the Mecholyl suppression test as a diagnostic tool in suspected cases of congenital megacolon. They claimed that the length of the aganglionic segment could be determined by moving the recording tips, but pointed out that the test could be expected to be of value in only one-half of the cases.

Results conflicting with those of Davidson et alii (1955) were published by Fink and Friedman (1960) who compared the effect of various drugs, amongst them Mecholyl, on the proximal and distal colon. To obtain pressure records from the proximal colon, these workers allowed a thin polythene tube with 2 windows 40 cm. apart to traverse the whole gastro-intestinal tract and connected each end of the tube to a pressure transducer.

According to Fink and Friedman (1960) Mecholyl constantly augmented the motility of the proximal colon, although the distal colon was less sensitive. However, a dose sufficient to cause definite systemic effects - comparable to that used by Davidson and his colleagues (1955) enhanced motor activity throughout the colon and rectum. In no instance was Mecholyl observed to cause suppression of motility. Since Prostigmine had the same qualitative action as Mecholyl and since both direct cholinergic stimulation and cholinesterase inhibition were more effective in the proximal colon, Fink and Friedman (1960) suggested that the distal colon contained more cholinesterase. They were strengthened in this belief by finding that bethanechol (Urecholine) - allegedly acting directly on the neuro-effector cells - had a more pronounced stimulating effect on the distal colon than either Mecholyl or Prostigmine.

They found that the dividing line between the two territories of different quantitative response was immediately to the left of the mid-transverse colon. This conforms well with existing knowledge of the parasympathetic innervation of the large bowel, the proximal colon being supplied by vagal fibres and the distal colon and rectum by the sacral out-flow.

Chaudhary and Truelove (1961b,c,d) made substantial contributions towards our knowledge of the motility of the large bowel in a series of well planned and carefully analysed experiments. They used three water-filled polythene catheters with the recording tips 7.5 cm. apart. The catheters were connected to photoelectric transducers coupled to a Cambridge three-channel recorder. Like Davidson et alii (1956b), Chaudhary and Truelove (1961b) found themselves unable to separate waves into strict categories, and therefore subdivided them on an amplitude-duration basis for the purpose of analysis. They introduced a "colonic motility index" to make rapid comparison of different tracings possible. This parameter was obtained by adding the amplitude-duration products of all waves and taking the average value in normal subjects as 100.

Chaudhury and Truelove recorded resting patterns of motility as well as changes induced by Prostigmine or by an "emotionally charged" interview. They studied normal subjects, patients with the irritable colon syndrome, and patients with ulcerative colitis.

In the first study, Chaudhary and Truelove (1961b) discussed resting patterns of motility. They showed that patients with the irritable colon syndrome whose chief symptom was abdominal pain (spastic colon) and who had symptoms at the time of study, showed hyperactive resting patterns. Patients with the irritable colon syndrome with active diarrhoea as their only symptom (pure diarrhoea) showed a slight decrease in the number of short waves, but no other deviation from normal. Furthermore, patients with the irritable colon syndrome who were without symptoms at the time of the pressure recordings had essentially normal resting patterns.

The patients with ulcerative colitis were subdivided according to the severity of the disease. Those with severe or moderate symptoms were shown to have increased total activity mainly due to a marked excess of waves of high amplitude and long duration - probably corresponding to type IV of earlier workers (Spriggs et alii, 1951). Essentially normal patterns with only a slight reduction in the number of short waves characterised patients with mild symptoms, and those with no symptoms but with sigmoidoscopic evidence of inflammation. The last group, symptom-free patients with no sigmoidoscopic evidence of inflammation, had normal patterns.

Tracings from the descending and transverse colon in five patients with colostomies failed to reveal any increase in resting activity at these higher levels as compared to the resting activity of the sigmoid colon.

In their concluding remarks Chaudhary and Truelove (1961b) emphasised the large variation in colonic motor activity in normal subjects which rendered estimates of hyperactivity or hypoactivity on mere visual inspection "grossly inadequate".

In their second communication Chaudhary and Truelove (1961c) reported the effect of a standard intramuscular dose of 1 mg. of Prostigmine. Eighty-six tracings were obtained from the same groups of subjects as previously. In all groups Prostigmine caused augmented activity which, however, was most marked in patients with the spastic colon disorder in the stage of symptoms. When no symptoms were present the response, although not so marked, was still greater than that seen in normal subjects. Patients with pure diarrhoea responded less than those with a spastic colon, but more than normal subjects.

In contrast, patients with ulcerative colitis did not differ quantitatively in their response from normal controls with the exception of patients in group I (severe to moderate symptoms) who showed an increase in long waves of high amplitude.

The overall picture was thus one of an excessive response to Prostigmine by patients with the irritable colon syndrome, whether of the spastic colon type or with pure diarrhoea, and whether in the stage of symptoms or not. Chaudhary and Truelove (1961c) concluded that this finding favoured the theory that all the patients with the irritable colon syndrome shared a common factor which persisted even when the disorder was quiescent. They suggested that this factor might be an increased reactivity to parasympathetic stimulation. On the other hand, there was little evidence for undue susceptibility to such stimulation in patients with ulcerative colitis.

The third study by Chaudhary and Truelove (1961d) concerned the effect of emotions on colonic motility. The method used to induce emotional stress under experimental conditions was a discussion with the patient of topics with an 'emotional loading'. They found that the frequency with which augmented motor activity was induced by the emotive interview was the same in all groups of subjects. Thus 25%

of the normal subjects, 26% of the patients with the irritable colon syndrome and 28% of the patients with ulcerative colitis showed a positive response. Patients with the irritable colon syndrome in the stage of symptoms reacted with enhanced motility more frequently than did symptom-free patients, but the numbers involved were small.

It is interesting to note that Chaudhary and Truelove (1961d) made no mention of a decrease in colonic motility induced by emotions. Such an occurrence was repeatedly described by Almy and his colleagues (Almy, Abbott and Hinkle, 1950; Almy, 1951) and abolition of motor activity was usually associated with feelings of guilt or inadequacy in the patient. However, since motor activity was normally seen in the colon for only about 13% of the recorded time (Chaudhary and Truelove, 1961b) it is possible that the periods of quiescence observed by Almy et alii (1950) bore no more than a temporal relationship to the interview.

More recently, Truelove and his co-workers (Ritchie, Ardran and Truelove, 1962) have reported the use of a balloon and an open ended catheter forming a differential unit in the study of motility. The differential unit was considered to be of value in detecting expansion of the bowel, and enabled waves caused by a contraction of the bowel in the neighbourhood of the recording device to be distinguished from those caused by transmission of the pressure generated by a contraction well above the differential unit. Ritchie et alii (1962) offered a classification of the different types of colonic motor activity based on simultaneous manometric studies and cine-radiology.

Kim and Barbero (1963) investigated the pattern of recto-sigmoid motility in children and showed that in children over six months of age the large bowel was active for a greater proportion of time than in adults. However, from their published results it is evident that they did not calculate the percentage activity in the same manner as did Davidson et alii (1956b) or Chaudhary and Truelove (1961b-d) rendering a comparison of the results of these three studies invalid.

3. Gastro-intestinal Radiotelemetering

The necessity of intubation was until recently the most serious disadvantage of assessing intestinal motility by measuring intra-luminal pressure fluctuations. Tubes were needed either to conduct the intra-luminal pressure changes to external transducers or to carry energy to transistors placed inside the intestine. The discomfort caused by the tubes made patients less inclined to undergo repeated or prolonged studies. Furthermore, nausea which was sometimes induced by tubes could alter the behaviour of the bowel.

The introduction of the ingestible radiotelemetering capsule in 1957 by two independent groups of workers (Farrar, Zworykin and Baum, 1957; Mackay and Jacobson, 1957) was therefore a significant advance in the methodology of gastro-enterological research. The approach of the two groups differed somewhat. Although both made use of frequency modulation radio transmitters, Farrar et alii (1957) enclosed a power supply in the capsule making it independent of external sources of energy, whereas Mackay and Jacobson chose to employ a passive transmitter consisting of a resonant circuit, the frequency of which was sensed from the outside.

The ingestible telemetering capsules in use today are essentially frequency modulation transmitters powered by small electric cells and have been used mainly for measurements of pressure fluctuations within the digestive tract. There are, however, reports of modifications which permit measurements of acidity and temperature (Connell and Rowlands, 1960; Rowlands and Wolff, 1960).

Basically, a telemetering capsule or 'radio-pill' adapted for pressure measurements consists of three components: the transducer, the transmitter and the power supply.

The transducer is a ferrite core, the disc of which carries the pressure sensitive component. This may be either a perspex diaphragm (Rowlands and Wolff, 1960) or a silver plated copper diaphragm. Alternatively, the pressure sensing device may be a bellows mechanism (Horowitz and Farrar, 1962).

The transmitter is usually designed to operate on a frequency between 300 Kc/s and 10 Mc/s (Watson, Ross and Kay, 1962). All circuits use the variation in inductance which results when intraluminal pressure fluctuations cause a movement of the pressure sensitive diaphragm or bellows and thus of the attached ferrite disc. The change in inductance results in a change in the frequency of oscillation of the transmitter. The radio signal is picked up by an aerial system outside the body and the frequency change demodulated by a receiver and recorded in a suitable way - usually by a direct writing recorder (Rowlands and Wolff, 1960).

Most radio pills are powered by a standard hearing aid mercury cell. This power supply will last 40 hours (Rowlands and Wolff, 1960) 80 hours (Watson et alii, 1962) or 4 to 5 days (Horowitz and Farrar, 1962) depending on the current required to operate the transmitter.

Technical Considerations in Radiotelemetering

The pressure sensing mechanism must give a stable performance to ensure reliable recording. A perspex diaphragm tends to undergo dimensional changes caused by the action of digestive secretions on its outer surface (Connell and Rowlands, 1960). Unless this is prevented, for example by covering the diaphragm with silicone grease, a baseline drift will develop during the recording. Alternatively, the diaphragm may be made of a more durable material, such as silver plated copper (Watson et alii, 1962); the bellows mechanism, if used, may be protected from blockage by intestinal contents by enclosing the capsule in a rubber bag (Horowitz and Farrar, 1962).

Voltage decay of the power supply is another possible cause of baseline drift. However, Watson et alii (1962) showed that the commonly used Mallory RM 312 mercury cell had a stable voltage curve as the current was drained from it. After an initial fall in the first 30 minutes, the voltage remained within 0.5% of the specified level of 1.32 volts, and the variation in frequency caused by this degree of decay was negligible. During actual recordings baseline drift, including drift in the receiver, was found to amount to less than a 3% change in carrier frequency. Thus the stability of the system was adequate.

It is well known that variations in environmental temperature influence the performance of radio-pills (Farrar, 1961). Watson et alii (1962) showed that frequency changes of up to 1 Kc/s could be caused by variations in environmental temperature within the physiological range. Each capsule was found to have its own temperature characteristics and thus had to be calibrated individually before use.

Another reason for calibrating each radio-pill separately is the fact that the change in frequency caused by a given pressure varies from one pill to the next. The range of pressures which can be recorded with acceptable linearity depends on the nature of the pressure-sensitive mechanism. A perspex diaphragm 0.2 mm. thick has been found suitable for pressures between 0 and 100 cm. of water (Rowlands and Wolff, 1960). The metal diaphragm 0.001 inches thick used by Watson et alii (1962) was reported to record up to a pressure of 50 cm. of water with a non-linearity error of less than 5%. Higher pressures could be recorded accurately by increasing the thickness of the diaphragm.

Practical Aspects of Telemetering from the Gut

The two main difficulties encountered in gastro-intestinal telemetering are the localisation of the capsule in the intestine and the phenomenon of 'loss of contact'.

The capsule is radio-opaque and its exact position in the large bowel can be easily ascertained by fluoroscopy. Localisation in the small intestine is more difficult, and even radiological contrast studies may not be wholly satisfactory if several loops of intestine are superimposed upon each other. Furthermore, the examination may have to be repeated at frequent intervals because the capsule, unless anchored by a thread, often moves rapidly through the upper small bowel.

Familiarity with the wave patterns usually found at different levels of the digestive tract is of help because gastric, small intestinal and colonic wave patterns are easily distinguished from one another. Indeed, Connell and Rowlands (1960) found themselves able to localise the capsule with a fair degree of accuracy from the nature of the pressure waves, and thought that with further experience fluoroscopic control might become unnecessary. However, most workers agree that radiology is still essential for accurate localisation (Horowitz and Farrar, 1962; Smith, 1962; Smith and Ridgway, 1962).

'Loss of contact' occurs when movement of the capsule causes a fall in signal strength. The strength of the radio signal depends on the position of the non-homogeneous field of the capsule in relation to the receiving aerial, being greatest when the aerial intercepts the maximum number of lines of force. If the capsule spins around the signal strength may fall below a critical level, causing an artefact in the pressure trace resembling a small bowel pressure wave (Connell and Rowlands, 1960; Sprung and Roisch, 1960).

Loss of contact may be prevented by the use of an omnidirectional aerial (Connell and Rowlands, 1960; Connell, McCall, Misiewicz and Rowlands, 1963). Alternatively, distortion of the pressure record may be avoided through the use of an electronic clamp which momentarily interrupts the recording when signal strength falls below the critical level (Smith, 1962; Smith and Ridgway, 1962).

On the other hand, loss of contact may provide information about movement of the capsule (Sprung and Roisch, 1960; Smith, 1962). If a contour map of signal strengths is plotted and the recording aerial purposely placed at the periphery, even slight changes in the position of the capsule will result in marked variations in signal strength. These variations can be recorded simultaneously with pressure fluctuations (Smith, 1962).

A further refinement was introduced by Connell et alii (1963) who combined pressure recording through an omnidirectional aerial with recording of signal strength through both an omnidirectional and a unidirectional aerial. Unfortunately the amount of electronic equipment necessary for this procedure may limit its acceptance in clinical practice.

While the position of the capsule in relation to the receiving aerial is constant, the signal strength depends on the distance between capsule and aerial. Thus the signal strength may be used to localise the capsule. Smith (1962), using a number of interchangeable aerials placed over the abdomen, found that signal strength was maximal through the central or left-sided aerial when the capsule was in the upper small intestine. When it had progressed to the caecum, the strongest signal was recorded through the lower right aerial loop.

The transit, recovery and possible re-use of the capsule also need to be considered. Transit though the gastro-intestinal tract is almost invariably uncomplicated, but if it is unduly long the 'life' of the power supply may be exceeded. Farrar and Bernstein (1958) reported one patient with an unsuspected carcinoid tumour in whom the capsule was arrested at the level of the tumour, and Connell and Rowlands (1960) had a similar experience in a case of unsuspected Crohn's disease. In both instances the provoked laparotomy led to a definitive diagnosis; nevertheless, radiotelemetering capsules should not be used in patients with suspected strictures of the intestine.

Recovery of the capsules presents no problem, but opinions differ on the question of repeated use of a capsule. Rowlands and Wolff (1960) used a 'one journey pill' and considered that the advantages of complete sealing and permanent connection of the battery outweighed the economic disadvantages. On the other hand, Farrar et alii (1957) preferred capsules with a replaceable power supply. Naturally the possibility of using the same capsule for a number of experiments is financially attractive, and even though adequate sealing of the battery end is difficult, it can be achieved (Watson et alii, 1962).

Results of Gastro-intestinal Telemetering

It is natural that many of the reports dealing with gastro-intestinal telemetering should have a strong methodological bias (Rowlands and Wolff, 1960; Mackay, 1961; Watson et alii, 1962; Smith, 1962; Connell et alii, 1963). However, the radio-pill has come into use as a tool for clinical research.

Farrar and Bernstein (1958) published a qualitative description of the motility of the small bowel in 10 normal subjects and 3 patients with functional alimentary disorders, but attempted no detailed analysis of their results. They also compared the tracings obtained through simultaneous recording with radio-pills and open ended catheters and found them to be virtually identical. Similarly, Sprung and Roisch (1960) described the small bowel patterns of 20 normal volunteers without attempting a quantitative appraisal. Connell and Rowlands (1960) published representative tracings from different levels of the gastro-intestinal tract and confirmed that tracings obtained with open ended catheters and with radio-pills were identical, though miniature balloons produced tracings with minor quantitative differences. Groisser and Farrar (1962) made use of the telemetering capsule in investigating the effect of small bowel motility on the absorption of radioactive sodium.

In 1962 Horowitz and Farrar reported quantitatively analysed results of the motility of the small bowel in 10 patients with functional gastro-intestinal symptoms and 12 normal subjects. Resting and post-cibal patterns were recorded. In their analysis the authors classified the waves into types I and III, and further subdivisions were then made on the basis of amplitude. Horowitz and Farrar found no difference between patients with functional alimentary disorders and control subjects in regard to the number and amplitude of type I waves. However, only 4 of the control subjects but all of the patients with functional alimentary symptoms showed type III waves.

Ross, Watson and Kay (1963) reported an elegant application of radiotelemetering to a clinical problem. They studied the return of intestinal peristalsis after gastric surgery with and without vagotomy. Eleven patients in whom gastric surgery was combined with vagal section showed a return of small bowel peristalsis after a mean of 10.2 hours; in the same number of patients who had gastric surgery without vagotomy, the corresponding time was 4.2 hours. The mean amplitude of the peristaltic waves was not influenced by vagotomy, and Ross and his colleagues concluded that the vagus exercised little control over the motility of the small bowel.

4. Radiology

Although radiological methods are a valuable aid in the diagnosis of gastro-intestinal disease, they have not been equally successful in elucidating the nature of normal and disturbed intestinal motility. Prolonged observation is necessary to observe the relatively slow and complex movements of the gut and its contents, and the amount of radiation involved made it impossible for the early investigators to study intestinal motility in man with any degree of safety.

Cannon (1902) studied motility in the cat and described in detail the fluoroscopic appearance of the different types of motor activity: segmentation, peristalsis and pendulum movement in the small bowel; peristalsis, anti-peristalsis and tonic constrictions in the large bowel. He also noted the abolition of all intestinal motility except the tonic constrictions of the colon in the excited or enraged animal, and was thus the first to draw attention to the fact that emotions influence motility. It is of some interest that the contrast medium used by Cannon (1902), a mixture of food and bismuth subnitrate, was probably more physiological than the pure barium suspensions of latter days which are not well suited for an investigation of the physiological behaviour of the gut. However, recently a standardised barium-food mixture has been introduced by Swedish workers (Mattsson, Perman and Lagerlöf, 1960) and found satisfactory.

An approximate estimate of motility can be made by using serial 'spot' films at regular intervals to decide on the progress of the contrast medium through the intestine. With this method Kirsh (1956) found a wide variation in the time taken for non-flocculating barium sulphate to reach the caecum. In 173 patients without known gastro-intestinal disease, the median transit time was 120 minutes, but in only 53% of the patients was the transit time between 90 and 180 minutes. It is clear that only gross deviations from the normal will be detected by this technique. However, transit times in normal people are claimed to be more constant if a 'physiological contrast medium', prepared by mixing the barium suspension with known quantities of carbohydrate, protein and fat, is used (Mattsson et alii, 1960). With this contrast medium the Swedish workers found slow small bowel transit in pancreatic steatorrhoea and non-tropical sprue, but normal transit in ulcerative colitis even when diarrhoea was present. In a later paper, Perman and Mattsson (1962) confirmed the slow small bowel transit in steatorrhoea. They found that the transit time was prolonged whether the steatorrhoea was of small bowel origin or secondary to pancreatic disease.

Abnormal small bowel transit times have also been reported in patients with the dumping syndrome following partial gastrectomy by Mattsson et alii,(1960) and Mattsson and Perman (1962). They reported that in patients with the dumping syndrome the 'head' or first part of the contrast medium traversed the small bowel at an extremely rapid rate, although the transit time for the remainder of the contrast was normal. Gastric emptying was equally rapid in patients with and without dumping.

Intermittent fluoroscopy may be used instead of serial 'spot' films, and is obviously more suitable for the observation of a dynamic process. However, with conventional equipment, the radiation hazard is not negligible. Using this method, Duthie and McKellar (1960) studied 35 patients who had undergone gastric surgery and in whom they attempted to induce dumping with hypertonic glucose. They found a mean small bowel transit time of 20 minutes in the patients who experienced dumping compared with 45 minutes when dumping did not occur. Hypermotility of the small intestine was noted in 12 of the 13 subjects in whom dumping was induced, but was also seen in the absence of dumping. Confirming the observations of Perman and Mattsson (1960), Duthie and McKellar did not find any evidence of more rapid gastric emptying in the presence of dumping.

In contrast to these findings, Cox and Allan (1960) reported complete stasis, dilatation and lack of peristalsis of the gastric remnant, duodenum and jejunum in four patients in whom dumping was reproduced by the particular food known by the patient to precipitate an attack. Two patients with less severe symptoms showed similar but less marked radiological changes.

Realising that most other workers had reported increased motor activity in the small bowel in the presence of symptoms of dumping, Cox and Allan (1960) attributed the discrepancy to the way in which dumping was induced. While other investigators had provoked the attacks with hypertonic glucose, Cox and Allan (1960) used 'natural foods', for example, sweetened egg-flip. However, the results of Jordan, Overton and De Bakey (1957a), Mattsson et alii (1960) and Mattsson and Perman (1962) were obtained with a food mixture of a composition similar to that used by Cox and Allan (1960).

Another possible explanation is that since Cox and Allan (1960) screened their patients at regular intervals and on the first symptoms of a dumping attack, the initial hypermotility and rush of contrast through the small bowel described by Mattsson et alii (1960) may already have occurred and thus escaped notice. This hypothesis receives some support from the manometric studies of Christoffersson, Kewenter and Kock (1962) demonstrating abolition of all small bowel motor activity after an initial period of hypermotility lasting from 2 to 8 minutes.

Of the radiological techniques available for the study of gastro-intestinal motility, only cineradiography combines the opportunity for prolonged observation with availability of permanent records for later analysis. However, although feasible for many years, cineradiography could be used only for animal work (Gianturco and Alvarez, 1932) until the recent development of X-ray image intensification. Image intensification reduces the amount of surface radiation received by the patient during the exposure of the cine film to the order of 20 r/min. (Liljedahl, Mattsson and Pernow, 1958) or 2.5 r/min. (Texter, 1961) depending on the type of X-ray plant, the filter and the film used.

In the field of gastro-enterology, X-ray cine films have been used to study the function of the oesophagus (Vantrappen, Liemer, Ikeya, Texter and Barborka, 1958; Vantrappen, Texter, Barborka and Vandenbroucke, 1960), the biliary tract (Caroli, Porcher, Pequignot and Delattre, 1960), the stomach, and the small and large intestine.

Liljedahl et alii (1958) described the radiological appearances of the small bowel in 11 persons before and after the administration of drugs enhancing motility. Another group of Swedish workers, Wallensten, Garsten, Jonson and Saltzman (1959) studied the activity of the small bowel after partial gastrectomy. They found hypermotility of the small bowel during glucose-induced attacks of dumping, and claimed good correlation between the degree of hypermotility and the severity of the attack. Liljedahl, Mattsson, Pernow and Wallensten (1959) showed that rapid small bowel transit was a characteristic radiological feature in patients prone to dumping even when the examination was made with the patient supine and no attempt was made to provoke an attack. They also remarked on the development of a "pyloric sphincter substitute" after a Billroth I gastrectomy and contrasted this with the absence of a closing mechanism and the resultant rapid gastric emptying seen after the Billroth II operation.

The development of a closing mechanism following partial gastrectomy with jejunal transplantation was described by Hedenstedt, Liljedahl and Mattsson (1961). The new 'sphincter' appeared at the site of the gastro-jejunal anastomosis. The transport of contrast medium through the small bowel was described as 'slightly livelier' in patients who experienced dumping after this particular operation than in those who did not.

Rothnie, Kemp-Harper and Catchpole (1963) combined the use of fluoroscopy, serial spot films and cineradiography in an investigation of the return of the motility of the stomach and small bowel after abdominal surgery. They found that both mixing and peristaltic activity was present in the upper small intestine within 24 hours and that neither surgical vagotomy nor surgical procedures directly involving the stomach influenced the rate of return of motor activity.

Although radiological techniques enable observation of the behaviour of the gut under physiological conditions, they have some distinct disadvantages.

Firstly, as already mentioned, even with modern equipment the time of observation is limited by the amount of radiation the patient receives.

Secondly, even when permanent records are obtained - for instance during cineradiography - the analysis of the records is largely confined to a subjective impression of the degree of motility present. 'Blind', preferably dual readings by experienced radiologists will reduce the error, but the opinions given must by necessity still be subjective.

Thirdly, unless transit times to set levels of the intestine are determined, there is no basis for comparison of results of different groups of workers. However, transit times are only a gross indication of gut motility, and vary considerably even in normal subjects (Kirsh, 1956). Differences between the results of two authors may also be due to the nature of the contrast medium used in each particular study. Kirsh (1956) found that small bowel transit was faster for non-flocculating contrast than for the standard flocculating barium suspensions, and Mattsson et alii (1960) claimed a more rapid transit when a food-barium mixture was substituted for conventional contrast media.

Combined Studies

Important information should be obtained from radiological methods when they are used in combination with pressure recording from the gut. For instance, if during manometric pressure recordings the bowel in the region of the recording device is visualised by means of contrast fluoroscopy or cineradiography, it should be possible to interpret the recorded wave patterns in terms of function such as propulsion and segmentation.

There are few reports of investigations in which the combined technique has been applied to the study of the motor activity of the digestive tract. The physiology of the oesophageal contractions and the closing mechanisms at the gastro-oesophageal junction were clarified by Vantrappen and his colleagues (Vantrappen et alii, 1958; Vantrappen et alii, 1960). Lorber and Shay (1954) investigated the effect of posture, barium ingestion and air insufflation on the intra-gastric pressure. Chapman and Palazzo (1949) combined balloon kymography and fluoroscopy and described the propulsive and non-propulsive wave patterns of the small intestine. Propulsion was said to be associated with tall sustained waves lasting longer than 2 minutes although the authors later stated that no contractions of this duration appeared during the fluoroscopic observations.

Smith, Texter, Stickley and Barborka (1957) studied the effect of an acid barium suspension on gastro-duodenal motor activity in patients with peptic ulceration and in normal controls. They showed that although basal activity was similar in both groups, ingestion of the acid contrast medium caused a greater increase in motility in patients with active ulceration than in the control group. The increase in activity was greatest when ulcer type distress was produced.

The combined technique has also been used to investigate gastro-intestinal function after partial gastrectomy. Jordan, Barton and Williamson (1957b) studied 46 patients in the second post-operative week, although radiology and pressure recording was done simultaneously in only two. They found no correlation between the rate of gastric emptying and the degree of gastric motility and considered that the gastric remnant emptied largely because of the effect of gravity. They demonstrated that gastric emptying was significantly more rapid after a gastro-jejunal anastomosis than after a gastro-duodenal one.

Glazebrook and Welbourn (1952) reproduced dumping in 3 of 23 patients after gastrectomy by distension of the jejunum with a balloon. This manoeuvre resulted in increased small bowel motility, although it might not be valid to draw conclusions from this study, because distension of the gut to the point of obstruction normally leads to increased motility proximal to the obstruction. When dumping was induced by jejunal instillation of hypertonic glucose, increased motility again resulted and the change could be reversed by the instillation of tap water. Radiologically the increased motor activity was reflected in 'violent peristalsis' with rapid small bowel transit. Jejunal dilatation was not seen. Penta- and hexamethonium bromide, which normally depress motility, prevented hypermotility and the onset of dumping when given before the hypertonic glucose solution. These results tend to incriminate hypermotility as a causative factor in the production of dumping symptoms, but one aspect of Glazebrook and Welbourn's (1952) work is open to criticism. Dumping was induced in all the patients given hypertonic glucose: thus there was no way of comparing the motor activity during an attack of dumping with the response of the small bowel to glucose in the absence of symptoms of dumping. On the other hand, it should be remembered that the radiological findings of Glazebrook and Welbourn (1952) receive support by some later work (Wallensten et alii, 1959).

The combined method has also been used to study the motility of the colon. Chaudhary and Truelove (1961b) published a preliminary report on the simultaneous use of intra-luminal pressure tracings and cineradiography. The presence of a wave on the tracing was associated with movement of the colon in the vicinity of the recording tip; the higher the wave the more pronounced was the movement. Big waves were associated with propulsion of bowel contents. In a later report Ritchie, Ardran and Truelove (1962) enlarged on these findings and submitted a classification of the various types of motor activity seen in the colon together with a discussion of their physiological significance.

5. Electromyography

This method of studying intestinal motor activity has been widely used in animal work (Milton and Smith, 1956; Holaday, Volk and Mandell, 1958; Daniel, Carlow, Wachter, Sutherland and Bogoch, 1959), and it is of fundamental importance in allowing motility to be studied by a different approach. It provides information about the electrical events which precede and coincide with the contraction of smooth muscle cells rather than about the pressure changes which result from this contraction as manometric studies do. Its application to man has so far been rather limited, although studies have been performed on the exposed gut during laparotomy (Daniel et alii, 1959) and also on the small bowel in its natural state (Colcher, Goodman and Katz, 1959; Daniel, Honour and Bogoch, 1960).

Milton and Smith (1956), working with exteriorised small bowel loops in dogs, described two kinds of electric potentials; a slow wave-like regular potential and a rapid spike potential. Milton and Smith (1956) were particularly interested in the nature and origin of the slow potential which, as they observed, occurred at a faster rate in the duodenum than in the ileum. They showed, that if the gut was clamped transversely or if ring infiltration with a local anaesthetic was performed, the rate of the slow potentials decreased distal to this 'functional block'. This, in their opinion, supported the concept of a pace-maker area of the small bowel, probably located in the duodenum in the region of the ampulla of Vater. The pace-maker was thought to control the frequency of the rhythmical contractions of the small bowel although ectopic foci could easily be produced by the local application of heat to the duodenal wall at any level.

Holaday et alii (1958) were of a different opinion regarding the origin of rhythmicity in the small bowel. In addition to animal work, they described a method suitable for electromyography of the intestine in unanaesthetised humans. By securing unipolar electrodes to the surface of balloons attached to a double lumen tube, they were able to make simultaneous recordings of electrical activity and intra-luminal pressure fluctuations. The recordings were said to have been successful although none were published. Holaday et alii (1958) agreed on the two basic types of electrical activity, the slow regular fluctuations and the rapid spike potentials. In exteriorised bowel loops the latter were invariably accompanied by visible contractions and were thus action potentials of the muscle fibres. They were augmented by drugs known to increase intestinal motility such as acetylcholine and Prostigmine and abolished by atropine and Banthine, both known depressants of intestinal motor activity. Action potentials were not seen when the tonus of the bowel was raised by morphine, providing that the tonus rise was not accompanied by contractions.

The low potentials, Holaday et alii (1958) postulated, represented cyclic alterations in the resting potential of the smooth muscle fibres rendering these alternatively excitable and refractory. They were thus considered to originate in the muscle fibres themselves and as expected, were not affected by drugs. Holaday and his colleagues (1958) believed that the capability of altering its state of electrical excitability was inherent in each smooth muscle fibre, and hence disagreed with the concept of a pace-maker controlling the rhythmicity of small bowel movements. For movements necessitating the participation of a number of bowel segments simultaneously or in rapid succession, such as the peristaltic rush and gastro-colic reflex, they postulated a mechanism subserving the coordination of multiple segments. They suggested, that the extrinsic nerve supply of the bowel together with the intra-mural plexuses of Auerbach and Meissner assumed this function, particularly as they could show that intra-arterial procaine which blocked the intra-mural plexuses led to a disruption of coordinated movements without affecting rhythmic contractions. Thus, Holaday et alii (1958) concluded that one mechanism, probably inherent in smooth muscle, was responsible for rhythmic contractions and another governed coordinated activity.

Daniel et alii (1959) accepted the concept of a pace-maker in the duodenum, but considered that the slow potentials were under the control of a pace-maker only in the upper part of the small bowel. They confirmed the finding of Holaday et alii (1958) that rapid spike potentials only occurred when the gut was demonstrably active.

In summary then, it appears that the slow potentials represent fluctuations in the resting potentials of smooth muscle cells. Whether a pace-maker exerts any influence on the rate of these cyclic fluctuations or not remains a matter of argument. There seems, however, to be no doubt that spike potentials represent muscular activity, whether they originate in the longitudinal muscle or in the myenteric plexus (Daniel et alii , 1959). As the action potentials are presumably governed by the slow waves and occur only in the relatively positive phases of the slow waves, and as the smooth muscle is probably in itself capable of altering its state of excitability (Holaday et alii, 1958), it seems likely that action potentials do originate in the muscle cells. The role of the intra-mural plexuses and the extrinsic nerve supply is most likely that of a coordinating mechanism for motor activity involving the integrated action of multiple bowel segments, although surgical vagotomy does not alter the electromyographic pattern of the small intestine (Colcher et alii, 1959).

6. Miscellaneous

The extensive literature concerning *in vitro* studies of motility and studies on experimental animals will not be reviewed in detail. *In vitro* studies using isolated human intestine (Streeten, Hirschowitz, Henley and Pollard, 1957; Fishlock and Parks, 1963) and animal intestine (Koelle, Koelle and Friedenwald, 1950) have provided information about the effects on motility of acetylcholine (Fishlock and Parks, 1963), cholinesterase inhibitors (Koelle et alii, 1950), noradrenaline, histamine, and serotonin 5-hydroxytryptamine (Fishlock and Parks, 1963) and afferent and efferent vagal stimulation (Harper, Kidd and Scratcherd, 1959). *In vitro* work has also clarified the intrinsic reflex arc which mediates the peristaltic reflex (Bülbring, Lin and Schofield, 1958) and *in vitro* studies led Alvarez (1914, 1919) to postulate the presence of a metabolic gradient as the cause of peristalsis.

In vivo animal studies have been undertaken to elucidate the effect of induced hyperthyroidism (Fetter and Carlson, 1932; Fetter, Barron and Carlson, 1932) and of surgical vagotomy (Muren, 1956) on gastro-intestinal motility. Reid, Ivy and Quigley (1934) used a simple but ingeniously devised 'spiral bolus' or 'gyrometer' to prove that, at least in the dog, propulsion along the small intestine was always associated with counter-clockwise rotation.

There are four methods of studying human gastro-intestinal motility (apart from those described in sections 1 to 5 of this Chapter) which are no longer in use, but nevertheless merit a brief commentary.

The advances in the design of external pressure transducers led to the development of miniature electric and electromagnetic transducers for use in the lumen of the intestine (Abbott, Hartline, Hervey, Ingelfinger, Rawson and Zetzel, 1943; Quigley, Brody, McKay, Landolina and McAlister, 1950; Hightower, 1952). These enjoyed a short vogue but the technical problems of supplying electrical energy through a swallowed cable prevented their general use.

Farrar and Ingelfinger (1955) made a study of gastro-intestinal motor activity by strapping a microphone to the abdominal wall of their patients and recording the sounds produced in the stomach and intestine on magnetic tape. This method led to the introduction of a new classification: instead of referring to waves of types I, II and III, Farrar and Ingelfinger (1955) now spoke of "staccato pops", "musical pings" and "series of pops". However, since sounds are produced by contractions only if the intestine contains gas, the method was not accurate enough to warrant further development.

Wenger, Engel, Clemens and Cullen (1961) let their patients swallow a small magnetic rod. The contractions of the stomach caused changes in position of the rod which were detected by a magneto-meter outside the body and recorded. The sensitivity of the equipment was high and movements of less than one degree could be detected; however, the amplitude of the contractions could not be measured. Although not suitable for use in the small bowel, this method appears to be quite a sensitive indicator of gastric motor activity which, because of the low pressures generated, is difficult to assess by more conventional means.

Direct observation is the simplest and easiest method of assessing the motility of the gut. However, objective measurements cannot be made by this method alone. Its applicability to unanaesthetised human beings is obviously limited and observation of the gut at laparotomy tells us little about normal bowel function. In animals, however, direct observation of exteriorised intestinal loops can be combined with photographic recording (Faik, Grindlay and Mann, 1950).

Weeks (1946) had the opportunity of studying a wounded Arab soldier in whom two loops of ileum, the transverse and sigmoid colon and a subsequent colostomy were visible. Weeks observed the reaction of the bowel to various drugs, local stimulation and changes in the patient's mental attitude.

Prolonged sigmoidoscopic observations of the motor activity, vascularity and secretion of the colon were made by Almy and his co-workers (Almy and Tulin, 1947; Almy, Hinkle, Berle and Kern, 1949b; Almy, Kern and Tulin, 1949a; Almy, 1951). They were particularly interested in the response of the colon to stress such as conflict-producing interviews, immersion of the hand in ice water, or headache induced by a headband. Such measures induced spasm of the sigmoid colon in all of a group of seven normal volunteers (Almy and Tulin, 1947). Later the study was extended to include 39 patients with spastic constipation (Almy et alii, 1949b) and 39 normal subjects (Almy et alii, 1949a). In both of these studies balloon kymography was used as an ancillary in the assessment of motility. Increased motility under stress was found in a proportion of the subjects in both groups but comparison is made difficult by the unequal and often small numbers subjected to the various kinds of stress. A further similar study was undertaken in 1951 (Almy, 1951). As a result of these investigations Almy and his associates made the following conclusions.

1. Both in healthy persons and in patients with spastic

constipation the nature of the reaction to experimentally induced stress is the same. The difference between the two groups is in the degree of reactivity, patients with colonic symptoms reacting more easily because of a difference in personality (Almy et alii, 1949b).

2. Patients with spastic constipation are tense and react to stress with hostility, aggression and sigmoid spasm. In contrast, patients with functional diarrhoea are soft-spoken with superficial attitudes of guilt, a sense of personal inadequacy and reduced colonic motility (Almy, 1951).

3. Functional colonic disorders are thus no more a disease of the colon than blushing is a disease of the skin (Almy, 1951).

However, although Almy and his associates carried out their experiments with great persistence and ingenuity, their results are mainly presented in the way of isolated illustrative case reports. Most of their measurements were subjective and the balloon studies are inadequate, because only one balloon was used and no attempt was made to quantitate the total duration of activity. Furthermore, the manner by which they produced stress seems far removed from natural stress, though it must be conceded that it is probably impossible to quantitate stress and often difficult to judge its presence.

Wener and Polonsky (1950) and Wener, Morton and Polonsky (1952) made prolonged observations on one patient with ulcerative colitis who had had a colostomy. They attempted to correlate the vascularity and motility of the colon with the emotional state of the patient. They observed their patient both before and after a surgical vagotomy had been performed for the disease, and found that the reaction of the colon to emotions was similar in both instances, though the degree of mucosal vascular reaction was somewhat reduced after vagotomy. Supporting Almy (1951), Wener and Polonsky (1950) found that feelings of resentment and hostility in their patient were generally associated with increased motility. However, whereas Almy and Tulin (1947) noted only increased motility under conditions of painful stress, Wener and Polonsky (1950) observed reduced motility.

A modification of direct observation was employed by Faik et alii (1950) who studied the effect of vagotomy on small bowel activity in dogs. They recorded photographically the movements of exteriorised loops of duodenum, jejunum and ileum for three months before and six months after the dogs had been submitted to surgical vagotomy. They found that vagal section abolished the normal increase in motility brought on by the sight and smell of food though not the increase in motility in response to feeding. Furthermore, peristaltic waves were fewer and of smaller amplitude after vagotomy. Though having the attraction for permanent objective records, this method is for obvious reasons restricted to animal work, and it seems unlikely that direct observation will be of practical value in the study of human intestinal motility.

7. Commentary

It has been shown that a great number of methods have been applied to the study of intestinal motor function in man. Direct observation of the gut, large and small balloons, ingestible electrical transducers, electromyography, microphones attached to the abdominal wall, catheters, radiology and radiotelemetering capsules have all been employed to furnish information about the motor function of the digestive tract. Many of these methods are now of historical interest only, rendered obsolete by the progress in medical physics. Those that remain in use all have their limitations which must be clearly appreciated if reliable information is to be gained.

As large as the number of methods that have been used is the field to which they have been applied. Motility has been investigated in conditions such as peptic ulceration, idiopathic and tropical sprue, coeliac disease, mucoviscidosis, ulcerative colitis, congenital megacolon and the irritable colon syndrome. The effect of drugs such as morphine, atropine, adrenaline, prostigmine, mecholyl, probanthine, 5-hydroxytryptamine and placebos has been studied. So has the response of the gut to food, sleep, pain and emotional upsets; also alterations in motor function following vagotomy, splanchnic resection and partial gastrectomy.

In spite of the time and effort spent in these studies and the mass of data accumulated by a large number of workers, our progress in the understanding of the motor function of the gut has been disappointingly slow. Already in 1898 Grützner forecast that "many a flash must come from the Röntgen tube before the normal movement of the intestinal contents is made entirely clear by this method". Perusal of some of the more recent reviews of intestinal motility reveals that Grützner's feelings are still echoed by workers in this field (Code, Hightower and Morlock, 1952; Chaudhary and Truelove, 1961a; Connell, 1961a; Texter, 1963).

To make further progress in the field of intestinal motility, the following points need consideration:

Firstly, the classification and analysis of pressure waves must be uniform if comparison between the results of different workers is to be possible. Templeton and Lawson (1931) classified the waves recorded from the large intestine of the dog into types I, II and tonus changes. This division was later adapted for work in man by Adler, Atkinson and Ivy (1941), the tonus change being called type III. Later type IV waves were described both in the small bowel (Code et alii, 1957) and large bowel (Spriggs et alii, 1951; Kern et alii, 1951). The classification of waves has been done by inspection of pressure tracings obtained with widely different techniques, and it is therefore not surprising that the characteristics of waves of types I to IV differ markedly from one author to the next. It is now generally agreed that although it is frequently possible to recognise waves corresponding to types I, II and III respectively, accurate classification of all waves is not possible (Davidson et alii, 1956b; Chaudhary and Truelove, 1961b; Barbero et alii, 1958; Farrar and Bernstein, 1958; Connell, 1962). The only objective way of analysis is to measure the amplitude and duration of all waves and to plot their distribution according to these characteristics.

Secondly, information is needed on problems of fundamental importance: what relationship do changes in intra-luminal pressure recorded as waves bear to motility of the bowel?; can the function of a wave in terms of propulsion, mixing etc. be inferred from its kymographic appearance?; and is movement of the bowel contents dependent not so much on the strength and duration of a contraction as on the resistance offered by adjacent segments of the gut?

To these questions we have as yet no valid answers. In the past the assignment of function to the various wave forms has come largely from the observation of expulsion of faeces or flatus through artificial stomas (Posey et alii, 1948) and is therefore of limited value. Recently, correlative cineradiographic and manometric studies of colonic motility have been done (Chaudhary and Truelove, 1961b; Ritchie et alii, 1962) but the technique has not yet been applied to the small bowel. With the exception of Chapman and Palazzo's (1949) work, already discussed in Chapter II (4), no information based on correlative studies of motility of the small bowel is available in the literature.

Thirdly, the pattern of motility in normal subjects must be established. This includes the range of variation between different subjects as well as the variation in repeated recordings done in the same person under identical conditions. As mentioned in Chapter II (2b), until recently most measurements of pressure changes in the intestine were done with the balloon-manometer system. This, although capable of detecting qualitative changes in motility, lacks the linearity and frequency response necessary for quantitative analysis of the data. Thus at the present moment there are only three quantitative reports of colonic motor activity in normal subjects: two concerning children (Davidson et alii, 1956b; Kim and Barbero, 1963) and one concerning adults (Chaudhary and Truelove, 1961b,c,d). In respect of the small bowel, information is even more meagre; the only quantitative analysis deals with duodenal activity monitored through a single recording tip in children (Barbero et alii, 1958).

Fourthly, with respect to intra-luminal pressure recordings, the greater part of the intestine is still terra incognita. This applies particularly to the lower small bowel and the proximal colon which, in the absence of surgically created stomas, are practically inaccessible to pressure recording. With the introduction of the radio-telemetering capsule, this matter will no doubt be rectified.

Attention to these four points is a prerequisite for the study of problems such as the physiological function of different wave forms, the relationship between motility and absorption, and the changes in motility in various disorders of the gut.

CHAPTER III

METHODS AND MATERIAL

Purpose of the Investigation

Alterations in intestinal motility have been postulated in a number of alimentary disorders. Two of the most common of these disorders are the dumping syndrome following gastric surgery and the irritable colon syndrome.

The early dumping syndrome is one of the most frequent and troublesome complications of partial gastrectomy. It is more common with the Polya than the Billroth I type of anastomosis (Capper and Welbourn, 1955). Following gastric resection most patients experience a sensation of abdominal fullness after eating. This can be regarded as physiological and tends to diminish with time. However, in many patients the ingestion of sweet or liquid foods is followed by a sensation of abdominal fullness, drowsiness, weakness, palpitations and sweating. Abdominal colic, borborygmi and explosive diarrhoea may also be present. These symptoms constitute the early dumping syndrome which in one particular study was found in 19% of patients who had had a Billroth I partial gastrectomy and in 24% of patients after the Polya operation (Capper and Welbourn, 1955).

The importance of the dumping syndrome is three-fold. Firstly, the subjective discomfort makes the patient less satisfied with the result of an otherwise successful operation. Secondly, the symptoms may be severe enough to decrease his capacity for work; this aspect is highly relevant as in many instances the operation has been performed to restore the earning capacity of a patient disabled by persistent ulcer pain. Thirdly, a restriction in food intake may be self-imposed by the patient with moderate or severe symptoms of dumping. Consequently his state of nutrition, which is often impaired at the time of operation, may not be corrected and may even deteriorate further. However, it should be emphasised that although at times severe symptoms persist long enough to warrant operative reconstruction of the anastomosis, this is the exception, and in most patients the intensity of the dumping syndrome diminishes with time.

The irritable colon syndrome is another condition in which disturbed motility has been considered of importance. The term embraces a number of manifestations of colonic dysfunction in which no organic disease can be demonstrated. The condition is characterised by abdominal pain, constipation and diarrhoea, alone or in various combinations. Many factors have been thought important in its aetiology: psychosomatic disturbance (Kalser, Zion and Bockus, 1956); previous bacillary and amoebic dysentery (Chaudhary and Truelove, 1962); intolerance to specific foods (Truelove and Reynell, 1963); previous abdominal operations; and the administration of broad-spectrum antibiotics (Kalser et alii, 1956). The irritable colon syndrome has many synonyms, some of which are mucous colitis, spastic colitis, colonic neurosis, the unhappy colon, nervous diarrhoea and dyssynergia of the colon. These synonyms reflect the wide range of clinical manifestations of the disorder and the many factors which have been implicated in its aetiology.

It is difficult to obtain an accurate impression of the prevalence of the irritable colon syndrome as a definitive diagnosis requires complete exclusion of organic alimentary disease. Therefore a well-documented diagnosis will usually be made only in those instances in which the symptoms are severe enough to make either the patient or his medical adviser request a full diagnostic study.

The work on which this thesis is based concerns a number of aspects of motility in health and disease:

the study of motility using intra-luminal pressure recordings and cineradiography, separately and together;

the quantitation of motility recordings by the measurement of the amplitude and duration of all waves, and the calculation of the percentage motor activity, the motility index, the mean amplitude of waves, the mean duration of waves and the distribution of waves on the basis of amplitude and duration;

the study of the range of motor activity of the small and large intestine in normal subjects and the effect on motility of emotion, food and Prostigmine;

the study of the behaviour of the small intestine in patients who have undergone partial gastrectomy with particular reference to changes in motility during the dumping syndrome;

the study of motility of the large intestine in patients with the irritable colon syndrome and in patients with a variety of diseases affecting the alimentary tract;

the study of the mechanism of constipation and diarrhoea;

the application of radiotelemetering to the study of relatively inaccessible parts of the intestine, in particular the proximal colon;

the correlation of wave forms in the motility tracings with the appearance of the intestine at cineradiography.

It is believed that the results of these studies have made a contribution to medical knowledge, particularly in the quantitative comparison of the motility of the small intestine in normal subjects and in patients following partial gastrectomy, the behaviour of the large bowel in conditions associated with diarrhoea, and the correlation of intra-luminal pressure recordings of the small intestine with their cineradiographic counterparts.

I declare that this thesis is my own composition and that none of the material contained in it has been submitted for any other degree or diploma in any University.

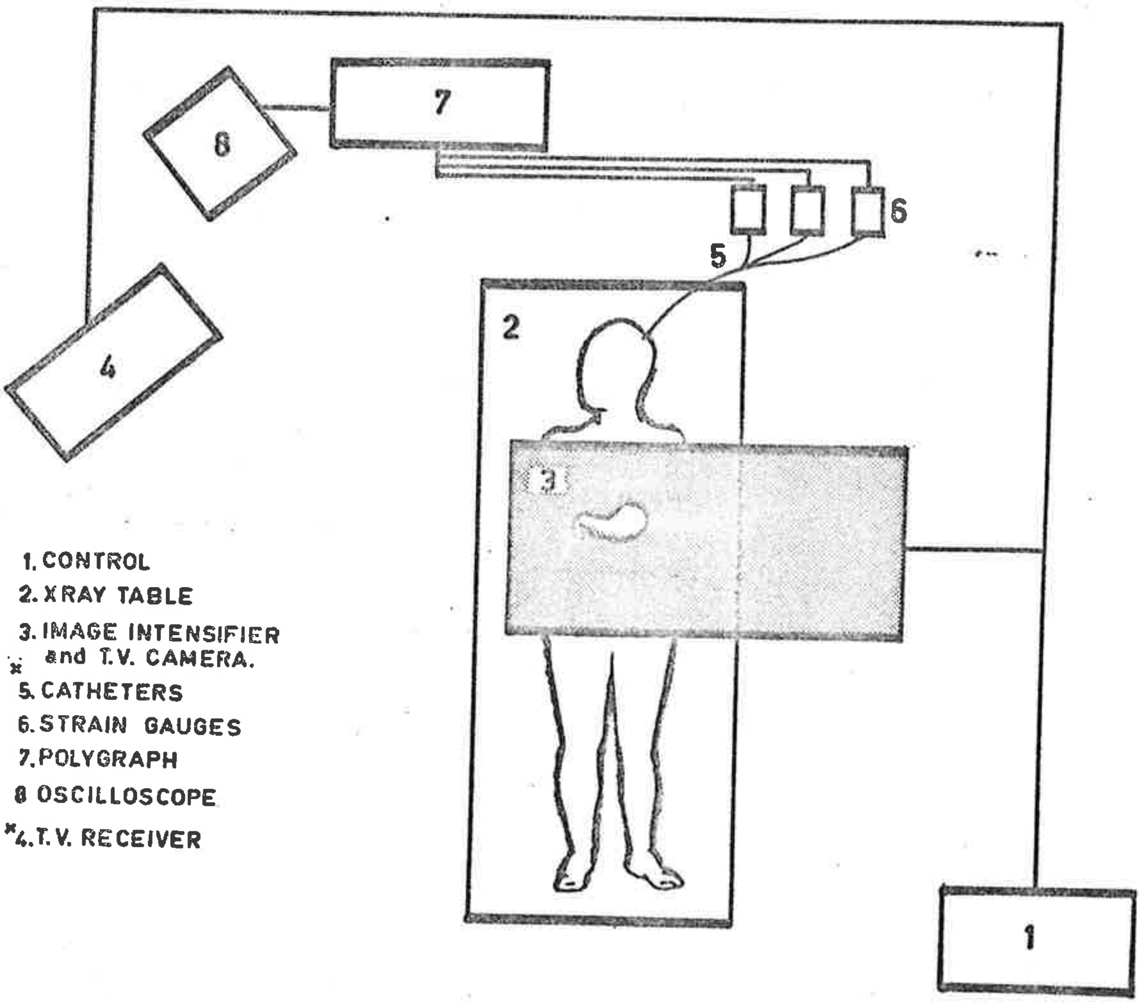


Figure 2: Diagrammatic representation of the equipment used in combined manometric and cineradiographic studies of motility.

Methods

In this study motility of the small and large intestine was assessed by two methods: by recording the intra-luminal pressure changes with either open ended catheters or radiotelemetering capsules or both of them; and by image intensification cineradiography. In many of the experiments pressure recordings and cineradiography were used simultaneously.

1. General Description

Figure 2 shows diagrammatically the general arrangement of the equipment that was used for studying motility. Three open ended polythene catheters filled with normal saline were placed in the part of the intestine to be studied. The catheters were connected to Statham strain gauges. The changes in pressure within the intestine were transmitted by the saline in the catheters to the transducer diaphragm of the strain gauges. The electrical current induced in the strain gauges by the changes in pressure was fed into a Grass four-channel polygraph where it was amplified and recorded by direct writing pen recorders. The fourth channel of the polygraph was either used to amplify and record the output from the radio-pill receiver or to record respiration. The pressure fluctuations could be monitored through the polygraph with a cathode-ray oscilloscope. A Philips 11 inch closed-circuit television image intensifier coupled to a 35 mm. Arriflex camera was used for simultaneous cineradiography.

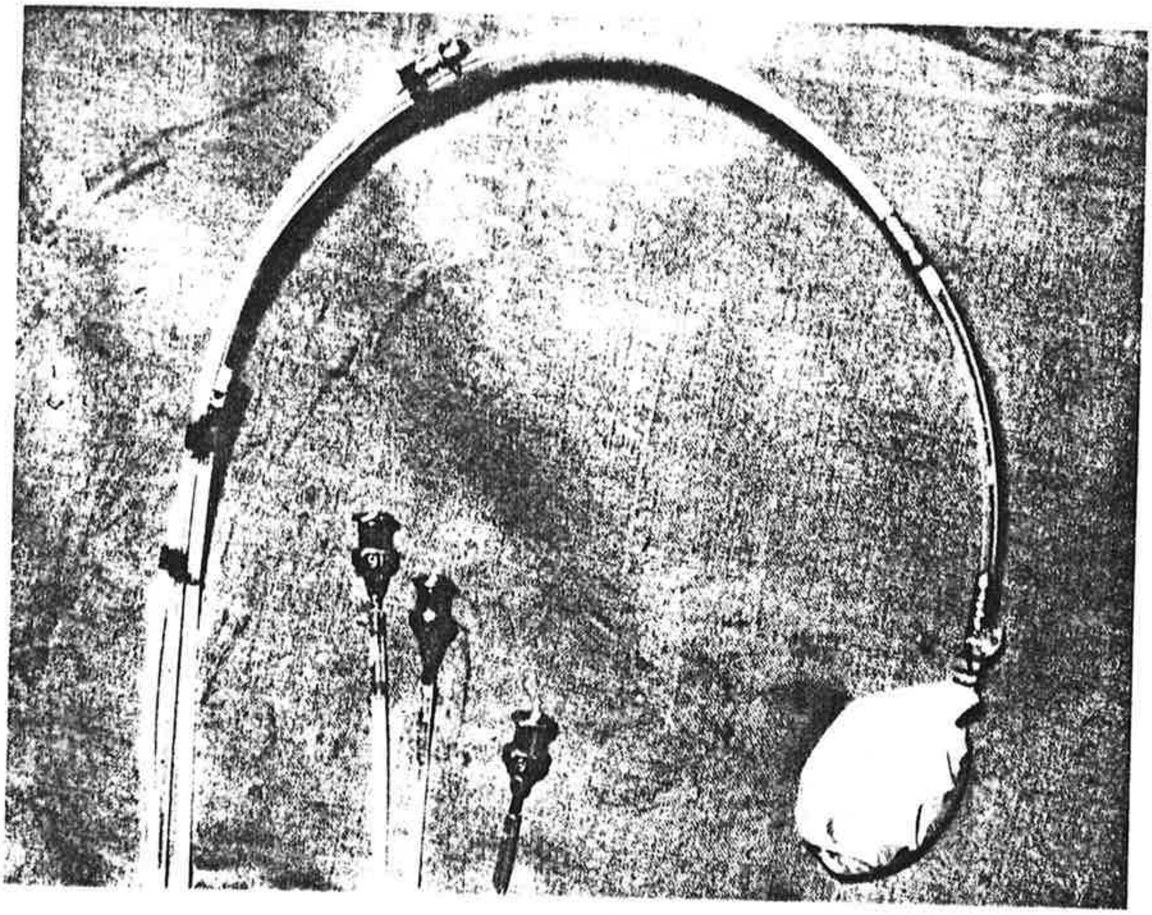


Figure 3: The catheters used to record intraluminal pressures in the small intestine.

2. Recording Catheters

In studies of the small bowel three flexible polythene catheters with an internal diameter of 1.5 mm. and an external diameter of 2.5 mm. were fixed together with ties of surgical silk. The most distal catheter carried a terminal perforated brass ring to which a latex balloon containing 2 - 4 cc. of mercury was attached to facilitate transport through the upper intestine (Blankenhorn, Hirsch and Ahrens, 1955). Eight centimetres from the attachment of the balloon two ports of 1.5 mm. diameter were drilled through the catheter and surrounding thin brass capsule to constitute the first recording tip. The lumen of the catheter between this tip and the balloon attachment was obliterated with a wooden plug. The tips of a further two catheters were covered with hollow brass cylinders through which lateral ports 1.5 mm. in diameter had been bored.

The catheters were tied to the first so that their open ends lay at distances of 7 cm. and 14 cm. from the first recording tip. The distance of 7 cm. from one recording tip to the next was chosen because the work of Posey and Bargen (1951) suggested that the length of the functional segment of the human small bowel was approximately 5 cm. The catheter assembly, shown in Figure 3, measured 150 cm.

The catheters which were used to record intra-luminal pressure in the large bowel were fashioned in a similar manner. Three lengths of 1.5 mm. bore polythene tubing were held together by brass rings in such a way that the three recording tips, each one covered by a brass capsule with terminal and lateral ports, were 7 cm. apart. The length of the assembly was 150 cm. The catheters were syringed gently with normal saline if the recording tips became blocked. The rate at which this occurred varied greatly, but such occlusion was rarely troublesome and its presence could easily be determined by inspection of the pressure tracing.

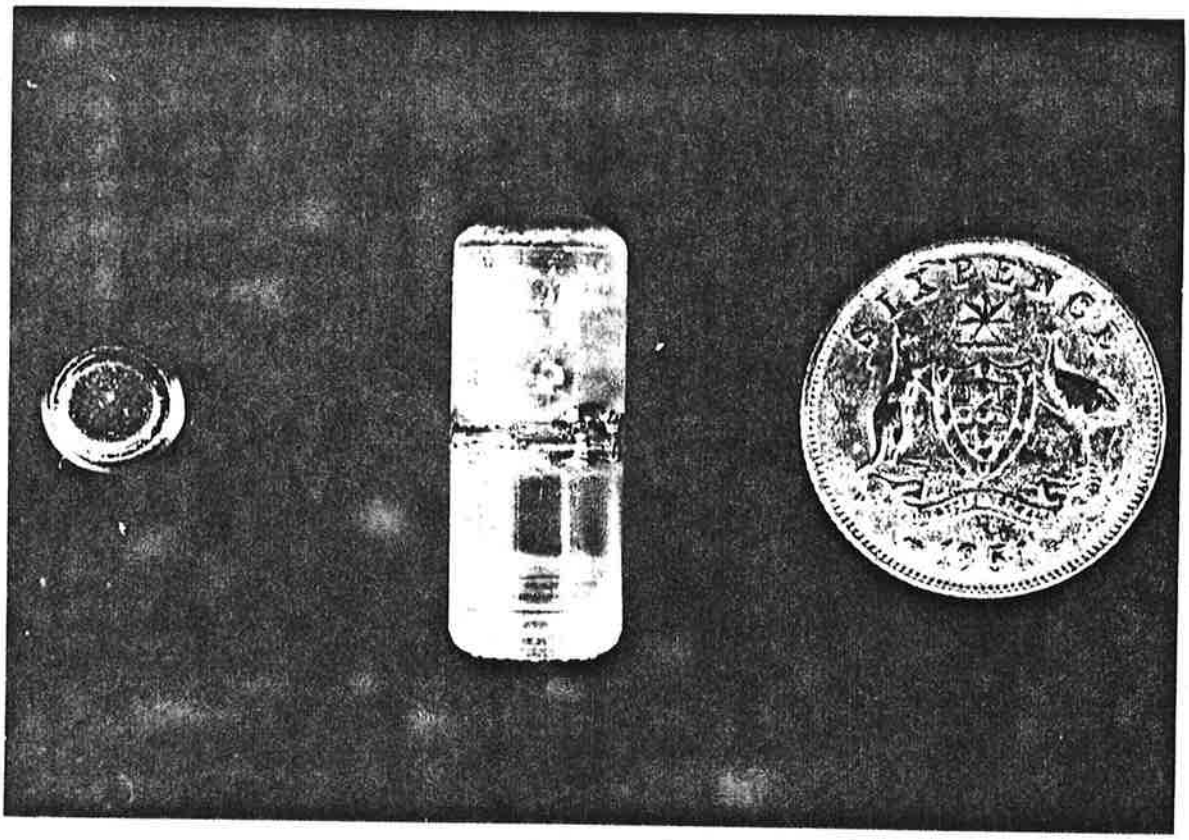
3. The Pressure Transducers

The P23AC strain gauges, manufactured by Statham Instruments Inc. of Puerto Rico, had a pressure range of 0 to 75 cm. Hg. They were connected to the catheters through three-way taps so that the catheters could be syringed without damage to the sensitive diaphragm of the strain gauge. The strain gauges were held by clamps to a moveable stand and adjusted vertically to the level of the recording tips.

4. The Polygraph

The four-channel polygraph used was manufactured by the Grass Instrument Co., Quincy, Mass., U.S.A. Each channel comprised a 5P 1 B or 5P 1 E low level D.C. preamplifier, a 5A driver amplifier and a direct writing pen recorder. Paper speeds could be varied between 0.25 mm. per second and 100 mm. per second. In this study the paper speed was 0.5 mm. per second. However, during exposure of the cine film speeds of 2.5 mm. per second and 5 mm. per second were used to facilitate subsequent correlative analysis.

The polygraph was calibrated before each recording. The sensitivity was chosen so that each millimetre of pen deflection corresponded



<u>Figure 4</u>: The comparative sizes of the radiotelemetering capsule (centre), the hearing aid battery used to power the capsule (left) and a sixpenny piece (right).

to a pressure of 1 mm. Hg. In the beginning of the work the fourth channel of the polygraph was used to record respiratory excursions and body movement. However, it was found early in the study that with experience continuous observation of the intra-luminal pressure traces allowed various artefacts to be distinguished from true intra-luminal pressure waves. The use of the stethograph was therefore discontinued; later in the study the channel was adapted to take the output from the radio-pill receiver for combined catheter and radio-telemetering studies.

5. Radiotelemetering equipment

The radiotelemetering capsule (Figure 4) used in this study was manufactured by the Solartron Electronic Group, Hants., England, and has been described by Connell and Rowlands (1960). It consists of a frequency modulation sub-miniature transmitter powered by a mercury cell (Mallory RM 312) and enclosed in a perspex casing measuring 25 x 8.8 mm. One end of the casing is formed by a pressure sensitive perspex diaphragm. The diaphragm carries the disc of the ferrite pot core which is the transducting element. When pressure is exerted on the capsule the diaphragm bends, the ferrite disc moves and changes the inductance and hence the frequency of oscillation of the transmitter. The radio signal is picked up by an external loop aerial which is held close to the patient's abdomen.

According to the manufacturer's specifications the capsule has a pressure range of 0 to 100 cm. of water with a mean sensitivity of 0.35 Kc per second per cm. of water. The 'life' of the battery is at least

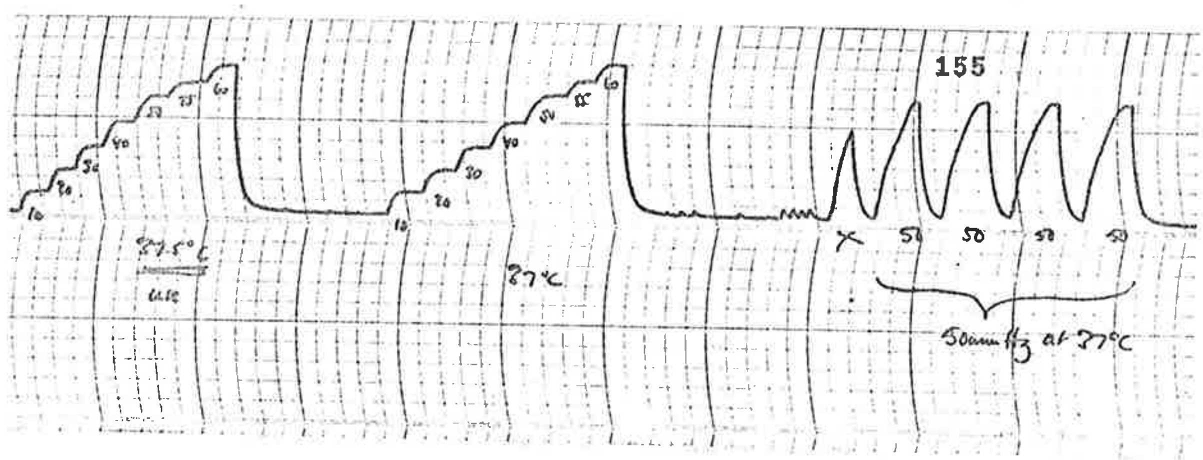


Figure 5: Calibration trace of radio pill. Calibration performed at 37.5°C and 37°C; thereafter intermittent pressures of 50 mm. Hg. were applied. Paper speed 2.5 mm. per second. Thus one small square equals 2 seconds.

36 hours, and in this study many capsules continued to operate after 50 hours.

The radio-pill receiver (Solartron E.I.L. Model 70A) was constructed by Electronic Instruments Ltd., Richmond, Surrey. It provided for recordings of signal strength as well as pressure. Audio monitoring of signal strength was also possible. In the present study it was found that positional changes of the pill leading to "loss of contact" could be identified through the audio signal of the receiver. Since the pill was used mainly to study the low ileum and proximal colon where positional and pressure changes are rather infrequent, the signal strength was generally not recorded. This allowed pressure traces from the capsule and the three catheters to be recorded simultaneously on the four-channel polygraph. Any one of the four channels could be monitored by connecting the corresponding driver amplifier to a cathode-ray oscilloscope with a five-second screen transit (Both Equipment Ltd., Adelaide, S.A.)

Each pill was calibrated before use. After activation the battery voltage was allowed to stabilise at body temperature over a minimum period of 30 minutes. The pill was then sealed and placed at a known depth in a container with water at 37°C. The container was enclosed in an airtight perspex box connected to a sphygomomanometer. By means of a hand bulb known pressure increments were added and the resulting graph (Figure 5) was kept for analysis of recordings made with that particular telemetering capsule.

6. Image Intensifier

A Philips 11 inch closed circuit television image intensifier was coupled to an Arriflex 35 mm. cine camera. For screening the image intensifier was operated at 100 KV and 0.5 mA with a half value thickness of 3.5 mm. Al. With these settings and a medium sized field the measured maximum dose rate to the patient's skin was 1.5 r per minute. In an attempt to reduce radiation the smallest field possible was used and screening time was kept to a minimum. No women in the reproductive age were subjected to cineradiography, and in male patients the gonads were protected by lead shields.

7. Quantitative Analysis of Motility Records

For quantitative analysis of intra-luminal pressure changes recorded with open ended catheters the tracings were inspected to identify and exclude artefacts due to body movements, coughing and deep respirations. Next, the amplitude and duration of all pressure waves were measured and the motor activity was calculated separately for each lead. In this thesis the term lead refers to the pressure trace recorded through a single catheter. Lead I, II and III thus refer to the traces recorded through the three catheters. Lead I is the trace obtained from the most distal catheter, and lead III is the trace from the most proximal catheter. Lead II refers to the record from the intermediate catheter. Thus in the small intestine, lead I would apply to the catheter furthest down the jejunum, whereas in the large intestine lead I would refer to the catheter furthest away from the anus.

The following parameters of motility were calculated separately for each lead:

Percentage activity: this represented the proportion of the recorded time during which motor activity was observed. It was calculated by adding together the duration of all waves and expressing the sum as a percentage of the recorded time;

Motility index: this was calculated by multiplying the amplitude and duration of each wave and dividing the sum of the products by the recorded time. The result of this division was then arbitrarily divided by 10 to yield a less cumbersome final figure. Thus:

$$\text{motility index} = \frac{\sum n \quad (A \times D)}{T \times 10}$$

where A = wave amplitude

D = wave duration

T = time of recording in minutes

n = number of waves during T

Consequently, the motility index was a means of expressing motility taking into account both the amplitude and the duration of the pressure waves;

The mean amplitude of the waves was obtained simply by adding the amplitude of all waves and dividing the sum by the number of waves;

Similarly, the mean duration of the waves was calculated by adding the duration of all waves and dividing the sum by the number of waves; and the distribution of waves was determined on the basis of amplitude and duration. As may be seen from the record sheet (Appendix A) subdivisions of 5 mm. Hg. were used for amplitude and subdivisions of 5 seconds for duration. However, it was found that the number of subdivisions became too large for graphic presentation of the results and thus in the final analysis all waves were subdivided as follows: The categories chosen for pressure waves from the small intestine were 0 to 10 mm. Hg., 11 to 20 mm. Hg. and over 20 mm. Hg. for amplitude; 0 to 10 seconds, 11 to 30 seconds and over 30 seconds for duration. In the distribution of waves from the large intestine the corresponding categories were 0 to 10 mm. Hg., 11 to 20 mm. Hg. and over 20 mm. Hg. for amplitude; 0 to 15 seconds, 16 to 30 seconds and over 30 seconds for duration. The number of waves in each category was expressed as number of waves per hour. For the large intestine, an attempt was made to make the subdivisions of duration conform with the reported durations of type I, II and III waves (Spriggs et alii, 1951; Code et alii, 1951). However, such a choice must remain arbitrary since there is not complete agreement on duration of these waves.

In regard to the small intestine, the first category (duration 0 to 10 seconds) corresponds to type I waves (Foulk et alii, 1954); waves of type III would be found in the subdivisions of 11 to 30 seconds and over 30 seconds (Code et alii, 1952; Foulk et alii, 1954).

Thus, to analyse catheter studies of motility, all waves in the tracings were measured and motility expressed separately for each lead as described above. Finally, the mean values for the three leads were calculated; these values were used in the preparation of graphs and tables.

Motility tracings obtained with the radio-pill were treated in the same manner except that the calculation of a mean for three leads could not be applied.

Results were analysed according to the statistical methods outlined by Bailey (1959).

The X-ray cine films were studied on a Philips viewing table and a number of the 35 mm. films were reduced to 16 mm. width to make screening with conventional projectors possible.

A record sheet (appended) was designed for the study. The clinical details, results of laboratory and radiological investigations, technical details of the procedure used in recording intraluminal pressure fluctuations and the data obtained were all recorded and coded on this sheet. For practical reasons the record sheet was designed and printed at the commencement of the study, and some of the sub-headings were found to be superfluous in the final analysis of the motility tracings. Nevertheless the record sheet greatly facilitated the rather complex and time-consuming analysis of the results.

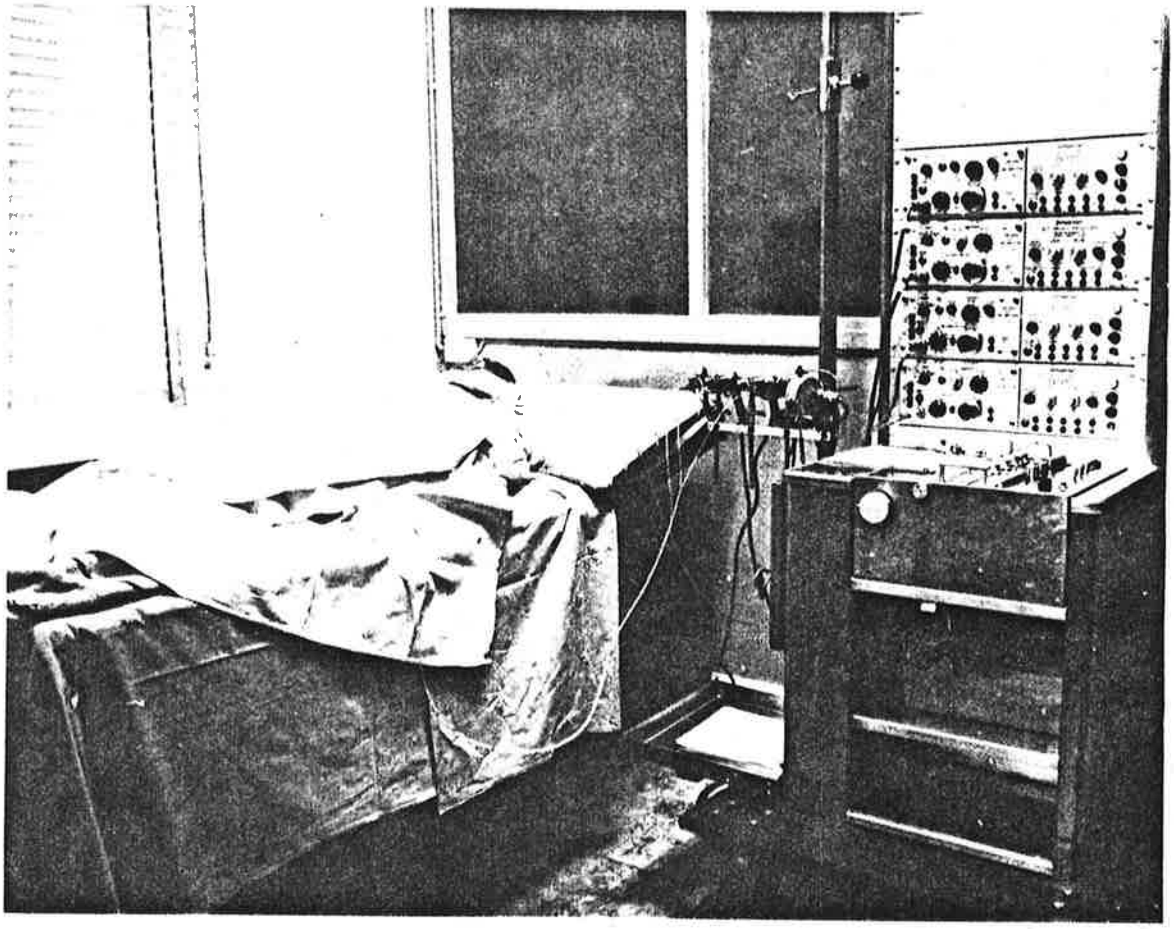


Figure 6: The arrangement of the recording equipment for catheter studies of the large intestine.

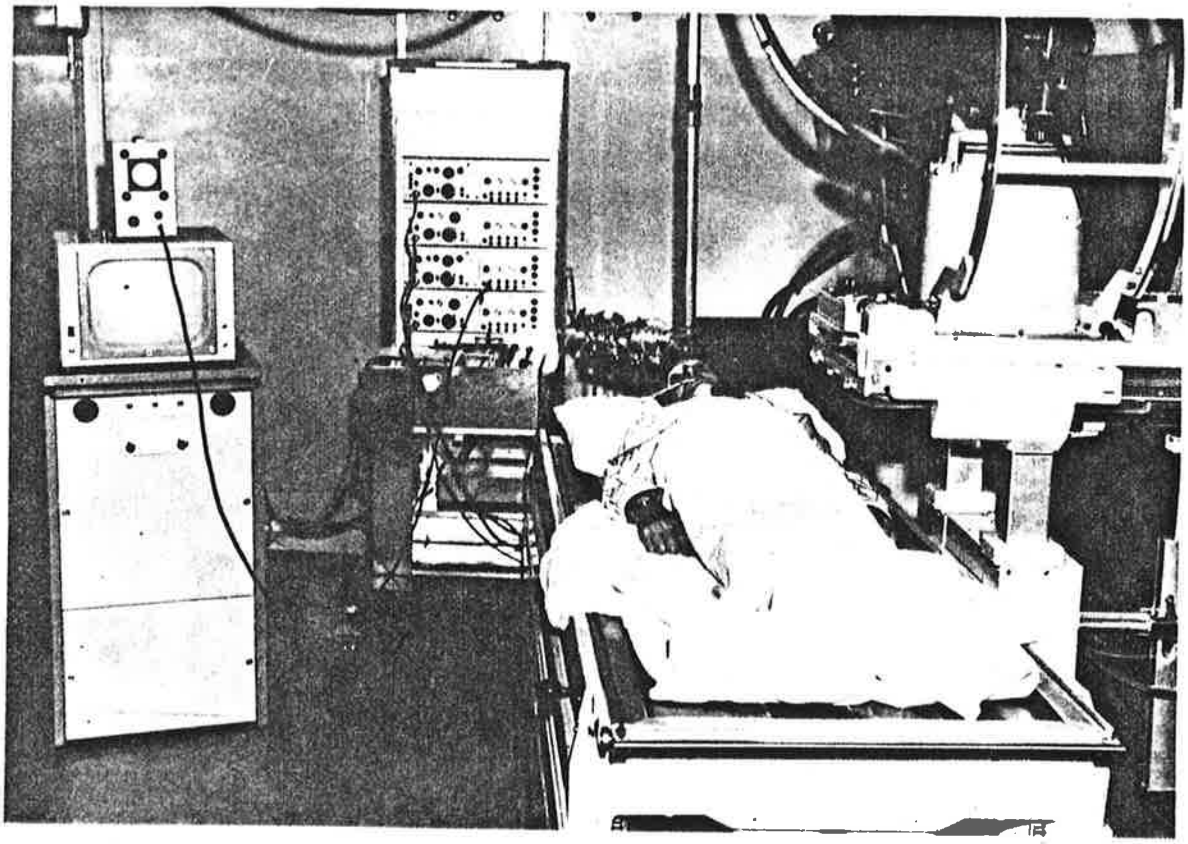


Figure 7: The equipment used for combined manometric and cineradiographic studies of motility.

Material

1. Procedure

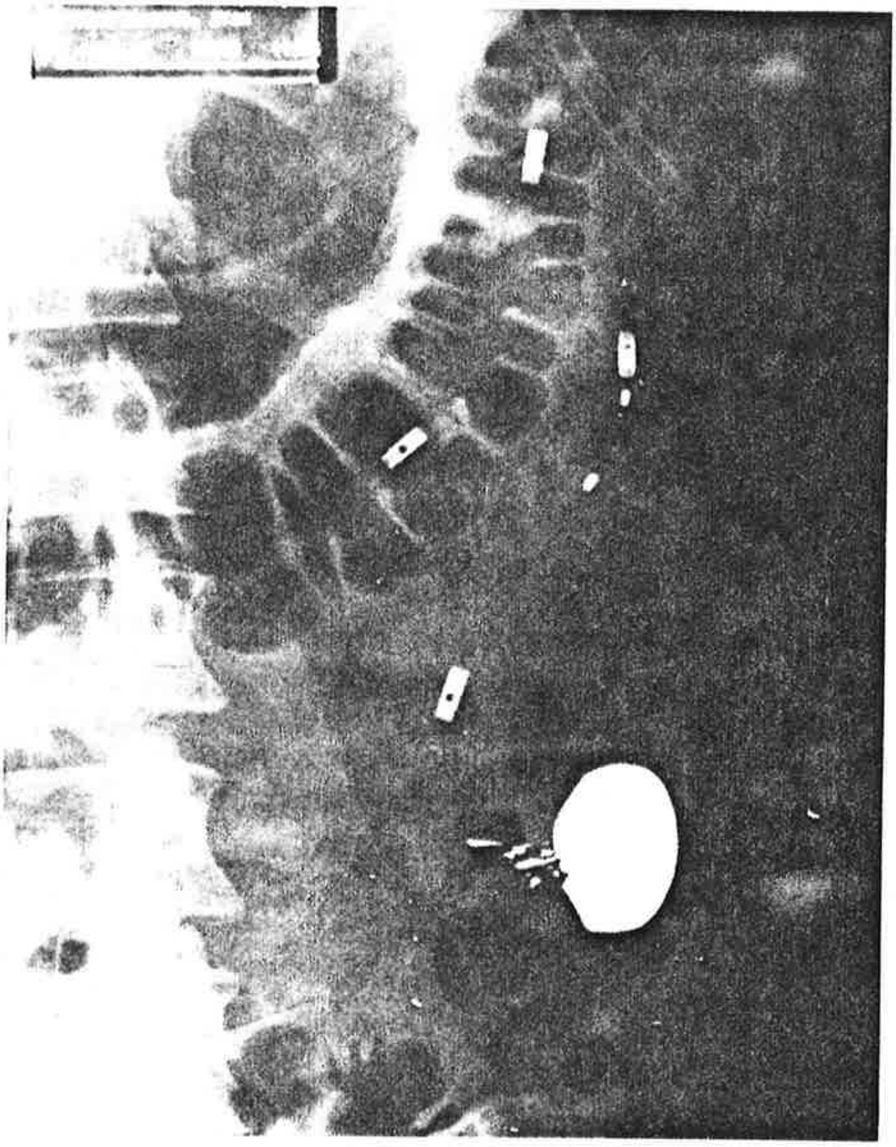
Preparation of patients

All small bowel studies were begun at 2 p.m., the patient having fasted after a light breakfast. The same procedure was followed in most studied of the large bowel, but in a few instances the experiments were commenced at 10 a.m. No enemata or aperients were used. Catheter studies of the large bowel were done with the patient lying supine on a couch in a quiet room in the Department of Medicine (Figure 6). Catheter studies of the small bowel and combined manometric and cineradiographic studies were done in the X-ray department of the Royal Adelaide Hospital (Figure 7).

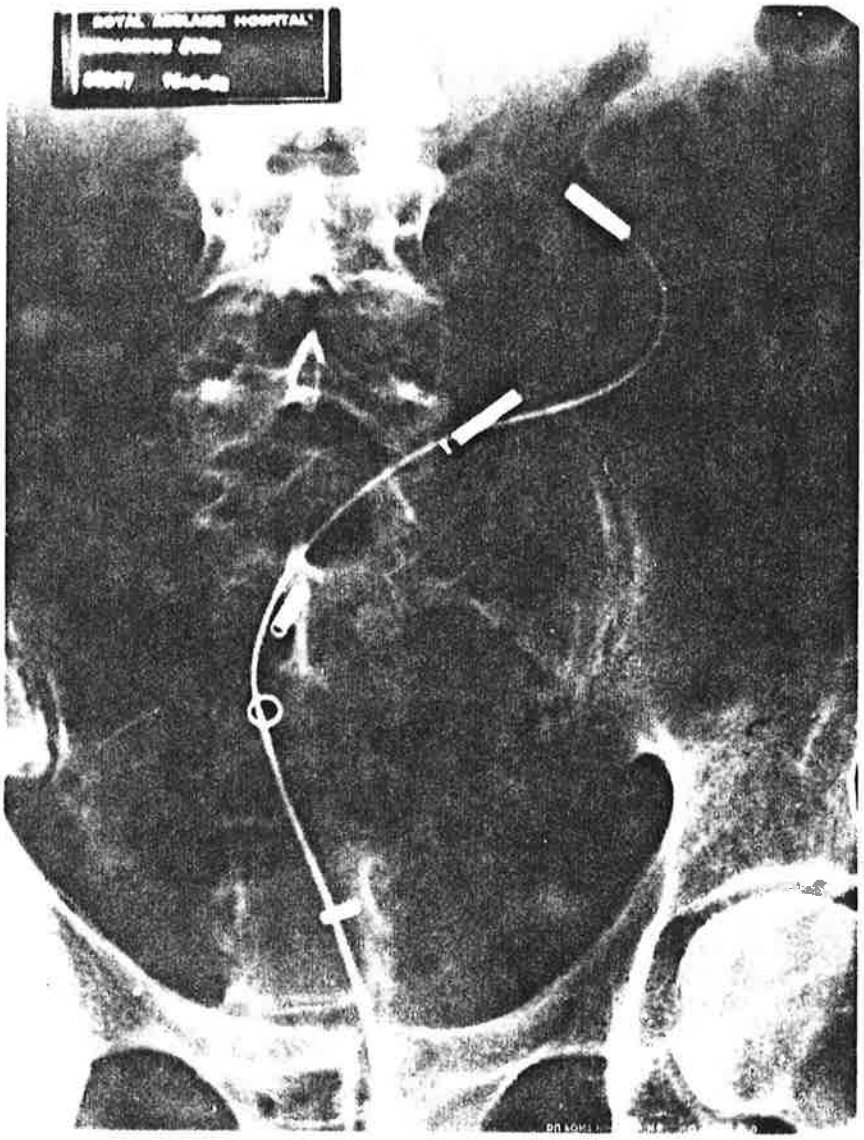
Introduction of pressure recording devices

At the beginning of the procedure of intubation of the small intestine, the pharynx was anaesthetised with a 4% solution of Lignocaine. The lubricated mercury bag and catheters were then introduced through the mouth. The catheters were guided into place under fluoroscopic control by positioning the patient. The duration of this procedure varied from two minutes (in some patients with a Polya-type partial gastrectomy) to one hour. If the catheters could not be made to pass the pylorus within one hour the attempt was abandoned.

Before experience had been gained with the technique, attempts at intubation were unsuccessful in three patients; these patients have been excluded from the study. Thereafter, in 33 of 36 consecutive



<u>Figure 8</u>: Radiograph showing the position of the catheters in the small intestine.



<u>Figure 9</u>: Radiograph showing the position of the catheters in the large intestine. The highest catheter is outlined by radio-opaque contrast medium.

patients the catheters were successfully introduced into the small bowel. However, in one study (case 7) a mechanical fault developed in the polygraph; hence 32 catheter studies of the small bowel were done. Of the three failed attempts at intubation, two occurred in patients with active peptic ulceration in whom the pylorus could not be negotiated; these patients were excluded from the study. The remaining patient had had a partial gastrectomy and was unable to swallow the catheters. In this patient only cineradiography was performed.

When the recording tips were in a satisfactory position the catheters were perfused with saline, connected to the strain gauges and the recording was begun. Figure 8 shows the mercury bag and the radio-opaque recording tips in the small bowel. The aim was to place all three tips in the jejunum, but on occasions this was not possible, one or two remaining in the duodenum.

In the large bowel studies sigmoidoscopy was performed and the appearances of the rectum and sigmoid colon were noted. The catheter assembly was introduced through the sigmoidoscope, and the highest recording tip came to lie at a distance of 20 to 25 cm. from the anus. The sigmoidoscope was withdrawn, the catheters were taped to the patient's buttocks, perfused with saline and connected to the strain gauges. Recording was begun half an hour later. Figure 9 shows the arrangement of the catheters in the large bowel.

In combined radiotelemetering and catheter studies of the large bowel the radio-pill was either swallowed "free" or attached to 13 feet of surgical silk. This length of silk was generally found to arrest the capsule in the proximal part of the colon. The position of the capsule was checked by fluoroscopy four to five hours after the patient had ingested a small amount of barium. When the radio-pill was in the desired position the catheters were introduced into the large bowel, as already described, and the recording started. There was considerable variation in the time taken for a capsule to pass through the small bowel. However, it was usually possible to obtain a record from the terminal ileum or proximal colon by allowing 36 hours for the passage of a capsule attached to silk.

Phases of pressure recording and cineradiography

A standard sequence of recording was followed, the experiment being divided into the following four phases:

1. the basal activity or "resting" pattern of motility;
2. the motor response of the intestine to a discussion of emotionally charged topics;
3. the response to a standard meal;
4. the response to a placebo and Prostigmine.

Cineradiography of the small bowel was usually done after phase 3 but it was often found that in the large bowel only phase 4 provided enough motor activity for cineradiography.

The resting pattern was recorded for at least half an hour to provide the basal level of activity of the intestine.

During the emotive interview, which lasted twenty minutes, both neutral topics and presumedly disturbing ones were discussed with the patient. These topics ranged from the patient's occupation and hobbies and his social and financial ambitions to fear of disease and traumatic experiences in adolescence and in married life. An attempt was made to conduct the interview at the same level of intensity with all patients rather than to try to elicit an obvious emotional response in every case. In studies of the small bowel the emotive interview was abandoned as the presence of the catheters in the pharynx made the patient disinclined to talk.

In the third phase of recording the response of the intestine to a standard meal was studied for 30 minutes. The meal consisted of one egg and two teaspoons of sugar beaten into eight ounces of milk of room temperature (Cox and Allan, 1960). Patients who had had a partial gastrectomy were positioned at a 45° head up tilt during this phase to encourage the onset of "dumping." All other patients remained supine.

Cineradiography of the small bowel was performed after the meal. The patient drank 50 to 100 ml. of a non-flocculating barium suspension (Alubar) and the progress of the contrast medium was followed on the television screen. The film was exposed when the contrast had reached the recording tips. On a few occasions, when gastric emptying was extremely slow, the contrast was injected through the most proximal recording tip. For cineradiography of the large bowel, 50 to 100 cc.

of Alubar diluted with saline was injected through the catheter furthest away from the anus. This catheter was then immediately perfused with saline and reconnected to the strain gauge for recording.

All cineradiographic studies were done with the image intensifier set at 80 Kv and 9.2 mA with a half-value thickness of 3.5 mm. Al. The film was exposed at 16 frames per second for studies of the small bowel and at 6 frames per second for films of the large bowel. The beginning and end of the cine period were marked on the pressure tracing to facilitate subsequent correlative analysis.

2. Patients investigated

Studies of the small intestine

The control group consisted of seven men. Five were volunteers from Yatala Labor Prison, Northfield. The other two were patients of the Royal Adelaide Hospital. Of the hospital subjects, one (case 2) was under investigation for haemoptysis; the other (case 6) had features of a paranoid psychosis. All the control subjects were ambulant. They did not have a past history of gastro-intestinal disease or alimentary symptoms at the time of this investigation.

The prison volunteers were all housed in minimum security wards; they performed light manual work on the prison farm and were given a normal diet. Most of the prisoners had been remanded for minor offences and none of them displayed obvious personality defects.

The mean age of the subjects in the control group was 28.7 years with a range of 20 to 42 years. They underwent the following tests:

	No. of Studies
Catheter Studies:	
Resting pattern	6 (a)
Response to food	6 (a)
Response to Prostigmine	5 (b)
Cineradiography	7

Nineteen patients were studied a number of years after partial gastrectomy. There were 16 men and 3 women. The ages of the patients ranged from 38 to 76 years with a mean of 58.7 years. The type of operation performed was partial gastrectomy with gastro-duodenostomy (Billroth I) in three patients (cases 8 to 10) and partial gastrectomy with gastro-jejunostomy (Polya) in 16 patients (cases 11 to 26). Surgical vagotomy had been performed on only one patient (case 25). The site of the peptic ulcer had been the stomach in 6 patients, and the duodenum in 13 patients. The time which had elapsed since the operation ranged from 1 to 17 years with a mean of 8.7 years. Thus most patients were investigated at a stage when adjustment to altered anatomy brought on by operation should have occurred; no attempt was made to study patients immediately after

---

(a): in case 7 intubation was successful but mechanical difficulties did not allow pressure recordings to be carried out. Hence only cineradiography was performed.

(b): Prostigmine was omitted at the end of a protracted study.

surgery.

The following post-gastrectomy late sequelae were present in this group:

	No. of Patients
Osteoporosis	4
Iron deficiency anaemia	3
Megaloblastic anaemia	1
Steatorrhoea	1

Eight patients were considered to have the early dumping syndrome (cases 8 to 12, 16, 17 and 25). This diagnosis was based on a history of abdominal fullness, sweating, weakness and palpitations following immediately or shortly after a meal and relieved by lying down. The severity of the attacks was arbitrarily graded as mild, moderate or severe on the number and intensity of the manifestations. On these criteria, the spontaneous attacks of dumping were mild in four patients (cases 10, 11, 12 and 16) and moderate in a further four (cases 8, 9, 17 and 25). Thus no patient in this study experienced severe manifestations of the dumping syndrome. Of the eight patients with the dumping syndrome, three had undergone a Billroth I partial gastrectomy and five the Polya operation. In six of the eight patients with the early dumping syndrome and attack was reproduced during the motility studies (cases 9, 10, 12, 16, 17 and 25). No patient who was not prone to spontaneous attacks of dumping experienced symptoms during the recording.

The following tests were carried out on the patients who had had partial gastrectomy:

		No. of Studies
Catheter Studies:		
	Resting pattern	18 (a)
	Response to food	18
	Response to Prostigmine	9 (b)
Cineradiography		17 (c)

Eight patients constituted the miscellaneous group, the composition of which was as follows:

Case No.	Sex	Age	Diagnosis
27	F	41	Irritable colon - functional diarrhoea (no symptoms at time of study)
28	M	32	Irritable colon - functional diarrhoea (no symptoms at time of study)
29	M	37	Irritable colon - spastic colon (no symptoms at time of study)
30	F	57	Longstanding constipation, chronic purgation, hypokalaemia

---

(a): intubation failed in one patient (case 18) and only cineradiography was done.

(b): Prostigmine was not given to patients who gave a history of ischaemic heart disease, hypertension or emphysema, or who in any way did not appear moderately robust.

(c): cineradiography was omitted in two pre-menopausal women (cases 11 and 26).

31	M	38	Hiatus hernia
32	M	57	Chronic gastric ulcer
33	F	65	Ulcerative colitis
34	F	52	Diverticulitis of the colon

Thus, in three patients (cases 27 to 29) a diagnosis of the irritable colon syndrome was made. This disorder is characterised by abdominal pain often related to defaecation; bouts of constipation with the passage of small pellet-like stools alternating with periods of diarrhoea and periods of normal bowel habits (Chaudhary and Truelove, 1962). The symptoms are often brought on or made worse by emotional tension. Furthermore, the patient can frequently identify particular foods which aggravate the disorder. Patients with the irritable colon syndrome usually fall into two groups. Patients with the spastic colon have abdominal pain as their main symptom, and in addition have constipation which alternates with diarrhoea or with periods of normal bowel habits. Patients with functional diarrhoea have little or no abdominal pain; their main symptom is constant or intermittent diarrhoea.

Of the three patients with the irritable colon syndrome, two (cases 27 and 28) had functional diarrhoea, and one (case 29) the spastic colon. All had normal bowel habits and were free of symptoms at the time of study. As all three also underwent colonic motility studies, a discussion of the clinical details of their cases will be found later in this section (page 92, 93).

One of the patients in the miscellaneous group suffered from constipation of more than 20 years' duration and from the effects of chronic purgation. At the time of study her serum potassium level was 2.5 mEq./1. as a result of longstanding misuse of purgatives.

One patient, (case 31) had a large hiatus hernia with a reflux oesophagitis. He complained of constipation for more than 10 years and used purgatives. He was receiving no drugs at the time of study.

The next patient, (case 32) had a radiologically proven chronic benign gastric ulcer on the lesser curvature of the stomach. At the time of study his bowel habits were normal, the stools were negative for occult blood and he was receiving no drugs.

There was one patient (case 33) with chronic ulcerative colitis of six months' duration. At the time of study she had normal bowel habits with no blood or mucus in the stools. The sigmoidoscopic findings were normal although a barium enema showed mild ulceration in the upper part of the sigmoid colon. There was no anaemia and the blood sedimentation rate was 16 mm. in the first hour.

The last patient (case 34) in the miscellaneous group had radiologically and clinically evident diverticulosis and diverticulitis of the sigmoid colon. She suffered from intermittent abdominal pain and diarrhoea, although at the time of study she was having only one formed motion every day without blood or mucus.

The patients in the miscellaneous group underwent the following studies:

	No. of Studies
Catheter Studies:	
Resting pattern	8
Response to food	8
Response to Prostigmine	7 (a)
Cineradiography	8

Thus studies of the small bowel were performed on 34 subjects comprising 7 normal controls, 19 patients who had undergone partial gastrectomy and a miscellaneous group of 8 patients. The methods of study were measurements of intra-luminal pressure fluctuations with open ended catheters, cineradiography and a combination of the two, distributed as follows.

	No. of Studies
Catheter Studies:	
Resting pattern	32 (b)
Response to food	32
Response to Prostigmine	21
Cineradiography	32

Studies of the large intestine

The control group consisted of 21 subjects of whom 19 were men and 3 were women. Their ages ranged from 18 to 79 years with a mean of

(a): omitted in case 28.

(b): in two patients (cases 7 and 18) only cineradiography was performed.

37.6 years. Fifteen of the control group were healthy volunteers from Yatala Labor Prison, Northfield. The diagnoses of the remaining six control subjects was as follows:

Diagnosis	No. of Patients
Multiple myeloma	1
Ischaemic heart disease	1
Cerebral arteriosclerosis	1
Post-infective polyarthritis.....	1
Post-pneumonic pleural effusion .	1
Bronchopneumonia	1

These six patients were all fully ambulant at the time of study. None of them had a past history of gastro-intestinal disease and none had any alimentary symptoms (indigestion, constipation or diarrhoea) at the time of study.

Twenty-seven catheter studies were done on the twenty-one subjects in the control group. Two subjects (cases 44 and 51) had two separate studies each; another two (cases 35 and 38) had three separate studies each. The control subjects underwent the following tests:

	No. of Studies
Catheter Studies:	
Resting pattern	27
Response to interview	16
Response to food	23

TABLE I - Clinical features of 18 patients with the irritable colon syndrome

		No. of patients	
A.	Subgroup		
	spastic colon	7	18
	functional diarrhoea	11	
B.	Sex		
	male	7	18
	female	11	
C.	Precipitating cause		
	emotional trauma	3	18
	unspecified gastro-enteritis	2	
	presumed bacillary dysentery	1	
	gastrointestinal surgery	1	
	not known	11	
D.	Duration of illness		
	$<$ 12 months	6	18
	1 - 5 years	5	
	5 - 10 years	3	
	$>$ 10 years	4	
E.	Symptoms aggravated by emotional stress	12	
F.	Intolerance to specific foods ... present	11	18
	absent	7	
	tomatoes	6	
	milk and milk products	4	
	acid fruits (apple, orange, lemon)	4	
	alcohol	3	
	onions, lemonade (each)	2	
	eggs, cabbage, tobacco, fish (each)	1	
G.	Past surgery on the gastrointestinal tract	8	
H.	History suggestive of irritable colon in either parent	2	

Response to Prostigmine	20
Response to 5-hydroxytryptamine ...	3 (a)
Radiotelemetering	10
Cineradiography	6

Eighteen patients with the irritable colon syndrome were studied. The group consisted of 11 women and 7 men. Their mean age was 48.6 years with a range of 23 to 75 years. Seven patients had the spastic colon (cases 29, 53, 54, 55, 58, 60 and 64). The remaining eleven had functional diarrhoea (cases 27, 28, 56, 57, 59, 61, 62, 63, 65, 66 and 67). Of 21 catheter studies performed in this group, 12 were done when the patients had symptoms of the colonic disorder; 9 studies were done at a time when symptoms were not present.

The diagnosis of the irritable colon syndrome was based on the clinical history and on the exclusion of organic disease of the alimentary tract.

The clinical features of the patients with the irritable colon syndrome are presented in Table I.

The condition had been present for less than 1 year in six patients, for 1 to 5 years in five, 5 to 10 years in three, and over 10 years in four patients. It was usually not possible to identify a cause which may have precipitated the disorder, although three patients

---

(a): The effect of 5-hydroxytryptamine on the motility of the large bowel was studied in three control subjects (cases 43, 45 and 51).

dated the onset of symptoms to major emotional upheavals, two to attacks of epidemic gastro-enteritis of uncertain aetiology, one to an attack of suspected but not proven bacillary dysentery and one to abdominal surgery (hysterectomy with division and re-suture of the lower small bowel).

Twelve patients stated that their symptoms were definitely aggravated by minor degrees of nervous tension; nine of these patients had functional diarrhoea and three the spastic colon.

Eleven patients gave a history of intolerance to particular foods, which invariably precipitated an attack or aggravated symptoms which were already present. Tomatoes, milk, acid fruits and alcohol were the foods most commonly incriminated. Six patients used aperients but none more frequently than three times weekly, and in no instance had laxatives been used by the patients in the days immediately preceding the present study.

Eight patients had had operations on the gastro-intestinal tract but in none of these patients were the operations performed for symptoms which they currently complained of. As already mentioned, there was a close relation in time between the operation and the onset of the irritable colon syndrome in only one patient (case 59). Only two patients gave a family history suggesting the presence of the irritable colon syndrome in either parent.

The exclusion of organic disease of the bowel was a pre-requisite for including the patient in the irritable colon group. Therefore a sigmoidoscopic examination was performed in all patients. If there was any doubt that the mucosa of the rectum and colon was not normal, the sigmoidoscopy was repeated on completion of the study and a specimen of mucosa obtained with Wood's gastric biopsy tube (Wood, Doig, Motteram and Hughes, 1949). No histological abnormalities were seen in any of the biopsy specimens taken from patients in this group.

A complete blood count, estimation of the erythrocyte sedimentation rate and stool tests for occult blood loss were performed in all patients.

Radiological examination of the large bowel served to exclude ulcerative colitis, diverticulitis and carcinoma of the colon. Barium meal and follow-through studies were done in all patients in whom the clinical features or examination of blood and faeces suggested the possibility of organic disease of the stomach or small intestine. In approximately half of the patients a barium meal and follow-through examination of the small intestine was performed. Estimations of faecal fat on three-day stool collections and examination of the stools for pathogenic bacteria and parasites were performed in most patients with diarrhoea. Patients in whom jejuno-ileal insufficiency was suspected on clinical, haematological or biochemical grounds, were subjected to further investigations. These included radio-active vitamin B_{12} absorption studies, the d-xylose excretion test, estimation of the serum folic acid level and, in selected cases, suction biopsy of the small bowel mucosa. Biopsy of the small intestine was carried out with the Baker-Hughes multiple retrieving tube (Baker and Hughes, 1960) or the Crosby capsule (Crosby and Kugler, 1957). Where appropriate, the presence of general medical disorders known to produce symptoms from the alimentary tract (e.g. hyperthyroidism, hypothyroidism and diabetes) was confirmed or refuted by the relevant diagnostic tests.

Thus a diagnosis of the irritable colon syndrome was made when the clinical features suggested this disorder and when organic disease of the alimentary tract had been excluded as far as it was possible.

The patients with the irritable colon syndrome took part in the following motility studies:

	No. of Studies
Catheter Studies:	
Resting pattern	21 (a)
Response to interview	18
Response to food	21 (a)
Response to Prostigmine	18
Radiotelemetering	1
Cineradiography	2

The miscellaneous group consisted of a total of 29 patients of whom 7 were male and 22 female. These patients were studied either because they had proven disease of the alimentary tract (ulcerative

(a): Three patients (cases 29, 61 and 67) were studied on two separate occasions.

TABLE II - Patients comprising the miscellaneous group

Case No.	Sex	Age	Diagnosis	Usual bowel habit*	Bowels at time of recording
33	F	65	Ulcerative colitis	D	N
68	F	36	Ulcerative colitis	CD	N
69	F	66	Ulcerative colitis	D	N
70	F	43	Ulcerative colitis	D	D
71	F	68	Ulcerative colitis	C	C
72	F	42	Small bowel resection; steatorrhoea	D	D
73	F	43	Malabsorption syndrome ?cause	D	N
74	F	62	Malabsorption syndrome ?cause	CD	C
75	F	60	Malabsorption syndrome ?cause	C	C
76	F	36	Idiopathic steatorrhoea	D	N
8	M	43	Partial gastrectomy (Billroth I)	N	N
9	M	45	Partial gastrectomy (Billroth I)	D	N
13	M	54	Partial gastrectomy (Polya)	N	N
26	F	45	Partial gastrectomy (Polya)	N	N
77	F	74	Hyperthyroidism	N	N
78	F	70	Hypothyroidism	C	C
79	F	40	Hypothyroidism	C	C
34	F	52	Diverticulitis of the colon	D	N
80	M	65	Diverticulitis of the colon	CD	N
30	F	57	Chronic purgation	CD	D
81	F	48	Uretero-colic anastomosis	D	D
82	F	39	Alcoholism; peripheral neuropathy	D	D
83	M	56	Systemic mastocytosis	D	D
84	M	57	Gastric ulcer	N	N
85	F	72	Scleroderma	N	N
86	F	83	Infective diarrhoea	N	D
87	M	13	Acquired megacolon	C	C
88	F	63	Diabetic ciarrhoea	D	D
89	F	58	Aperient-induced diarrhoea	N	D

*Symbols: C = constipation

D = diarrhoea

N = normal bowel habits

CD = alternating constipation and diarrhoea colitis, jejuno-ileal insufficiency) or because they had organic disease elsewhere which was capable of producing disordered bowel function (thyroid malfunction, scleroderma, diabetes mellitus). Table II lists the patients included in the miscellaneous group; further details of some individual cases will be presented in Chapter IV. It can be seen that at the time of study 6 patients were constipated, 9 patients had diarrhoea and 14 patients had normal bowel habits.

The following studies were done in the patients in this group:

	No. of Studies
Catheter Studies:	
Resting pattern	32 (a)
Response to interview	28
Response to food	30
Response to Prostigmine	24
Radiotelemetering	3
Cineradiography	1

Thus a total of 80 studies of the motility of the large bowel were done in 68 patients. There were 21 control subjects, 18 patients with the irritable colon syndrome and 29 patients with miscellaneous disorders. Open ended catheters, telemetering and cineradiography were used to study the large bowel as follows:

(a): 3 patients (cases 79, 83 and 87) were studied twice.

	No. of Studies
Catheter Studies:	
Resting pattern	80
Response to interview	62
Response to food	74
Response to Prostigmine	62
Response to 5-hydroxytryptamine ..	3
Radiotelemetering	14
Cineradiography	9

CHAPTER IV

RESULTS

TABLE III - The extent of the present investigation

Group	Patients	Studies	Catheter Studies Rest	Emotion	Food	Prostigmine	5-hydroxytryptamine	Radiotelemetering	Cineradiography
[Sm]all Intestine									
Control	7	7 (a)	6	-	6	5	-	-	7
Postgastrectomy	19	19 (a)	18	-	18	9	-	-	17
Miscellaneous	8	8	8	-	8	7	-	-	8
[La]rge Intestine									
Control	21	27	27	16	23	20	3	10	6
Irritable colon	18	21	21	18	21	18	-	1	2
Miscellaneous	29	32	32	28	30	24	-	3	1
TOTAL	89*	114	112	62	106	83	3	14	41

*Thirteen patients underwent studies both of the small intestine and the large intestine.

(a) of which one purely radiological.

Thirty-four studies of the small intestine were carried out on 34 patients and 80 studies of the large intestine were performed on 68 patients. Thirteen patients underwent studies of both the small intestine and the large intestine. One hundred and twelve pressure recordings were done with open ended catheters and the radio-pill was employed as well in 14 instances. The pressure recordings were combined with cineradiography in 39 studies and cineradiography alone was performed in 2 cases (Table III).

The total duration of the pressure tracings was 10,642 minutes (177.4 hours). Since each tracing consisted of at least three simultaneous pressure traces and since the minimum paper speed was 0.5 mm. per second, a total of approximately 960 metres of tracing were obtained and analysed.

Qualitative Aspects of the Pressure Tracings Obtained with Open Ended Catheters

The small intestine

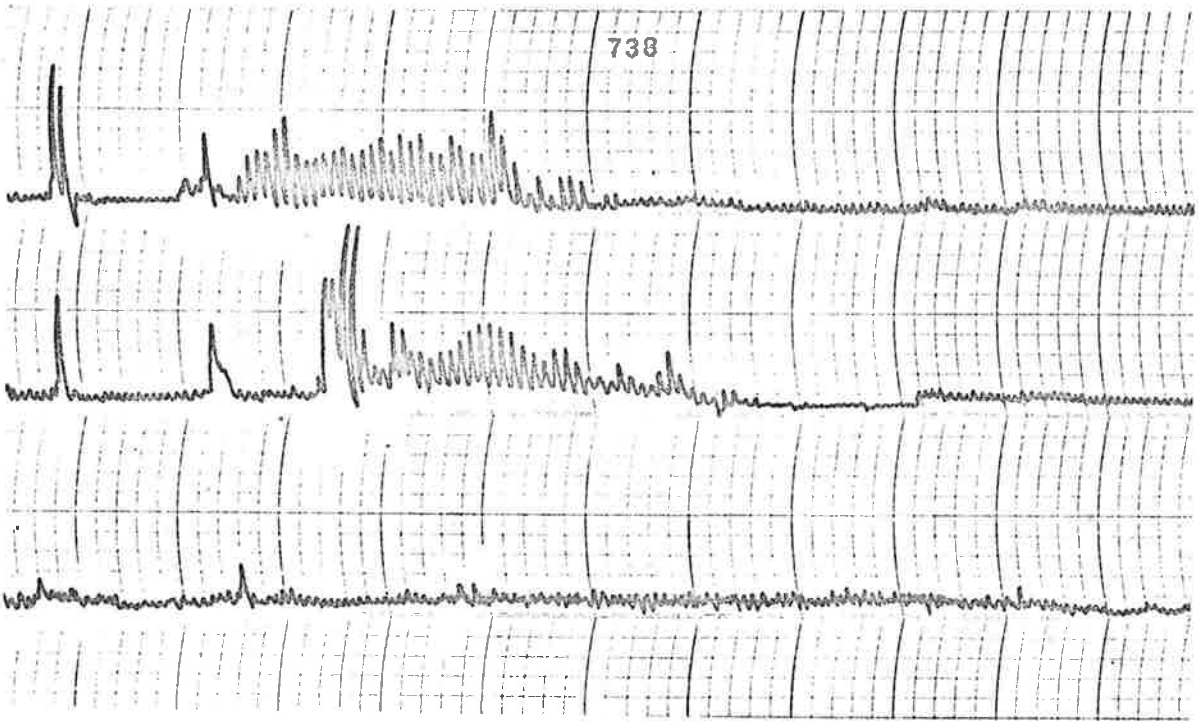
The outstanding feature of the intraluminal pressure recordings from the small intestine was the marked variation in motor activity not only between different patients, but also between different leads in the same patient and in the same lead over a period of time. Periods of activity were interspersed with periods of quiescence in an apparently random fashion.

Type I and type III waves were recognised in the tracings from the

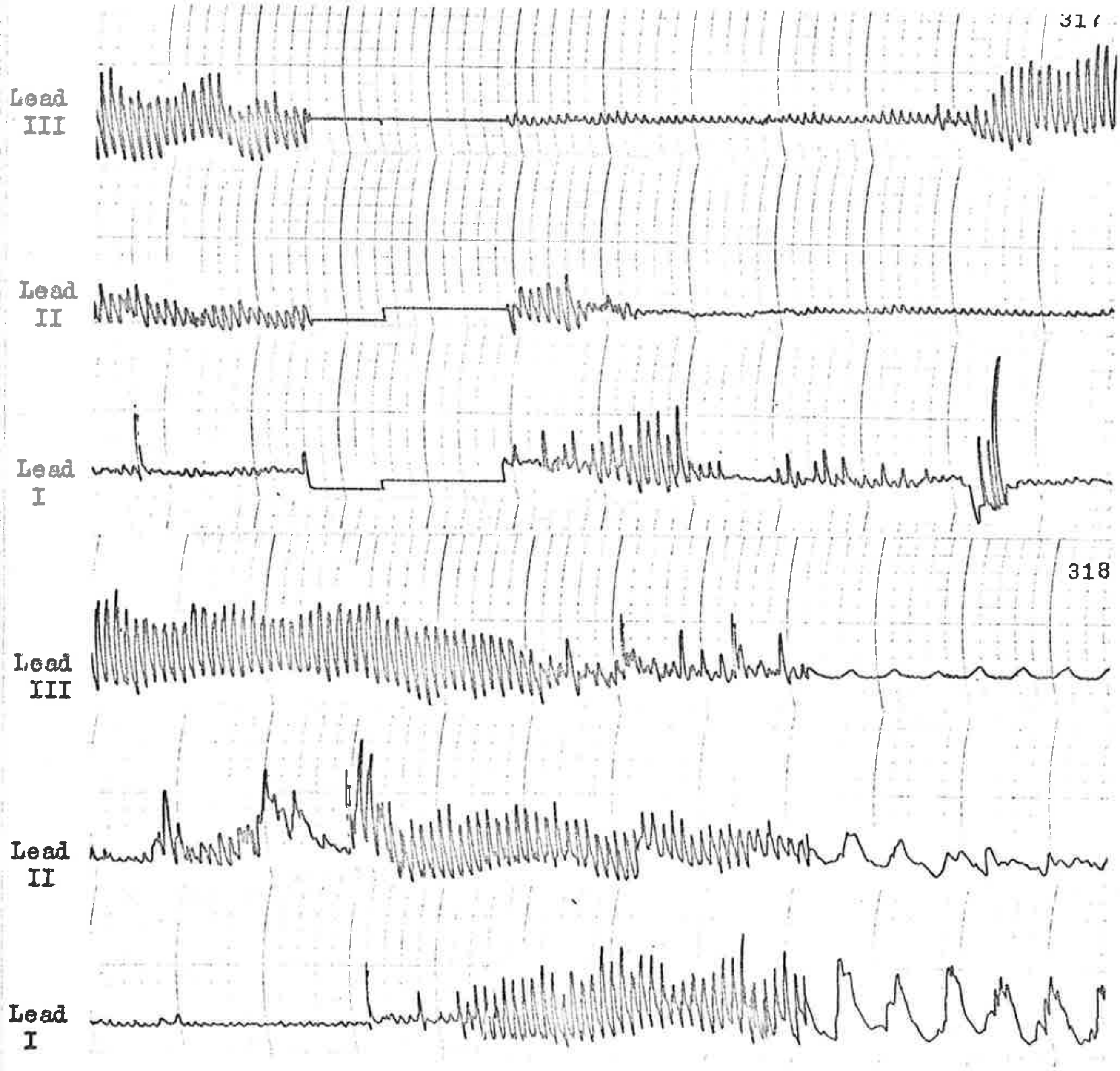
Lead III

Lead II

Lead I



<u>Figure 10:</u> The small intestine: basic rhythm occurring during the resting phase in a control subject (case 3). Unless otherwise stated in this and in all subsequent traces recorded by the catheters one small square has an amplitude of 5 mm. Hg. Paper speed 0.5 mm. per second (one small square equals ten seconds).



<u>Figure 11</u>: The small intestine: basic rhythm occurring during the resting phase in a patient who had had partial gastrectomy (case 12). Paper speed 0.5 mm. per second except during the last quarter of the lower panel where the speed was 2.5 mm. per second.

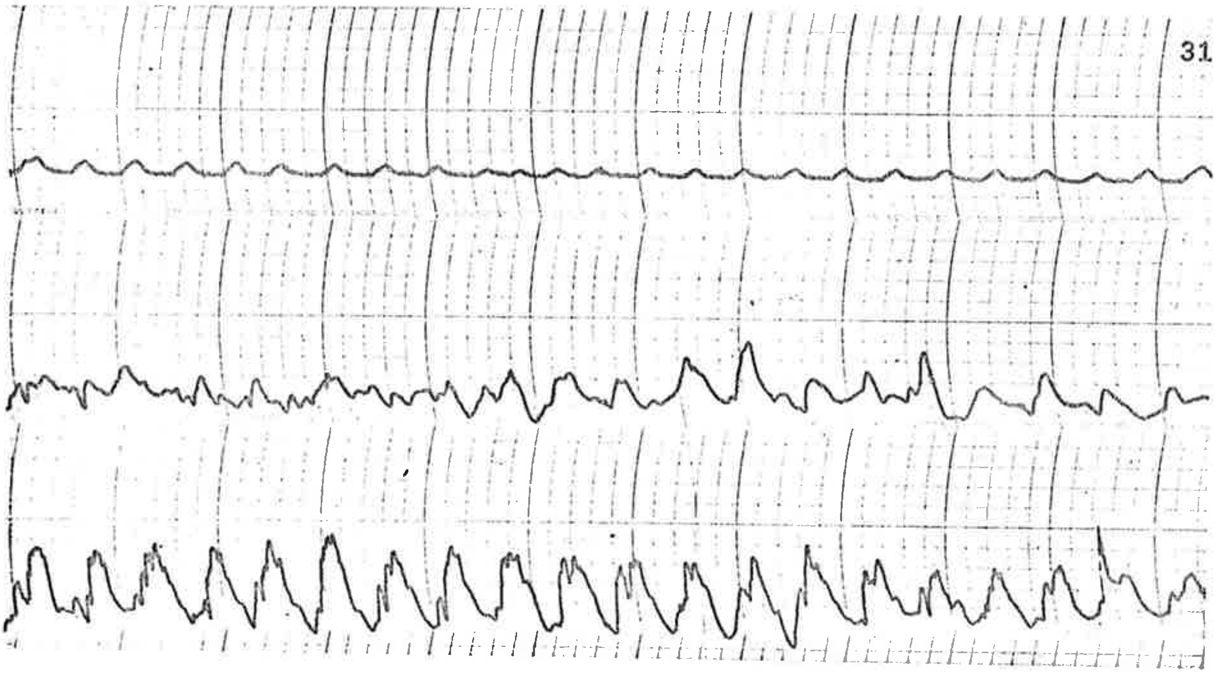


Figure 12: The small intestine: continuation of basic rhythm from Figure 11 at fast paper speed (2.5 mm. per second) showing the complex form of the type I waves.

small intestine (Figures 10 and 11). However, a distinction between waves of type I and type II could not be made. Type IV waves were not seen. Although type I waves appeared simple and monophasic at the usual recording speed, recording at higher speeds showed that they were, in fact, complex (Figures 11 and 12). Most of the activity recorded in the small intestine consisted of type I waves, singly or in groups. Type III waves were rarely recorded in normal subjects during the resting phase although they appeared after the stimulation of food and Prostigmine. However, they were observed quite frequently during the resting phase in patients who had undergone partial gastrectomy.

A qualitative comparison of the three leads showed that although the corresponding recording tips were only 7 cm. apart, the activity at these three different levels was usually markedly dissimilar. It was not uncommon to find that pressure changes were being recorded from solely the proximal, intermediate or distal catheter (leads III, II and I respectively). Alternatively, two of the leads at times showed activity independently of the third one which remained quiescent. In the control subjects lead III was almost invariably the most active lead, whereas patients after partial gastrectomy usually had more activity in lead II. Synchronous activity of the three leads was most evident after Prostigmine had been given, the activity being of type III. Progressive delay in the appearance of a wave in the three leads was only rarely observed. Progression was only seen with rhythmic type I

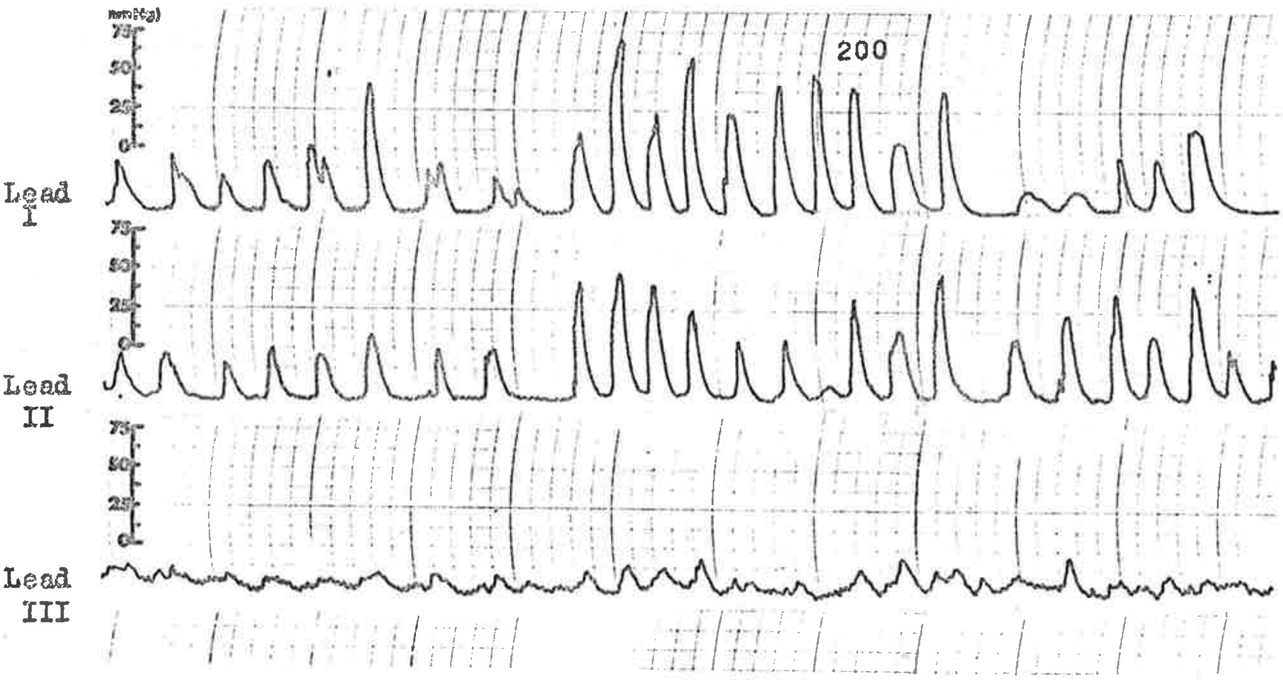


Figure 13: The large intestine: the effect of Prostigmine in a patient with the spastic colon (case 64). A dose of 1.0 mg. of Prostigmine was given intramuscularly 5 minutes after a similar volume of sterile normal saline had been injected. This procedure and this dose of Prostigmine were used in all experiments in which the drug was used. Paper speed 0.5 mm. per second (one small square equals ten seconds).

waves (basic rhythm) (Figures 10 and 11) and type III activity. Retrograde conduction of waves from the distal to the proximal lead was not encountered.

Basic rhythm was present only during the resting phase. It consisted of rhythmic type I waves at a constant rate of 11 to 12 waves per minute with or without a change in baseline (Figures 10 and 11). Negative pressure deflections were often seen during periods of basic rhythm (Figure 11) but were otherwise uncommon.

The amplitude of the pressure changes recorded from the small intestine varied greatly but only rarely exceeded 50 mm. Hg.; most waves had an amplitude of 10 to 30 mm. Hg.

The large intestine

In the large intestine the variation in activity from subject to subject was even more marked than in the small intestine. During the resting phase there were periods of quiescence as long as 10 to 15 minutes. The predominant activity was of type II (Figure 13). Type II waves were seen alone, grouped and in pairs. Type I waves were recorded more frequently from the rectum than from the distal colon. Type I and type III waves were comparatively rare. Type IV waves were not recognised.

Independent activity in the three leads was the rule during the resting phase and was more common in the colon and rectum than in the small intestine. The trace from the recording tip furthest away from the anus (lead I) was almost invariably more active than traces from the

TABLE IV - The motility of the small intestine. The means and ranges of the values for the percentage activity, the motility index, the mean amplitude of the waves and the mean duration of the waves in control subjects and patients after partial gastrectomy.

	Control (6 cases)		Partial Gastrectomy without "dumping" (12 cases)		Partial Gastrectomy with "dumping" (6 cases)	
	Mean	(range)	Mean	(range)	Mean	(range)
Motor activity (%)						
Rest	32.1	(19.6 - 48.2)	30.3	(8.4 - 70.7)	37.1	(25.7 - 43.4)
Food 1	40.0	(28.4 - 54.7	41.7	(13.4 - 92.3)	26.2	(0.0 - 61.2)
Food 2	38.2	(23.1 - 57.3)	59.2	(23.1 - 91.9)	46.6	(29.9 - 81.4)
Prostigmine	47.1	(20.2 - 74.0)	53.2	(38.1 - 76.5)	42.4	(41.5 - 43.2)
Motility index						
Rest	21.1	(10.6 - 32.6)	30.0	(2.6 - 74.4)	33.8	(23.9 - 46.8)
Food 1	23.6	(12.5 - 39.2)	37.0	(4.8 - 77.5)	22.5	(0.0 - 69.8)
Food 2	19.6	(13.5 - 26.7)	54.7	(22.9 - 105.7)	50.3	(17.3 - 156.2)
Prostigmine	35.3	(10.5 - 57.6)	76.0	(29.9 - 127.9)	41.6	(21.0 - 62.2)
Mean Amplitude (mm. Hg.)						
Rest	10.1	(7.7 - 13.6)	12.8	(4.6 - 22.3)	12.2	(9.4 - 15.5)
Food 1	9.1	(3.7 - 12.0)	12.9	(4.1 - 29.2)	11.9	(9.0 - 18.0)
Food 2	8.4	(5.7 - 12.1)	13.6	(6.5 - 20.0)	13.3	(7.3 - 29.1)
Prostigmine	10.5	(8.2 - 12.4)	20.7	(8.8 - 48.7)	14.9	(8.1 - 21.7)
Mean duration (seconds)						
Rest	13.2	(7.7 - 16.5)	11.6	(5.1 - 17.7)	12.1	(6.9 - 18.6)
Food 1	12.1	(8.6 - 16.7)	11.0	(5.3 - 18.6)	12.7	(6.8 - 18.7)
Food 2	12.9	(8.1 - 16.5)	10.3	(5.9 - 14.2)	11.3	(5.2 - 21.3)
Prostigmine	12.0	(8.7 - 21.3)	15.8	(6.8 - 22.9)	10.8	(5.6 - 16.0)

lower recording tips; this was so in all categories of patients studied.

Synchronous activity at two or more levels of the large intestine was particularly evident after Prostigmine had been given (Figure 13). The activity was usually of type II and often rhythmic at 2.8 to 3.0 waves per minute.

The pressure changes recorded from the large intestine varied from less than 5 mm. Hg. to over 110 mm. Hg. (Figure 13). However, waves in excess of 50 mm. Hg. were unusual and the waves of type II which constituted the greater part of the activity of the large intestine usually reached a height of 10 to 20 mm. Hg.

Quantitative Analysis of Catheter Studies

The small intestine

Control subjects and patients after partial gastrectomy

The results of the quantitative analysis of motility are summarised in Table IV. In this and other tables and in the graphs "Food 1" refers to the first 10 minutes following the standard meal and "Food 2" refers to the subsequent 20 minutes. "Food 1 + 2" embraces the entire 30 minutes following the meal. This subdivision was made to detect whether there was any abnormality in the response of the intestine to food during induced attacks of "dumping" in the patients after partial gastrectomy.

The values for the motility index in the control subjects are

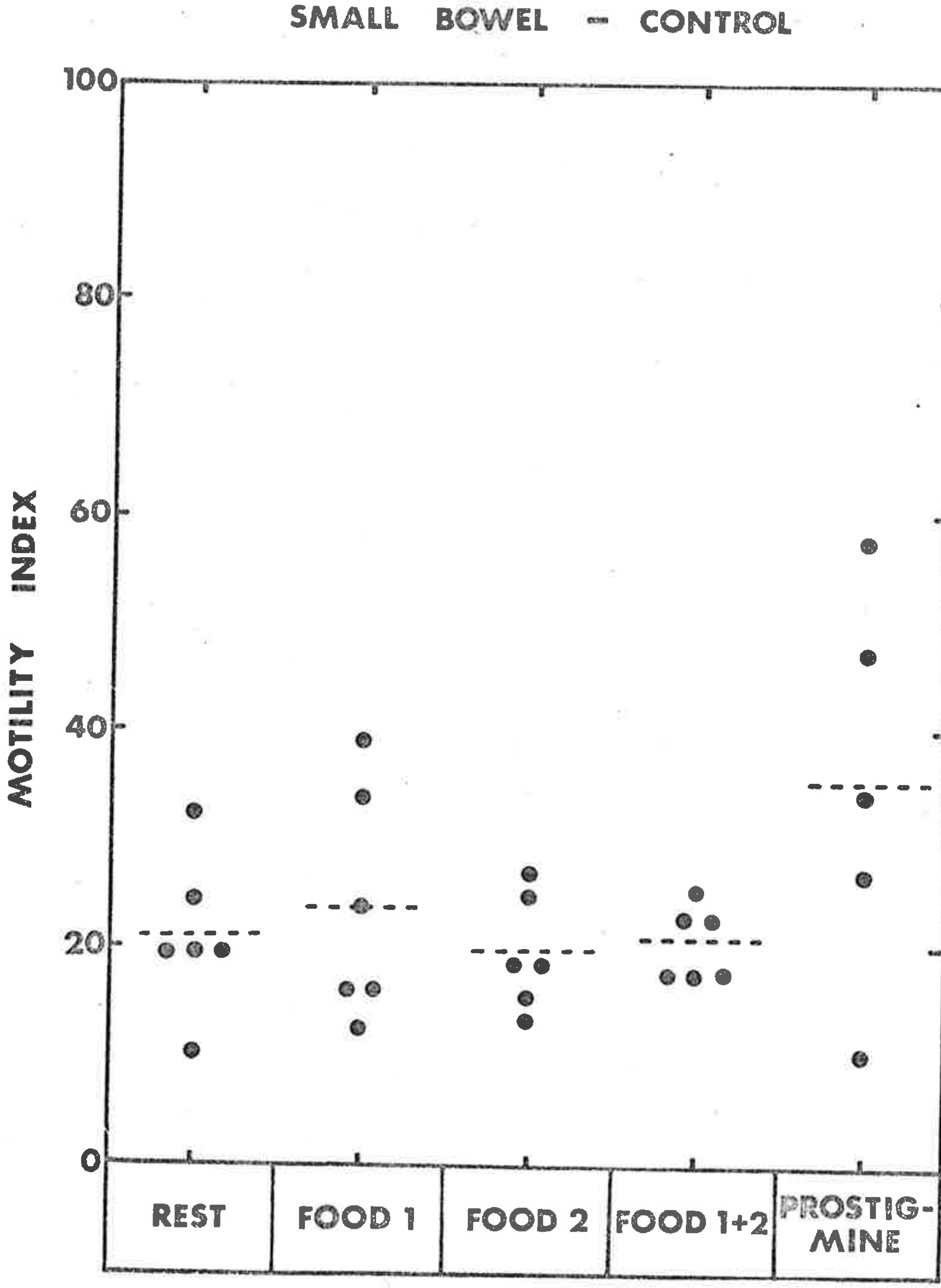


Figure 14: The motility index in six control subjects.

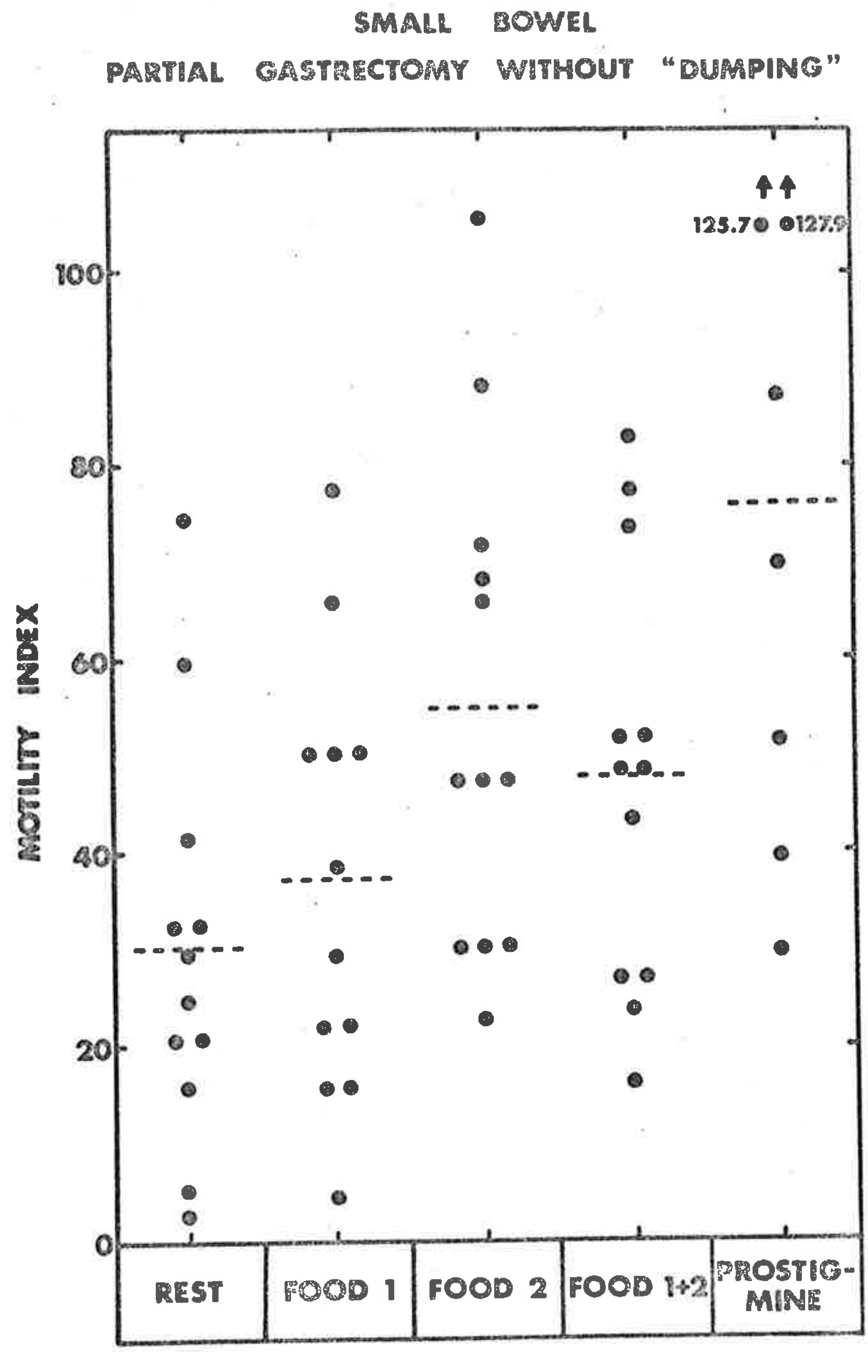


Figure 15: The motility index in twelve patients after partial gastrectomy in whom the dumping syndrome did not follow the administration of the meal.

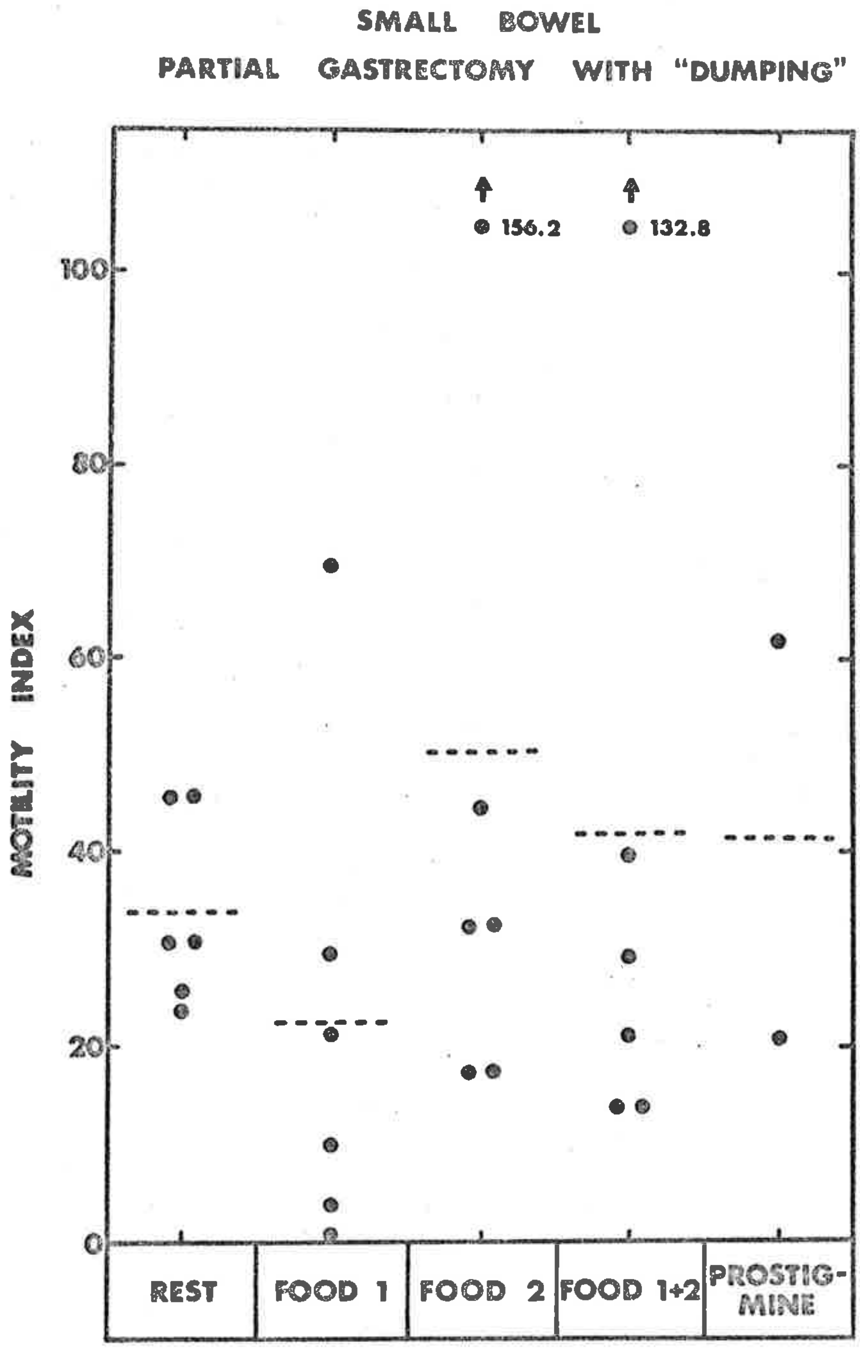


Figure 16: The motility index in six patients who had undergone partial gastrectomy and in whom the meal induced an attack of "dumping".

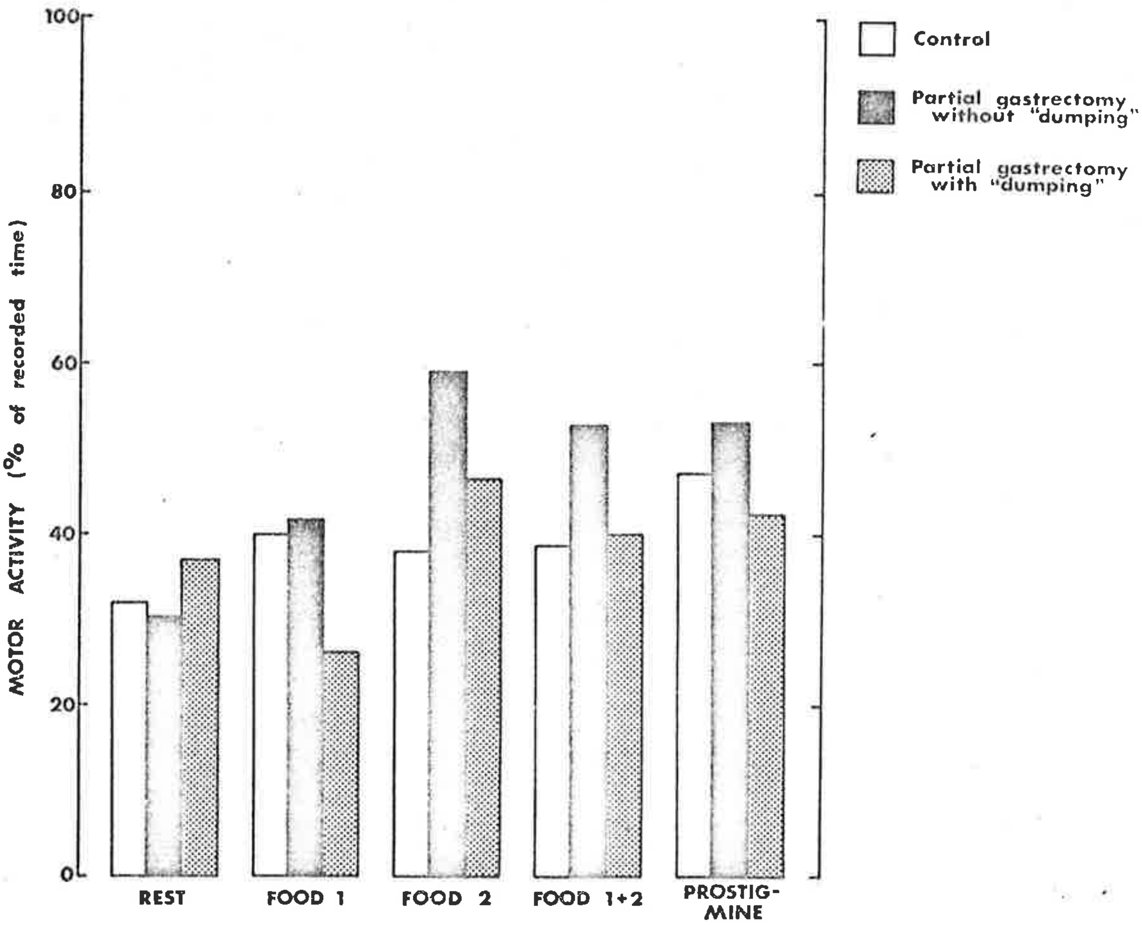


Figure 17: The motility of the small intestine: comparison of the percentage motor activity in the control subjects and patients after partial gastrectomy with and without the dumping syndrome.

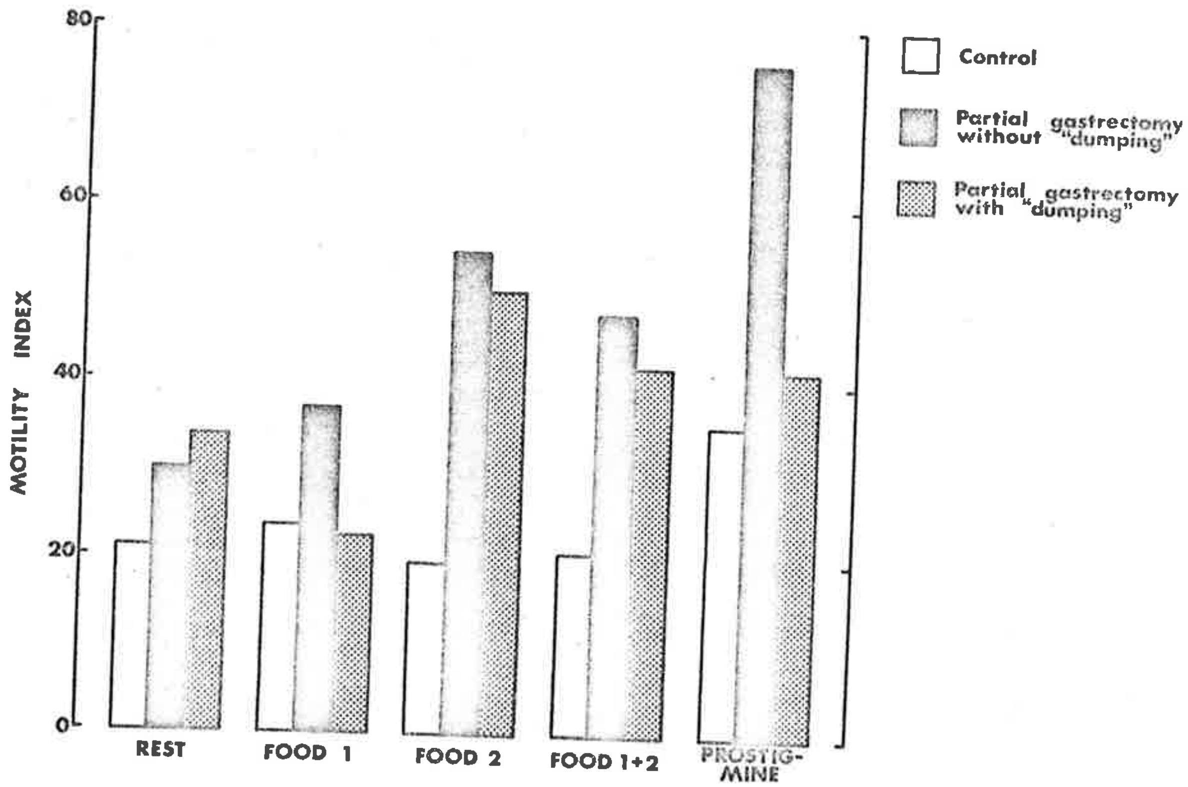


Figure 18: The motility of the small intestine: comparison of the motility index in control subjects and in patients after partial gastrectomy with and without the aumping syndrome.

presented in Figure 14. Unexpectedly food did not augment the motility of the small intestine. However, Prostigmine caused an increase in the mean motility index, although the variation in individual cases was considerable.

The range of the motility index of the patients after partial gastrectomy was considerably larger than in the case of the control subjects (Table IV). The values for the patients without the dumping syndrome after operation are illustrated in Figure 15 and the values for the patients with "dumping" in Figure 16.

Figure 17 illustrates the changes in percentage motor activity in the control subjects and in the two groups of patients who had had partial gastrectomy. There was little difference between the three groups during the resting phase and following Prostigmine. However, the patients in whom the dumping syndrome was induced showed a reduction in percentage activity immediately after the standard meal had been given. This reduction, although pronounced, was not statistically significant ($p > 0.05$). The patients with the dumping syndrome showed a greater delayed response to food than did normal subjects. However, their response was not as marked as that seen in patients without the dumping syndrome. The delayed response in this latter group was significantly greater than that in normal subjects ($p < 0.05$).

The differences between the three groups became more striking when the motility index was used as a basis for comparison (Figure 18). The resting activity in patients who had had partial gastrectomy and in

TABLE Va - The changes in the motility of the small intestine induced by food and by Prostigmine. A statistical comparison between the groups.

Phase of Recording	Control Mean motility index	Partial gastrectomy without "dumping" Mean motility index	Significance of difference between means
Rest	21.1	30.0	$p > 0.05$
Food 1	23.6	37.0	$p > 0.05$
Food 2	19.6	54.7	$p < 0.01$
Prostigmine	35.3	76.0	$p > 0.05$

Phase of Recording	Control Mean motility index	Partial gastrectomy with "dumping" Mean motility index	Significance of difference between means
Rest	21.1	33.8	$p < 0.05$
Food 1	23.6	22.5	$p > 0.05$
Food 2	19.6	50.3	$p > 0.05$
Prostigmine	35.3	41.6	$p > 0.05$

Phase of Recording	Partial gastrectomy without "dumping" Mean motility index	Partial gastrectomy with "dumping" Mean motility index	Significance of difference between means
Rest	30.0	33.8	$p > 0.05$
Food 1	37.0	22.5	$p > 0.05$
Food 2	54.7	50.3	$p > 0.05$
Prostigmine	76.0	41.6	$p > 0.05$

TABLE Vb - The changes in the motility of the small intestine induced by food and Prostigmine. A statistical comparison within each group.

Group	Rest: Mean motility index	Food 1: Mean motility index	Significance of difference between means
Control	21.1	23.6	$p > 0.05$
Partial gastrectomy without "dumping"	30.0	37.0	$p > 0.05$
Partial gastrectomy with "dumping"	33.8	22.5	$p > 0.05$

Group	Rest: Mean motility index	Food 2: Mean motility index	Significance of difference between means
Control	21.1	19.6	$p > 0.05$
Partial gastrectomy without "dumping"	30.0	54.7	$p < 0.02$
Partial gastrectomy with "dumping"	33.8	50.3	$p > 0.05$

Group	Rest: Mean motility index	Prostigmine: Mean motility index	Significance of difference between means
Control	21.1	35.3	$p > 0.05$
Partial gastrectomy without "dumping"	30.0	76.0	$p < 0.01$
Partial gastrectomy with "dumping"	33.8	41.6	$p > 0.05$

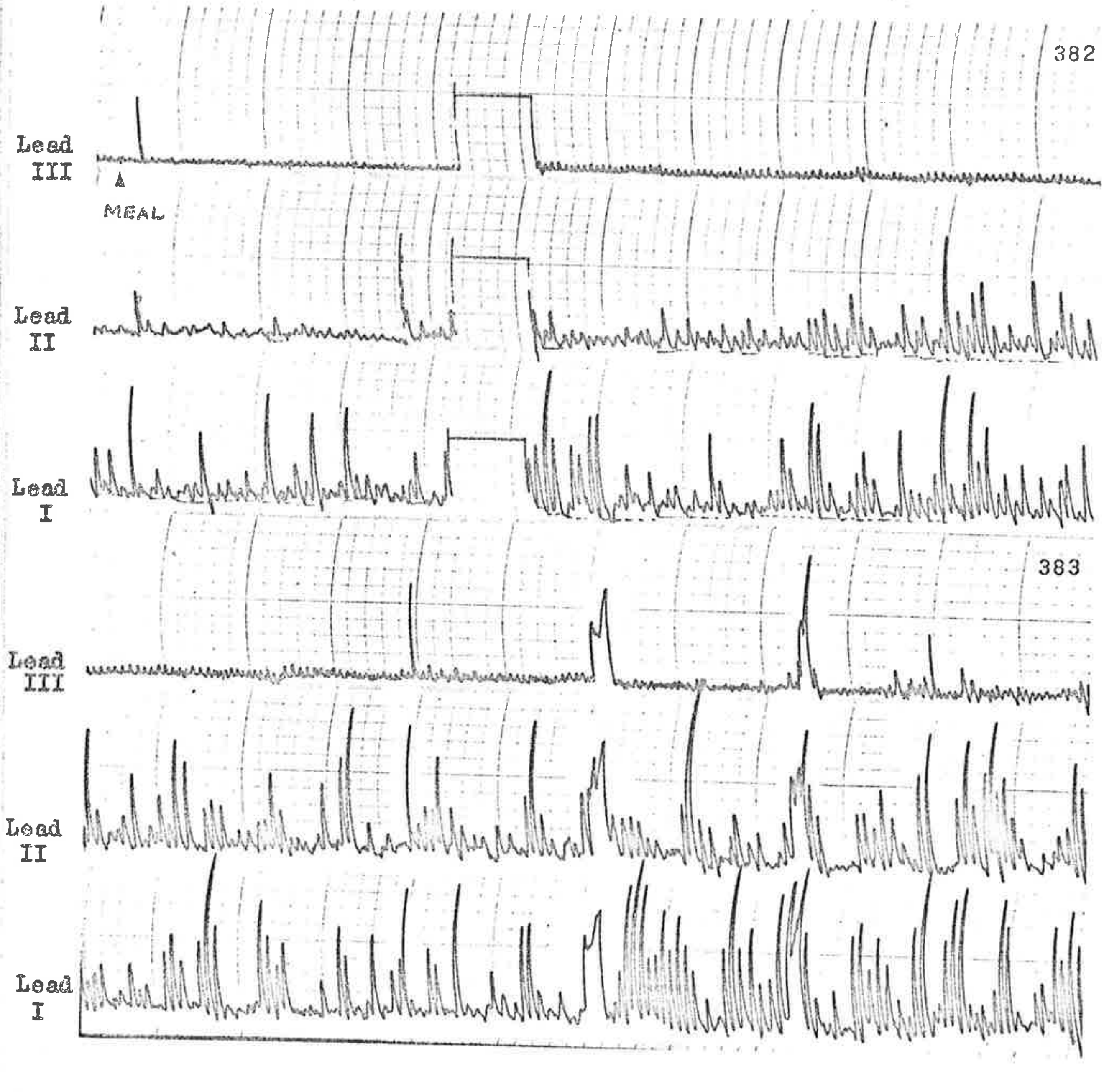


Figure 19: The small intestine: the response to the standard meal in a patient after partial gastrectomy in whom the meal did not provoke an attack of "dumping" (case 19). Paper speed 0.5 mm. per second (one small square equals ten seconds). The duration of the recording of the two panels is twenty minutes.

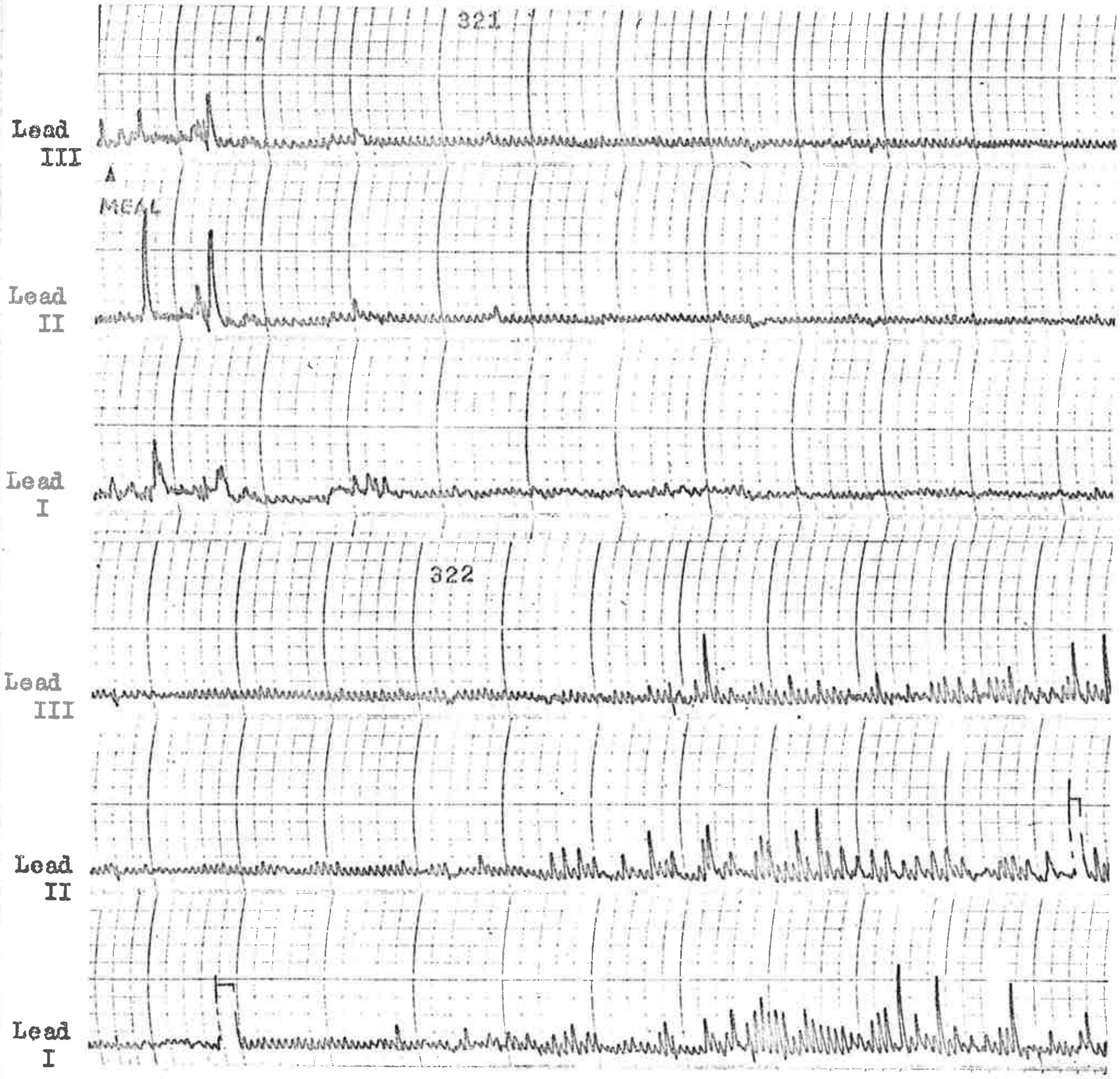


Figure 20: The small intestine: the response to the standard meal in a patient after partial gastrectomy in whom an attack of "dumping" followed the administration of the meal (case 12). Paper speed 0.5 mm. per second (one small square equals ten seconds). The duration of the recording of the two panels is twenty minutes.

whom "dumping" was induced by food was significantly higher than in the control subjects (Table Va). There was a marked reduction in the motility index with the onset of symptoms of "dumping", although this did not reach a level of statistical significance (Table Vb). However, the mean motility index of patients with symptoms of "dumping" was approximately the same as that of the controls but considerably less than that of patients without "dumping". Statistical analysis of the changes induced by food is presented in Tables Va and Vb.

Accompanying the subsidence of the attack of "dumping", the motility increased to a level well above that seen in the control subjects (Figures 17 and 18). The delayed response to food was of the same magnitude in both subgroups of patients after partial gastrectomy although it reached levels of significance only in the group without the dumping syndrome (Tables Va and Vb). By contrast the normal subjects displayed virtually no response to food. Prostigmine augmented motility in all groups but most markedly in the patients after partial gastrectomy in whom an attack of "dumping" was not induced by Food (Figure 18). In these patients the motility index was significantly higher after Prostigmine than during the resting phase (Table Vb). However, the differences between the groups were not statistically significant (Table Va).

The responses to food of two patients after partial gastrectomy are shown in Figures 19 and 20. The tracing in Figure 19 came from a patient (case 19) who did not experience symptoms of "dumping". Type I

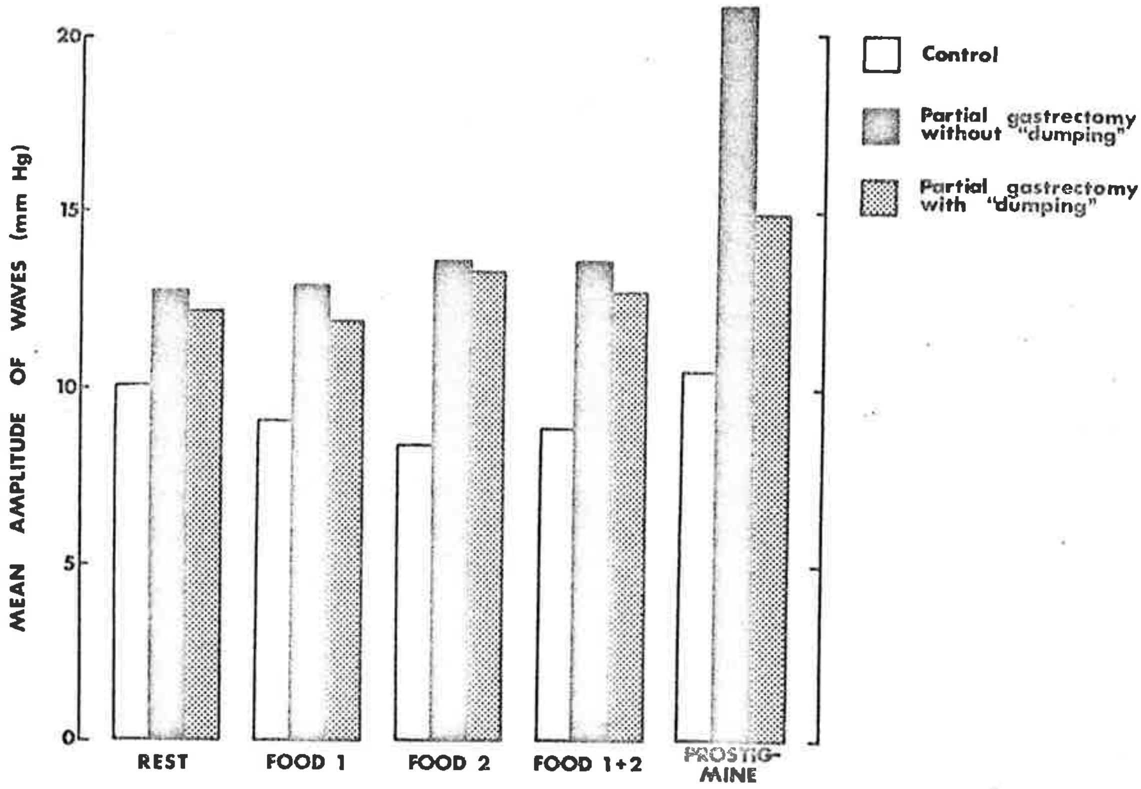


Figure 21: The motility of the small intestine: comparison of the mean amplitude of waves in control subjects and patients after partial gastrectomy with and without the dumping syndrome.

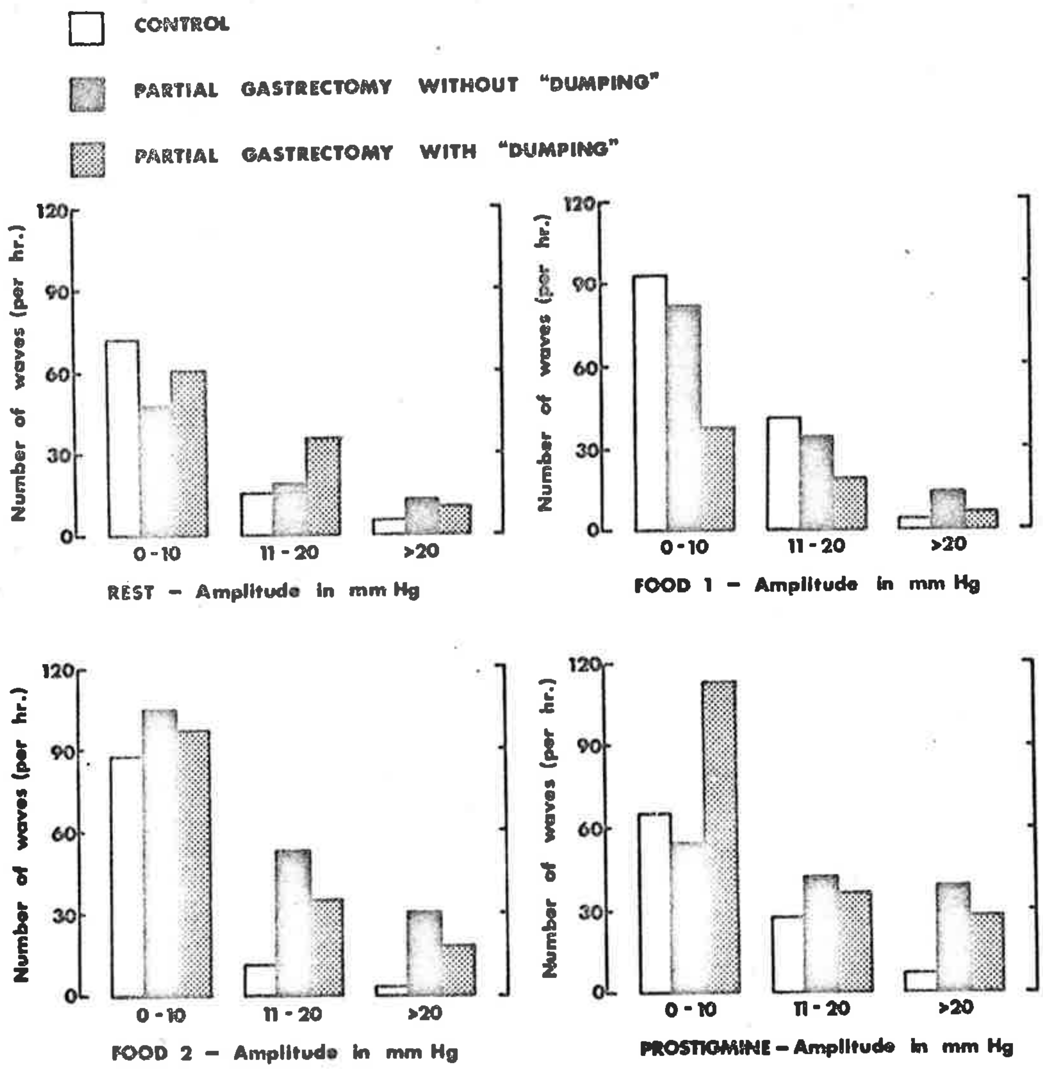


Figure 22: The motility of the small intestine: the distribution of the waves on the basis of amplitude in control subjects and patients after partial gastrectomy with and without the dumping syndrome.

activity was present throughout the tracing, although type III activity predominated towards the end of the recording period. In contrast, the tracing in Figure 20 was recorded from a patient (case 12) in whom the standard meal induced sweating, weakness and palpitations. It can be seen that after two waves appearing with progressive delay in all three leads, the small intestine remained completely inactive for nearly 15 minutes; a slow return of type I activity then accompanied the disappearance of the symptoms of "dumping".

The mean amplitude of the waves was consistently greater in both groups of patients after partial gastrectomy than in the control subjects (Figure 21). This was particularly marked after Prostigmine in patients without the dumping syndrome. The high mean amplitude in the patients without the dumping syndrome was reflected in an excessive number of waves of a high amplitude in this group (Figure 22). Figure 22 also shows that the patients who experienced an attack of "dumping" did not reach an equally high mean amplitude in response to Prostigmine because the increase in the number of high waves was masked by a more pronounced increase in the number of low waves. It can be further seen that both in the control subjects and in the patients after partial gastrectomy waves of low amplitude were the most common during all phases of the recording. Furthermore, the diminished motility of the small intestine during provoked attacks of "dumping" was due to a proportional decrease in waves of all amplitudes. Finally, the excessive late response to food in the patients who did not experience symptoms

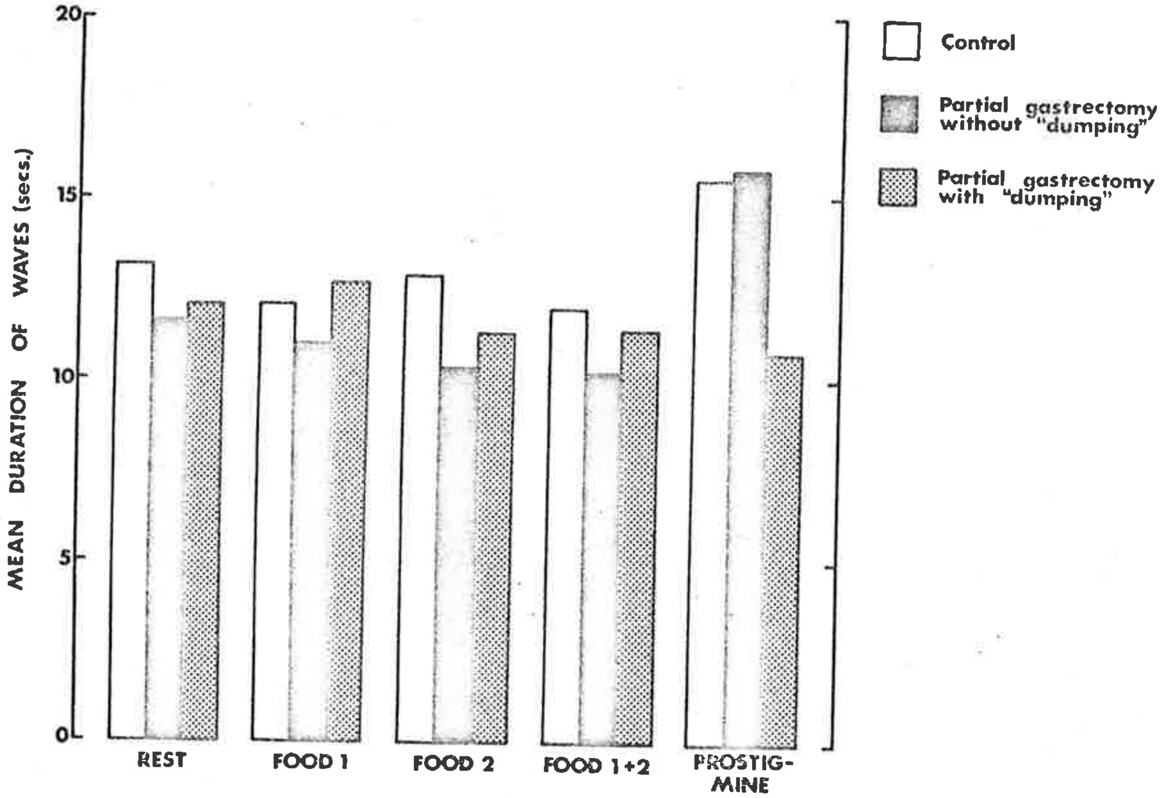


Figure 23: The motility of the small intestine: comparison of the mean duration of waves in control subjects and patients after partial gastrectomy with and without the dumping syndrome.

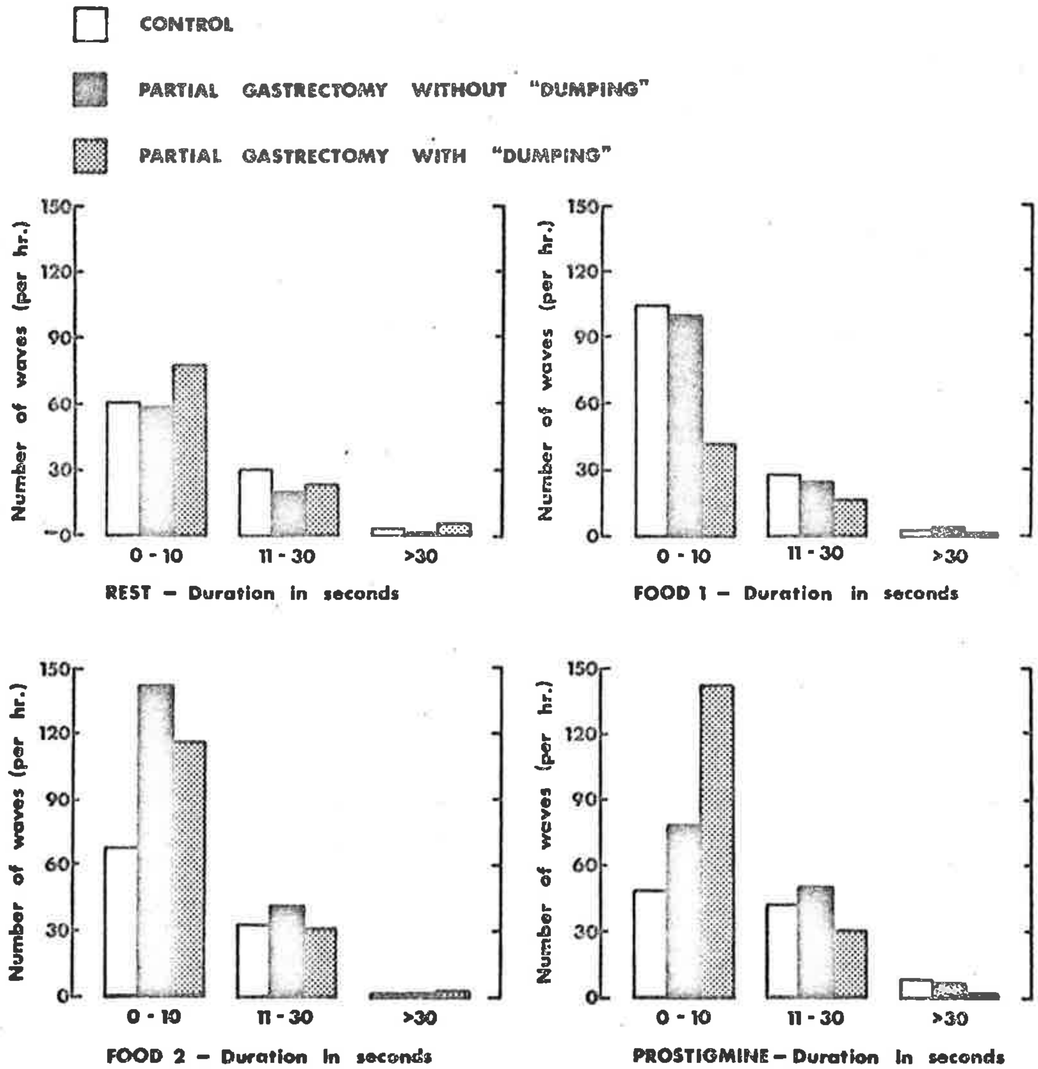


Figure 24: The motility of the small intestine: the distribution of the waves on the basis of duration in control subjects and patients after partial gastrectomy with and without the dumping syndrome.

TABLE VI - Catheter studies of the small intestine. The percentage motor activity, the motility index, the mean amplitude of the waves and the mean duration of the waves in a group of patients with miscellaneous alimentary disorders.

Case	Diagnosis	Bowel Habit* Usual	Bowel Habit* At study	Motor Activity (%) Rest	Motor Activity (%) Food 1	Motor Activity (%) Food 2	Motor Activity (%) Prostigmine	Motility Index Rest	Motility Index Food 1	Motility Index Food 2	Motility Index Prostigmine
27	Functional diarrhoea	D	N	38.7	71.5	76.7	76.1	23.8	63.2	45.9	73.1
28	Functional diarrhoea	D	N	36.3	30.7	57.6	-	32.2	25.2	56.5	-
29	Spastic colon	N	N	25.6	31.5	46.4	42.8	16.8	17.7	48.3	63.2
30	Chronic purgation	CD	D	8.2	-(a)	13.5	29.4	3.5	-(a)	8.2	13.1
31	Hiatus hernia	C	C	63.5	55.7	81.6	62.4	48.7	61.9	67.2	62.8
32	Gastric ulcer	N	N	40.7	51.8	53.6	54.8	24.6	39.2	38.0	146.8
33	Ulcerative colitis	D	N	35.2	39.5	48.4	54.7	40.2	23.2	32.9	91.0
34	Diverticulitis of the colon	D	N	16.7	10.2	50.5	31.1	12.1	6.4	26.4	36.7

*Symbols: C = constipation
D = diarrhoea
N = normal bowel habit
CD = alternating constipation and diarrhoea

(a) = not suitable for analysis owing to a technical fault in the recording equipment.

TABLE VI (continued)

Case	Mean amplitude (mm. Hg.) Rest	Food 1	Food 2	Prostigmine	Mean duration (seconds) Rest	Food 1	Food 2	Prostigmine
27	8.8	13.2	9.0	14.1	11.5	14.6	14.0	13.8
28	12.8	11.7	13.3	12.7	12.4	14.2	17.2	16.0
29	9.8	8.4	11.9	18.0	9.3	10.2	13.8	16.2
30	6.8	-[a]	9.3	6.6	8.2	-[a]	11.4	9.1
31	11.1	16.5	12.0	13.6	21.1	14.4	15.9	15.8
32	9.2	11.3	10.3	41.2	10.5	10.0	10.9	14.6
33	12.9	8.0	8.5	17.3	15.7	15.7	15.6	16.7
34	10.0	10.3	9.5	11.6	16.3	19.8	11.5	14.6

(a): Not suitable for analysis owing to a technical fault in the recording equipment.

of "dumping" was reflected in an increase in waves of all amplitudes.

There were no marked differences between the three groups of patients in respect of the mean duration of waves (Figure 23) or the distribution of the waves on the basis of duration (Figure 24). However, it can be seen that the mean duration of the waves recorded in patients without the dumping syndrome decreased in response to Prostigmine (Figure 23). This decrease was due to a marked rise in the number of short waves (Figure 24). Furthermore, short waves lasting less than 10 seconds (type I) were more numerous than waves of intermediate or long duration in all groups of patients during all the phases of the experiment (Figure 24).

Patients with miscellaneous alimentary disorders

Table VII lists the parameters of motility in the miscellaneous group. Although the small numbers do not permit statistical analysis, some interesting features of individual cases will be mentioned.

> Case 27 was a 41 year old woman with a diagnosis of functional diarrhoea. She had experienced almost continuous diarrhoea after an argument with her employer two months before her admission to hospital. She had no abdominal pain apart from a slight discomfort associated with a call to stool and promptly relieved by defaecation. The diarrhoea was aggravated by nervous tension and by ingestion of foods containing egg. The

results of a barium meal and a sigmoidoscopy were normal. The diarrhoea subsided without treatment during her stay in hospital so that her bowel habits were normal when the recording was made.

Table VI shows that the resting pattern of motility in this patient was normal in respect of the percentage activity and motility index. However, the response to the standard meal (one egg and two teaspoons of sugar beaten into milk) was greater than that seen in any of the normal subjects (Table IV). Likewise, the response to Prostigmine was in excess of normal.

Case 28 was a man of 32 years who had been subject to intermittent attacks of diarrhoea for five years preceding study. He was intolerant to milk and tomatoes and had learnt to avoid these foods because they aggravated his alimentary symptoms. Table VI shows that the late response to the standard meal in this patient was greater than normal.

Case 29, aged 38 years, had colonic pain with normal bowel habits diagnosed as the spastic colon. He was an interstate road transport driver and suffered marked exacerbations of pain with swelling in the left iliac fossa each time he had encountered a potentially dangerous situation on the road. The descending colon was firm and tender. Table VII shows that Prostigmine caused a greater rise in the motility index in his case than in any of the control subjects and that this rise was due to the high mean amplitude of waves, the percentage activity and mean duration of waves being within normal limits.

The patient with longstanding constipation (case 30) was a 57 year old woman. The constipation had led her to use increasing doses of aperients and to give herself enemata, almost every day. As a result her bowel habits alternated between severe constipation and spurious diarrhoea. She had undergone two laparotomies for the symptoms of intestinal obstruction and had had a further two episodes treated conservatively. Attempts to reduce the dose of purgatives resulted in increasing abdominal distension and vomiting with the radiological signs of low intestinal obstruction. However, barium studies of the gastro-intestinal tract revealed no organic obstruction. At the time of recording her serum potassium level was greatly diminished at 2.5 mEq. per litre.

Table VII shows that this patient had very little motor activity in the small intestine during the resting phase.

The percentage activity and motility index were both less than one-half of the lowest values encountered in the control group. There was also less activity after food than in any of the normal subjects and the response to Prostigmine was at the lower limit of normal.

The patient with a hiatus hernia (case 31) had sustained high levels of motility throughout the recording (Table VI) and the patient with a benign gastric ulcer (case 32) showed marked hypermotility in response to Prostigmine. In this latter patient the motility index reached a level of 146.8 compared with a maximum of 57.6 in the control group. This marked increase was due to an extremely high mean amplitude of waves; the percentage activity and mean duration of waves were both within normal limits.

The patient with ulcerative colitis (case 33) also displayed an excessive response to Prostigmine as judged by the motility index. The last patient in the miscellaneous group (case 34) showed no marked deviation from the normal.

The large intestine

Control subjects and patients with the irritable colon syndrome

The results of the quantitative analysis of the studies of the

TABLE VII - Catheter studies of the large intestine. The means and ranges of the values for the percentage motor activity, the motility index, the mean amplitude of the waves and the mean duration of the waves in control subjects and patients with the irritable colon syndrome.

		Control (27 studies)		Spastic colon (8 studies)		Functional Diarrhoea (13 studies)	
		Mean	(range)	Mean	(range)	Mean	(range)
Motor Activity (%)							
	Rest	13.2	(0.9 - 55.6)	17.9	(8.2 - 29.6)	5.7	(0.0 - 16.1)
	Emotion	19.9	(2.5 - 60.0)	19.0	(6.4 - 46.6)	9.6	(0.0 - 16.0)
	Food	15.4	(0.9 - 62.0)	22.0	(12.2 - 32.7)	9.7	(0.2 - 19.2)
	Prostigmine	32.1	(2.2 - 60.4)	47.1	(38.5 - 62.3)	23.1	(2.7 - 50.4)
Motility Index							
	Rest	8.6	(0.2 - 38.7)	12.5	(4.0 - 30.2)	2.4	(0.0 - 8.9)
	Emotion	18.4	(1.1 - 77.0)	15.3	(7.7 - 33.6)	5.9	(0.0 - 13.8)
	Food	15.0	(0.2 - 74.7)	18.4	(5.7 - 30.7)	5.3	(0.0 - 11.6)
	Prostigmine	34.0	(0.6 - 94.6)	58.3	(28.7 - 106.3)	17.8	(0.7 - 46.3)
Mean Amplitude (mm. Hg.)							
	Rest	7.7	(3.0 - 20.3)	10.4	(6.2 - 19.0)	6.0	(3.0 - 10.0)
	Emotion	10.3	(4.3 - 26.4)	12.7	(8.2 - 16.8)	8.7	(3.1 - 15.6)
	Food	9.5	(3.0 - 19.0)	11.0	(5.1 - 14.4)	7.5	(3.0 - 14.3)
	Prostigmine	13.0	(4.0 - 22.6)	18.6	(11.5 - 32.0)	9.9	(4.1 - 17.0)
Mean Duration (seconds)							
	Rest	16.9	(4.1 - 29.6)	18.1	(14.5 - 22.2)	15.8	(11.5 - 20.3)
	Emotion	19.0	(8.3 - 32.5)	19.7	(14.5 - 24.1)	16.8	(9.2 - 19.0)
	Food	17.7	(10.7 - 27.7)	18.5	(16.3 - 23.3)	15.6	(10.0 - 24.3)
	Prostigmine	19.0	(12.2 - 26.0)	18.8	(11.9 - 24.9)	16.9	(12.1 - 20.7)

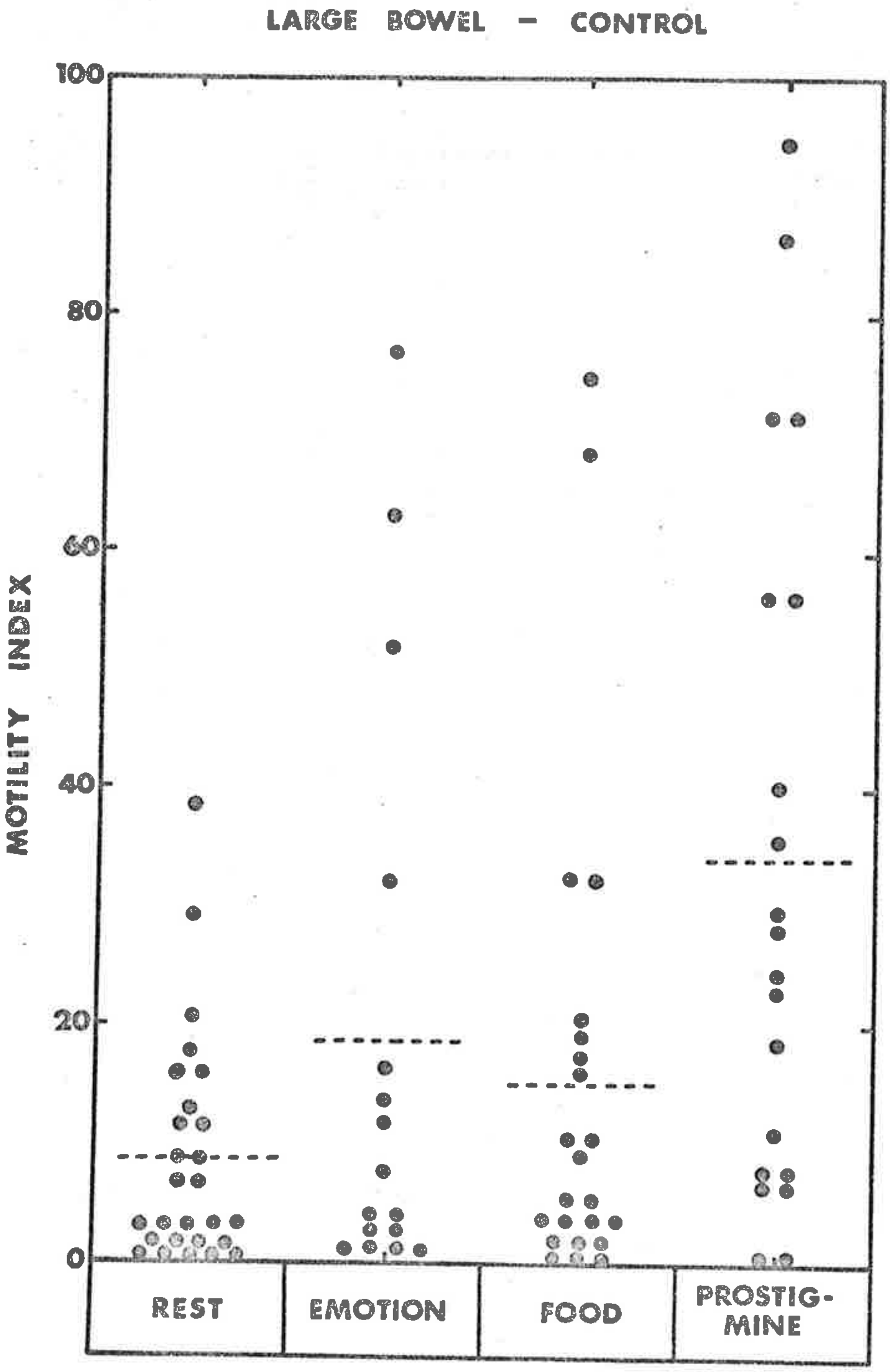


Figure 25: The motility index in twenty-seven studies of control subjects.

TABLE VIII - Variation in the resting pattern of motility of the distal large intestine. Comparison of separately analysed 30-minute periods of extended recordings in two normal subjects.

		Case 42	Case 45
Motor activity (%)			
	Rest 1*	15.3	55.6
	Rest 2	27.2	56.7
	Rest 3	32.3	
	Rest 4	33.3	
	Mean	27.0	56.2
Motility Index			
	Rest 1	16.5	38.7
	Rest 2	25.1	49.7
	Rest 3	25.6	
	Rest 4	17.3	
	Mean	21.1	44.2

*"Rest 1" refers to the first 30 minutes of the extended resting phase; "Rest 2" to the second 30 minutes, and so on.

TABLE IX - Variation in the motility of the distal large intestine. Comparison of repeated studies done on separate days in four normal subjects.

Case	No. of days between studies	Motor Activity (%) Rest	Emotion	Food	Prostigmine	Motility Index Rest	Emotion	Food	Prostigmine
35		9.3	3.0	2.9	11.9	4.0	1.8	0.3	7.8
	1								
"		10.7		8.6	7.8	12.7		2.3	7.1
	1								
"		3.7		8.6	11.9	1.0		4.1	6.7
38		6.2	10.3	15.2	18.1	2.4	3.4	5.8	7.8
	1								
"		5.4		3.7	2.2	1.7		1.4	0.6
	1								
"		3.3		0.9	2.7	3.3		0.2	0.8
44		20.8	46.5	61.4	59.0	11.5	52.0	68.3	86.6
	2								
"		21.0	9.7	10.5	60.4	15.7	4.7	5.2	40.4
52		22.1	43.8	32.9	48.3	29.3	77.0	32.3	71.6
	2								
"		7.9		16.5	37.9	11.5		19.1	56.6

large intestine are summarised in Table VII. The distribution of the values for the motility index in 27 studies carried out on control subjects is illustrated in Figure 25. Although there is considerable variation between different subjects, comparison of the mean values shows that the motor activity of the distal large intestine was augmented by emotion, food and Prostigmine.

Studies were performed to assess the constancy of the motor activity of the colon. Two normal subjects underwent prolonged recordings of the resting pattern of motility and the tracings were analysed in separate half-hour periods. The results of these studies are given in Table VIII. The agreement between the separate periods in the same individual was usually close, although the percentage activity in one of the subjects varied by as much as one hundred per cent.

In addition, four of the control subjects underwent a number of studies on different days. The result of these studies are presented in Table IX. It can be seen that with only two exceptions the level of motility expressed by the percentage motor activity remained relatively constant in any given person. The first exception occurred in case 38 where food and Prostigmine failed to augment motility during the second and third experiments. The second exception was seen in case 44 where the emotive interview failed to enhance motility when it was carried out for the second time. The motility index, being a compound expression of amplitude and duration, moved in parallel with the percentage motor activity but showed greater variation (Table IX).

Emotion augmented the motility in some of the control subjects. In 8 of 15 subjects the initial emotive interview (excluding re-studies) was associated with an increase in the motility index to 200 per cent. or more of the resting value. A decrease to 50 per cent. or less of the resting value was seen in one subject and in the remaining six the change during the interview was within these limits. During the interview, marked increases in activity were seen in patients with both high and low resting levels of motility. However, the increments were generally proportional to the resting values; the highest motility indices during the interview were found in the patients with high resting values. It was not possible to identify one particular mood in the person being studied with augmented motility and another mood with colonic inactivity.

On occasions hyperactivity of the large intestine was observed only while particular topics were being discussed:

> Case 52, a 36 year old man was serving a prison sentence for forgery. The large intestine began to show striking hypermotility during a discussion of the sentence, which the prisoner considered unduly harsh. The increased activity persisted while he commented on the disharmony between his wife and himself. The motility index increased from a resting value of 29.3 to 77.0. A

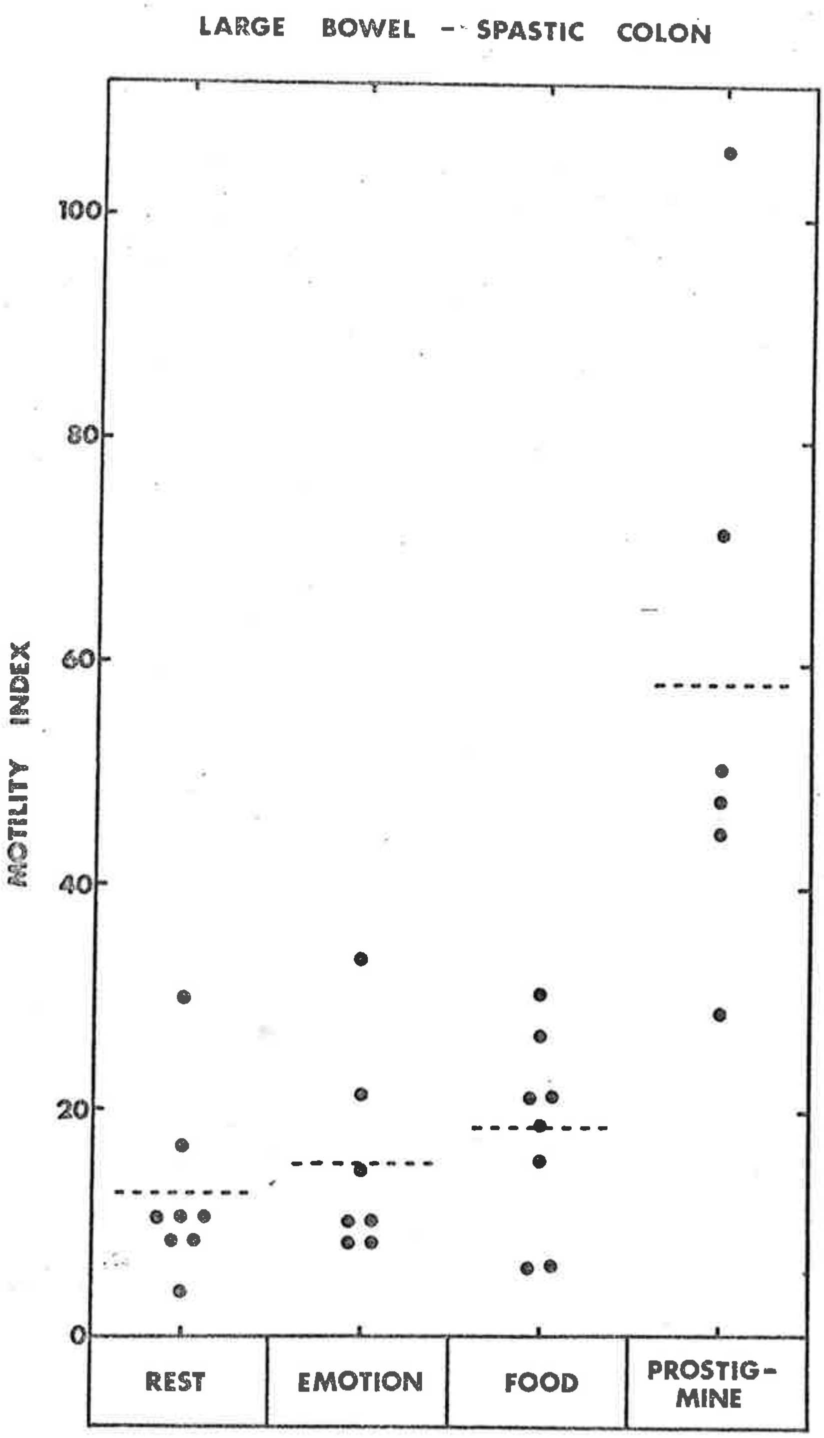


Figure 26: The motility index in eight studies of patients with the spastic colon.

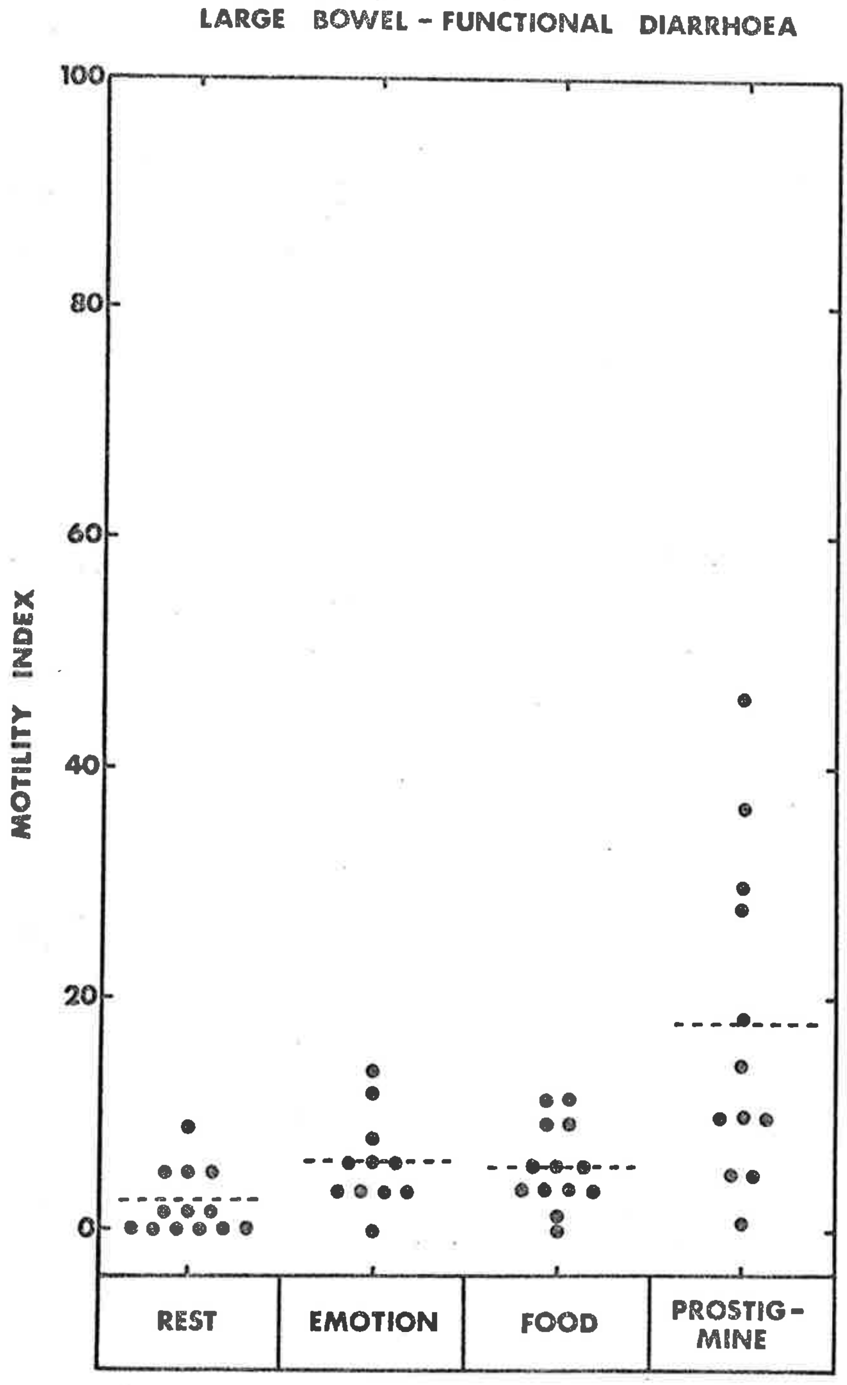


Figure 27: The motility index in thirteen studies of patients with functional diarrhoea.

> discussion of topics other than the two above mentioned did not augment motor activity.

However, on other occasions hyperactivity of the large intestine prevailed during the entire interview and was apparently unrelated to the emotional significance of the topics discussed:

> Case 36, a 40 year old man, had been imprisoned because of failure to pay alimony to his divorced wife. Excessive motor activity was present throughout the interview and did not abate when presumably neutral topics were discussed. The motility index for the interview was 63.2 compared to the resting value of 8.4.

Eight catheter studies were made of patients with the spastic colon and thirteen studies of patients with functional diarrhoea. The mean values and ranges for the percentage motor activity, motility index, mean amplitude of waves and mean duration of waves are presented in Table VII. Figures 26 and 27 show the means and distribution of the individual values for the motility index in these two groups. It can be seen that in both groups the motility of the large intestine increased in response to the interview, food and Prostigmine. However, patients with functional diarrhoea had less activity during all phases of the recording than patients with the spastic colon. The uniformly low resting level of motility in patients with functional diarrhoea was particularly striking (Figure 27).

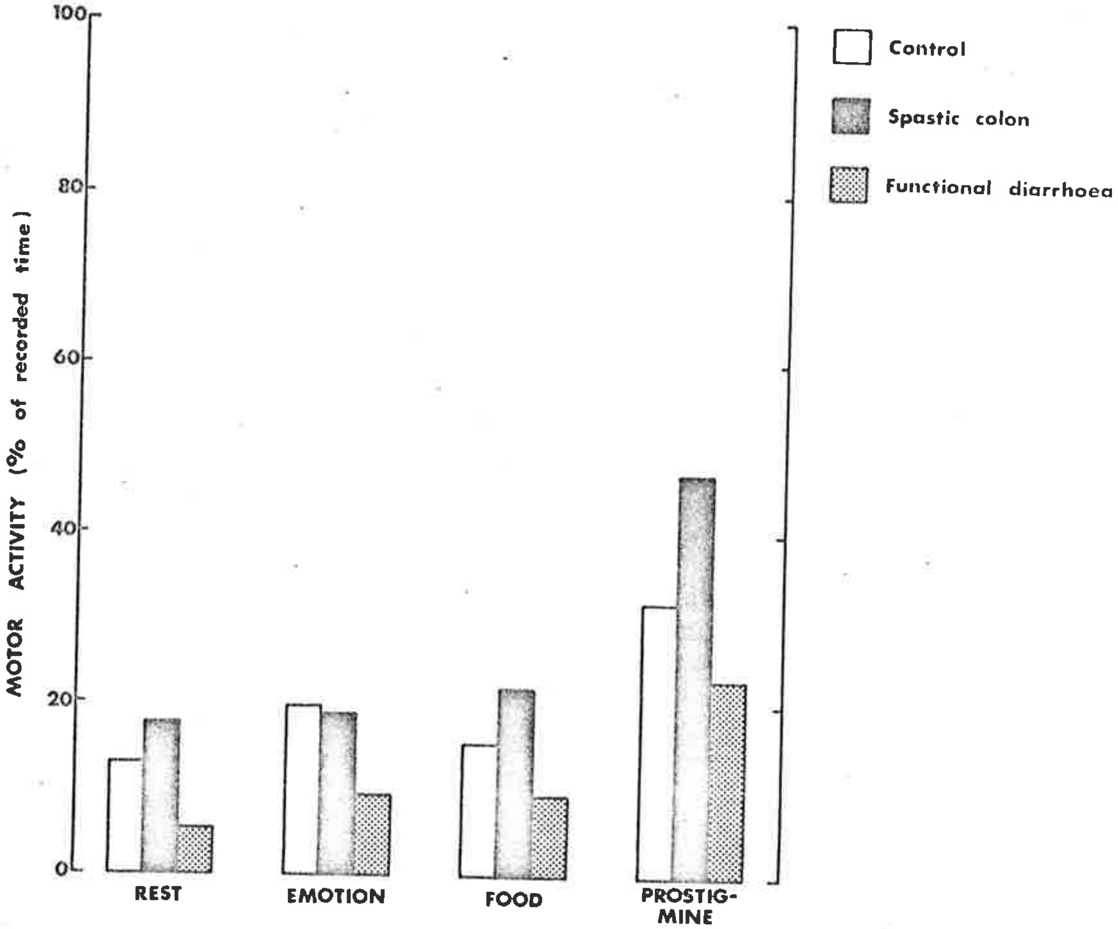


Figure 28: The motility of the large intestine: comparison of the percentage motor activity in control subjects, patients with the spastic colon and patients with functional diarrhoea.

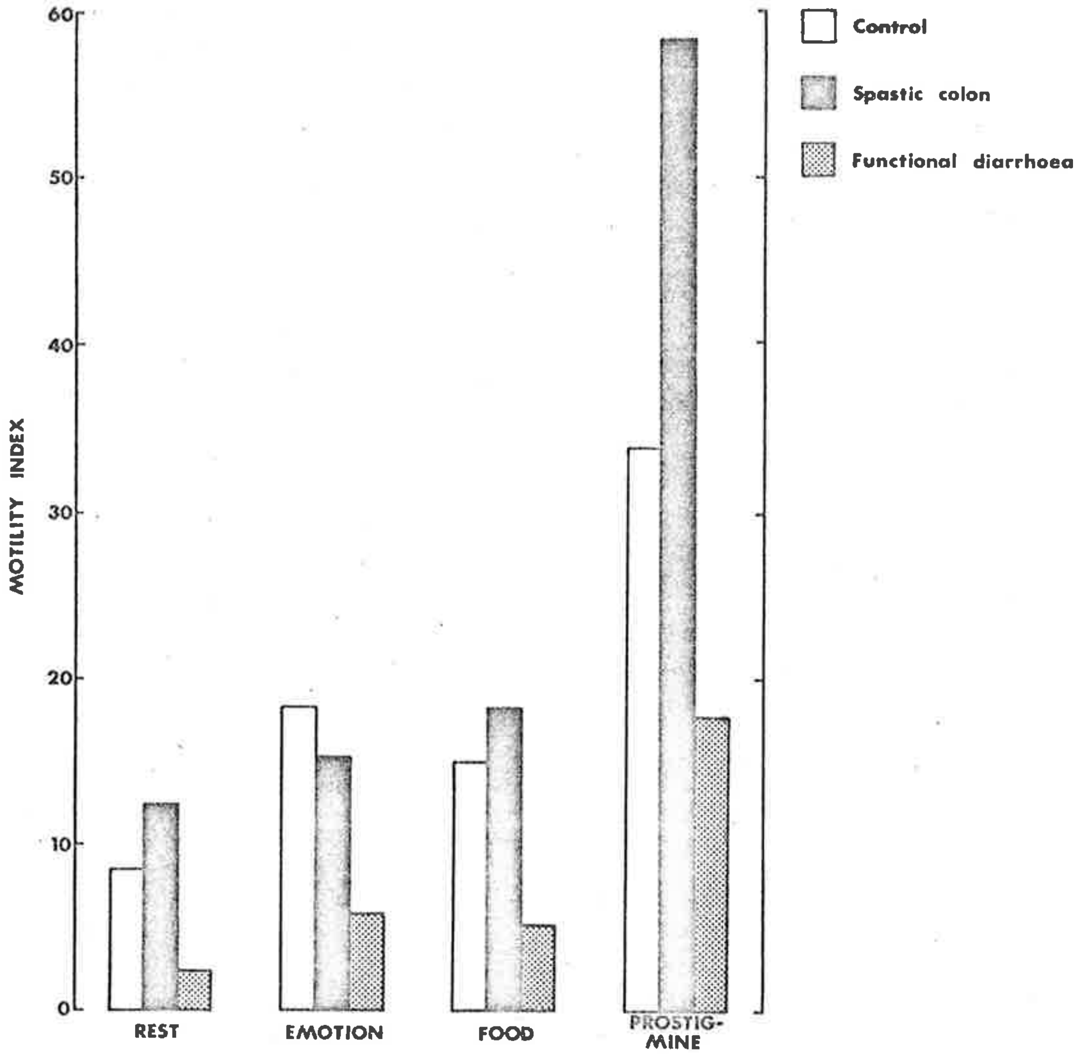


Figure 29: The motility of the large intestine: comparison of the motility index in control subjects, patients with the spastic colon and patients with functional diarrhoea.

TABLE X - Statistical evaluation of the differences between the mean motility indices of control subjects, patients with the spastic colon and patients with functional diarrhoea.

Phase of Recording	Control Mean motility index	Spastic Colon Mean motility index	Significance of difference between means
Rest	8.6	12.5	$p > 0.05$
Emotion	18.4	15.3	$p > 0.05$
Food	15.0	18.4	$p > 0.05$
Prostigmine	34.0	58.3	$p > 0.05$

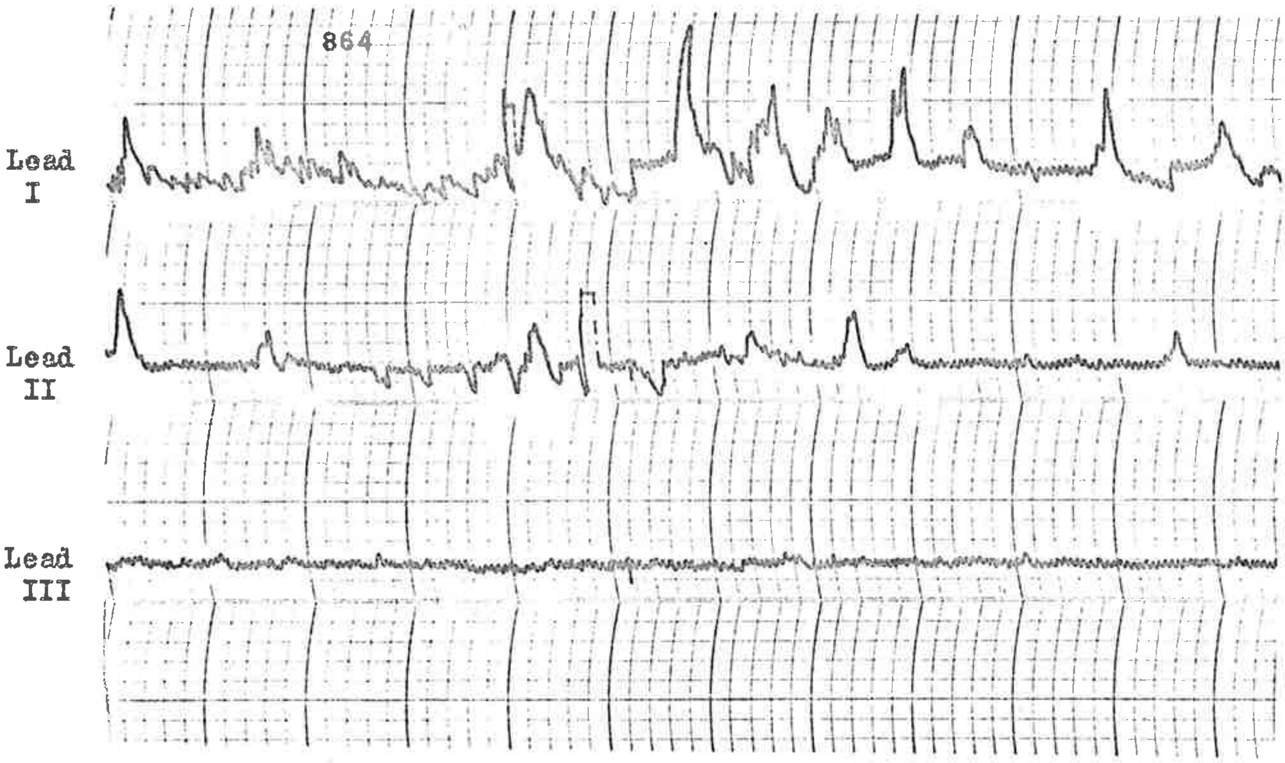
Phase of Recording	Control Mean motility index	Functional Diarrhoea Mean motility index	Significance of difference between means
Rest	8.6	2.4	$p < 0.05$
Emotion	18.4	5.9	$p \ngtr 0.05$
Food	15.0	5.3	$p > 0.05$
Prostigmine	34.0	17.8	$p > 0.05$

Phase of Recording	Spastic Colon Mean motility index	Functional Diarrhoea Mean motility index	Significance of difference between means
Rest	12.5	2.4	$p < 0.002$
Emotion	15.3	5.9	$p < 0.01$
Food	18.4	5.3	$p < 0.001$
Prostigmine	58.3	17.8	$p < 0.001$

Figure 28 illustrates the changes in percentage motor activity in the normal controls and in the patients with the irritable colon syndrome during the four phases of the recording. It can be seen that all three groups had more activity during the interview, after food and after Prostigmine than during the resting phase. The increase in percentage motor activity induced by Prostigmine was highly significant in all three groups ($p < 0.001$). The resting level of activity of patients with functional diarrhoea was lower than the levels of control subjects and patients with the spastic colon, and these differences were statistically significant ($p < 0.05$).

Figure 29 illustrates the mean motility indices of the three groups studied. The inactivity of the distal large intestine in patients with functional diarrhoea is again evident. Patients with the spastic colon had the highest levels of activity during all phases of the recording except the interview and the control subjects occupied the intermediate position. Table X presents the statistical evaluation of the differences between the means of the motility indices of the three groups studied. It can be seen that patients with functional diarrhoea had a significantly lower motility index than patients with the spastic colon during all phases of the recording. They also had a significantly lower motility index than the control subjects during the resting phase.

Figures 30 and 31 emphasise some of the differences between the two subgroups of the irritable colon syndrome. Figure 30 represents



<u>Figure 30</u>: The large intestine: the resting pattern of motility in a patient with the spastic colon (case 29) showing increased activity in lead I (from the sigmoid colon). Paper speed 0.5 mm. per second. Thus one small square equals ten seconds.

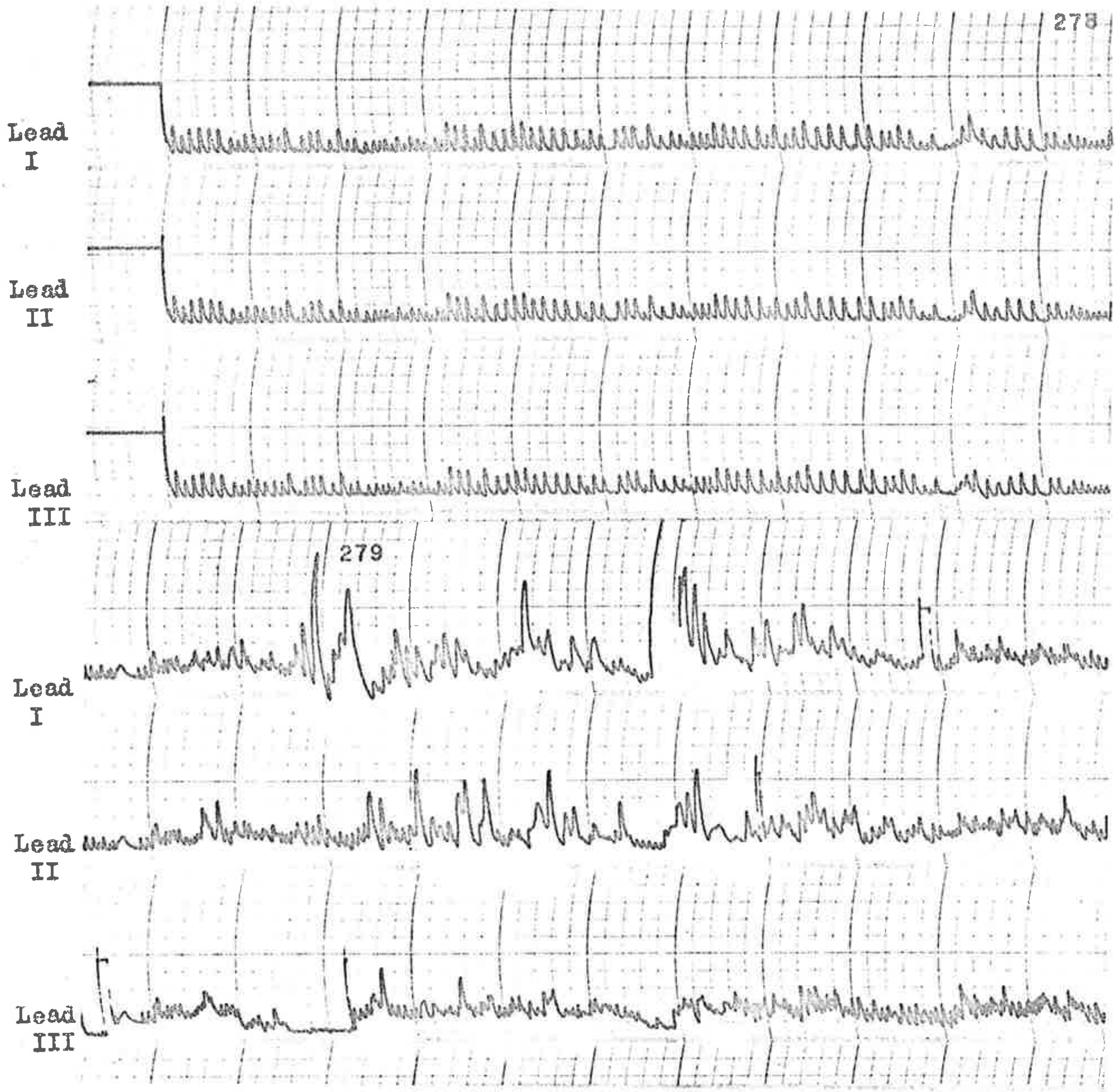


Figure 31: The large intestine.
Upper panel: the resting pattern of motility in a patient with functional diarrhoea (case 67). There are many transmitted respiratory fluctuations of varying amplitudes but only one small pressure wave recorded from the large intestine.
Lower panel: markedly increased motility in response to the emotive interview in the same patient.
Paper speed 0.5 mm. per second, thus one small square equals ten seconds.

the resting pattern of motility in a patient with the spastic colon (case 29) and Figure 31 illustrates the inactivity of the distal large intestine during the resting phase in a patient with functional diarrhoea (case 67).

> Case 67, with a diagnosis of functional diarrhoea, was a 70 year old Latvian woman who had been subject to recurrent attacks of diarrhoea for the two years preceding the present study. A sigmoidoscopy and barium studies of the stomach, small intestine and large intestine revealed no organic lesion. The stools were negative for occult blood and contained no pathogenic bacteria or parasites. The three-day faecal fat excretion was 8.0 grammes, and a biopsy specimen from the rectum showed normal mucosa. The serum level of protein bound iodine was 6.2 µg. per 100 ml. (normal: 3.5 to 8.0 µg. per 100 ml.). During the resting phase there was very little spontaneous motility. During the interview tall waves appeared in the tracing when the patient related her experiences during the German and Russian occupations of Latvia in the Second World War. The motility index increased to 13.8 from a resting value of 1.5.

Table XI presents the statistical evaluation of the changes in

TABLE XI - Statistical evaluation of the changes in the motility of the large intestine induced by emotion, food and Prostigmine

Group	Rest Mean motility index	Emotion Mean motility index	Significance of difference between means
Control	8.6	18.4	$p > 0.05$
Spastic colon	12.5	15.3	$p > 0.05$
Functional diarrhoea	2.4	5.9	$p < 0.02$

Group	Rest Mean motility index	Food Mean motility index	Significance of difference between means
Control	8.6	15.0	$p > 0.05$
Spastic colon	12.5	18.4	$p > 0.05$
Functional diarrhoea	2.4	5.3	$p < 0.05$

Group	Rest Mean motility index	Prostigmine Mean motility index	Significance of difference between means
Control	8.6	34.0	$p < 0.001$
Spastic colon	12.5	58.3	$p < 0.001$
Functional diarrhoea	2.4	17.8	$p < 0.001$

the motility index observed during the interview, after food and after Prostigmine in the three groups studied. It can be seen that compared to the resting values only the patients with functional diarrhoea had a significant increase in the motility index during the interview and after food. However, Prostigmine caused a highly significant rise in the motility index both in the control subjects and the patients with the irritable colon syndrome. Figure 13 shows the response to Prostigmine in one patient with the spastic colon (case 64).

The first emotive interview was associated with an increase in the motility index to 200 per cent. or more of the resting value in 2 of 7 patients with the spastic colon (28.6%) and 6 of 11 patients with functional diarrhoea (54.5%). Of the patients with functional diarrhoea who exhibited this increase, all but one had given a history of aggravation of the symptoms by nervous tension. The motility index decreased to 50 per cent. or less of the resting value in one patient with the spastic colon and in two patients with functional diarrhoea.

After food, two of seven patients with the spastic colon showed an increase in the motility index to 200 per cent. or more of the resting values; neither gave a history of intolerance to milk, egg or sugar. Seven of eleven patients with functional diarrhoea had a similar increase after the standard meal, and of these patients three were intolerant to milk.

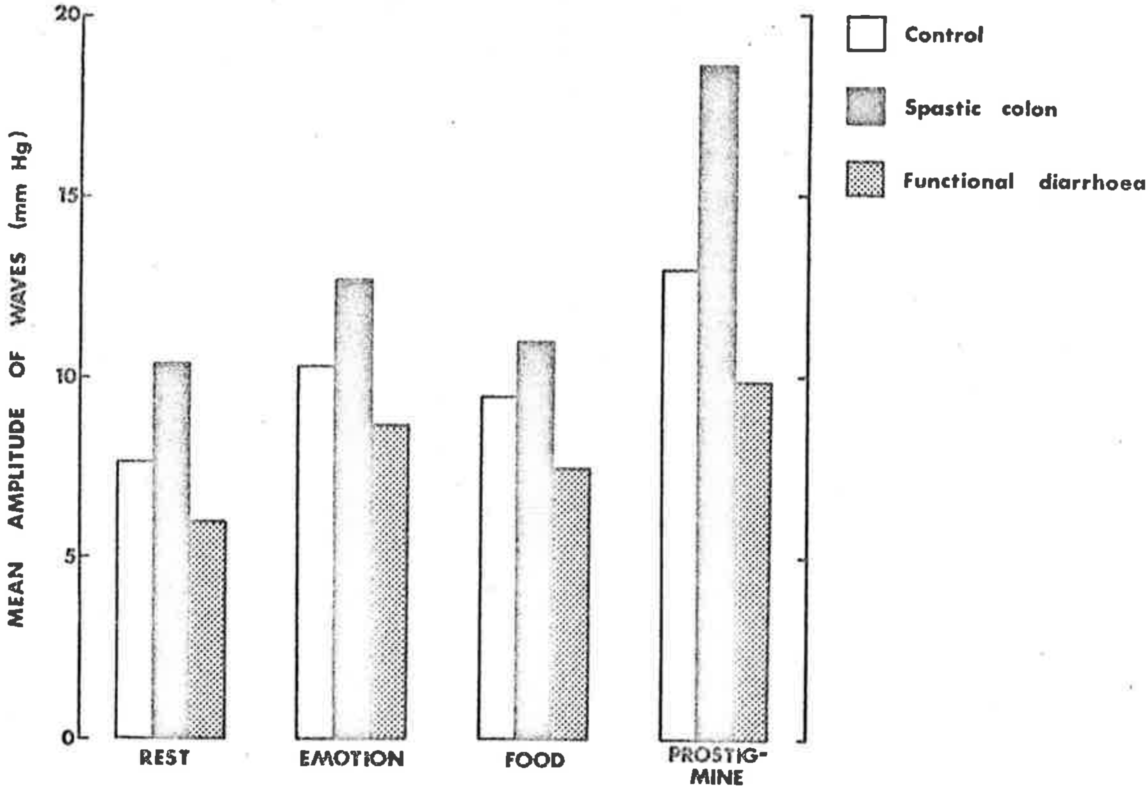


Figure 32: The motility of the large intestine: comparison of the mean amplitude of waves in control subjects, patients with the spastic colon and patients with functional diarrhoea.

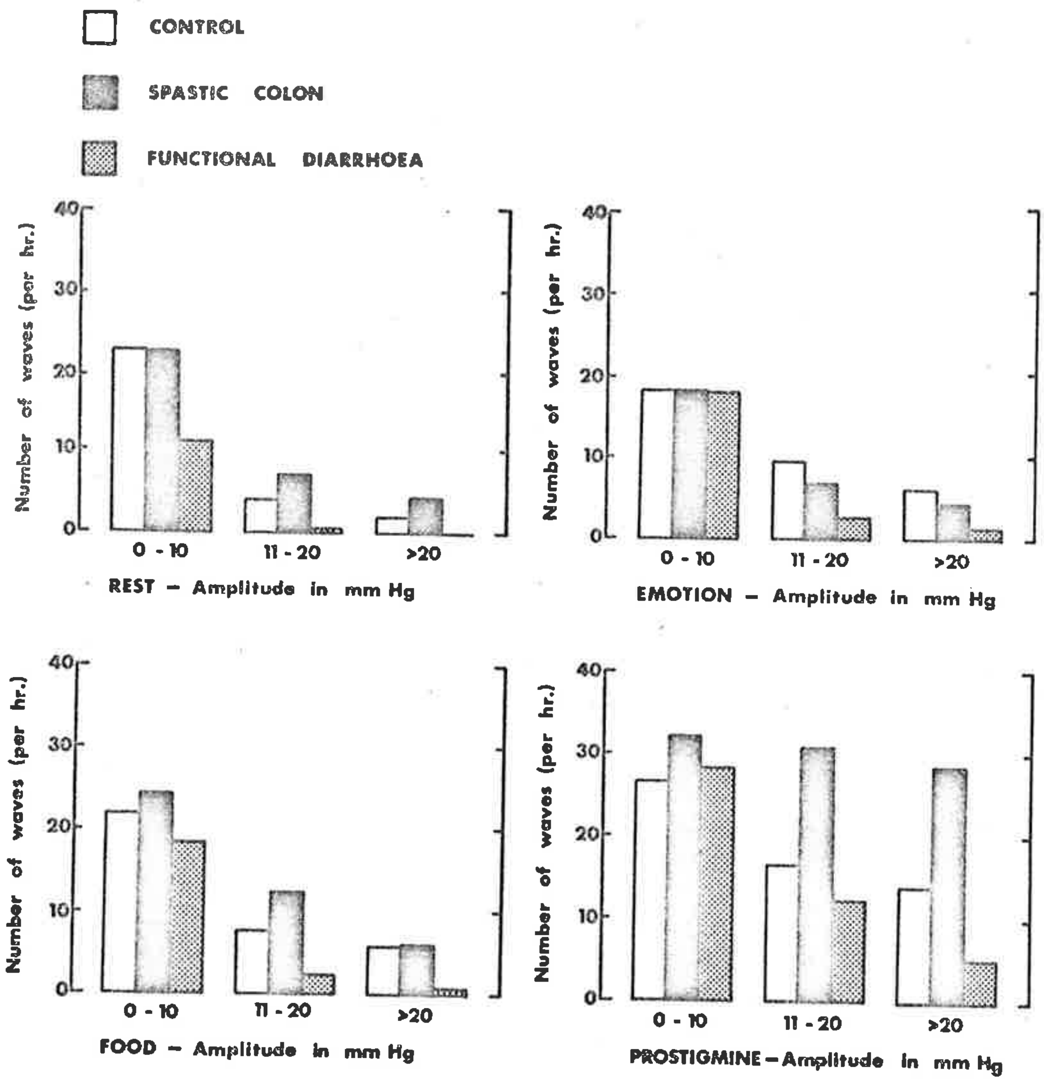


Figure 33: The motility of the large intestine: the distribution of the waves on the basis of amplitude in control subjects, patients with the spastic colon and patients with functional diarrhoea.

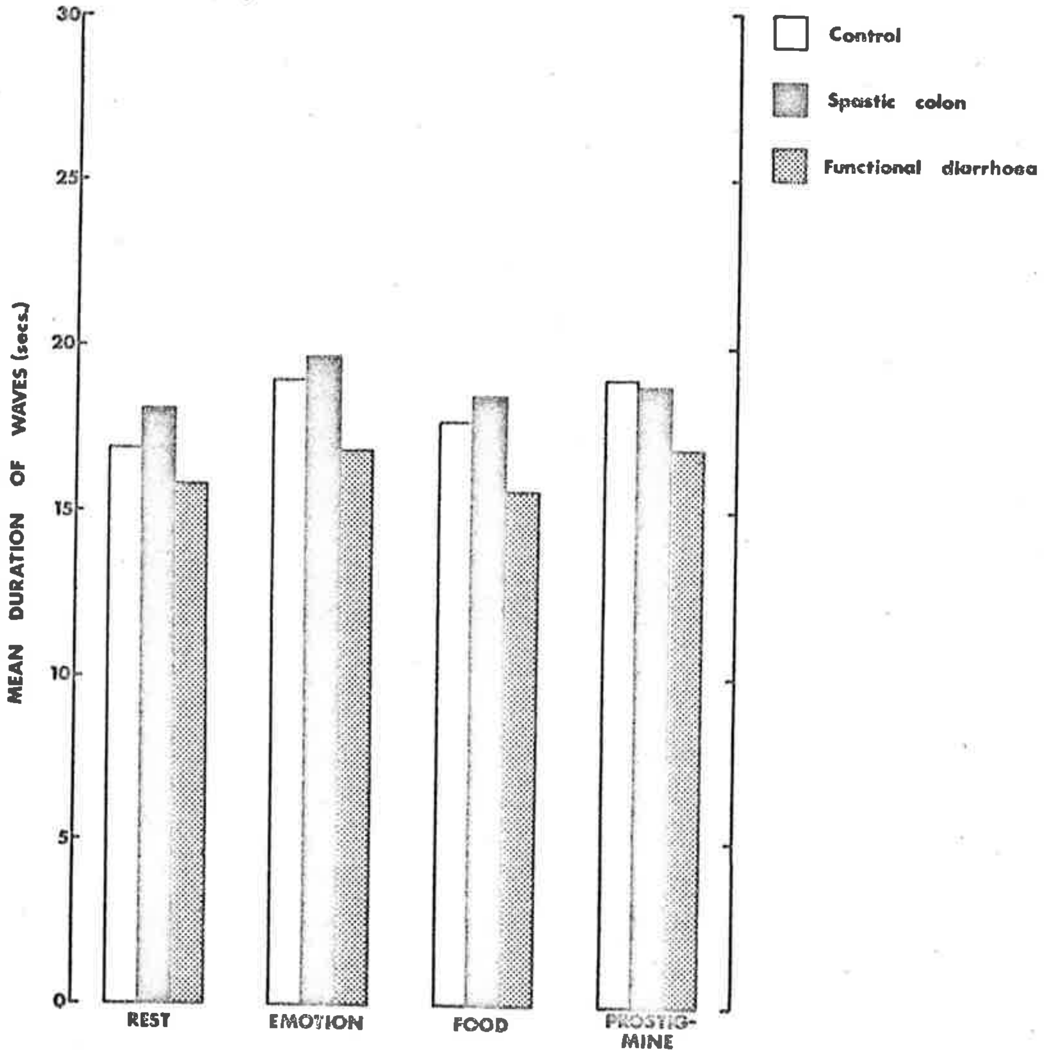


Figure 34: The motility of the large intestine: Comparison of the mean duration of waves in control subjects, patients with the spastic colon and patients with functional diarrhoea.

The remaining two patients with the irritable colon syndrome and an intolerance to ingredients of the standard meal had functional diarrhoea. In one patient the motility index after food was 143 per cent. of the resting value. The other patient showed a reduction in the motility index to 77 per cent. and 38 per cent. of the resting values in two separate studies.

The mean amplitude of the waves in the control subjects and the patients with the irritable colon syndrome is shown in Figure 32. Patients with the spastic colon had the highest mean amplitudes throughout the recording and patients with functional diarrhoea the lowest mean amplitudes, while the control subjects occupied the intermediate position. The reason for the low mean amplitudes in the patients with functional diarrhoea is apparent in Figure 33. Although low waves occurred with approximately equal frequency in all three groups, the patients with functional diarrhoea had considerably fewer waves of intermediate or high amplitude than did the control subjects or the patients with the spastic colon. Waves of the two latter categories were most frequent in patients with the spastic colon. Figure 33 also shows that Prostigmine caused an increase mainly in the number of waves of intermediate and high amplitude.

Figure 34 shows that the mean duration of the waves remained virtually constant throughout the phases of the recording and that it was approximately the same in the control subjects and in patients with the irritable colon syndrome. The distribution of the waves on the

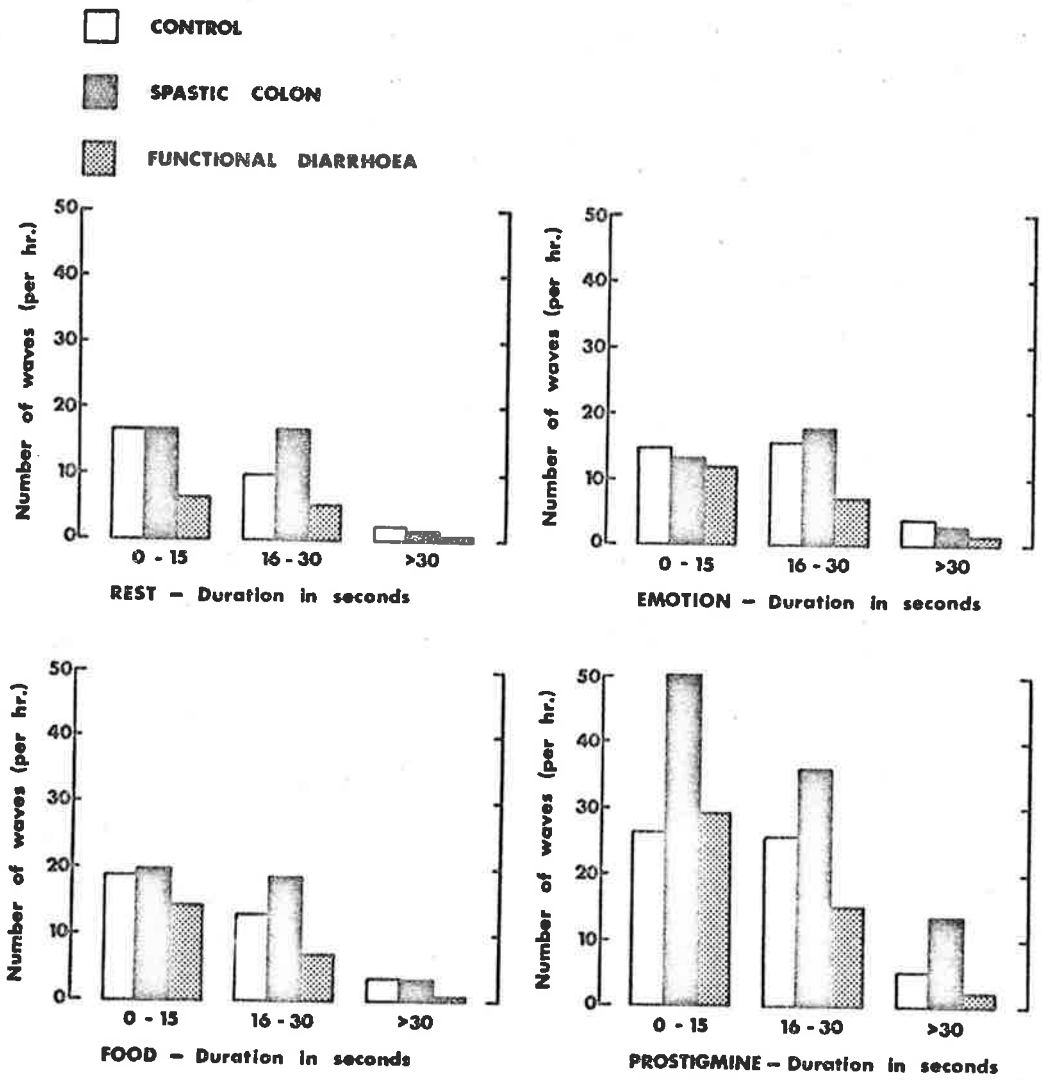


Figure 35: The motility of the large intestine: the distribution of the waves on the basis of duration in control subjects, patients with the spastic colon and patients with functional diarrhoea.

TABLE XII - Catheter studies of the large intestine. The means and ranges of the values for the percentage motor activity, the motility index, the mean amplitude of the waves and the mean duration of the waves in a group of patients with miscellaneous disorders

Diagnosis	Bowel Habit* Usual	Bowel Habit* At study	Motor Activity (%) Rest	Motor Activity (%) Emotion	Motor Activity (%) Food	Motor Activity (%) Prostig-mine	Motility Index Rest	Motility Index Emotion	Motility Index Food	Motility Index Prostig-mine
Ulcerative colitis	D	N	22.5	24.3	13.7	42.6	7.6	7.9	2.9	22.8
" "	CD	N	8.1	4.2	7.0	13.8	1.9	2.0	2.7	5.0
" "	D	N	22.2	15.1	19.1	52.3	26.1	18.9	17.1	84.4
" "	D	D	0.0	0.0	-	-	0.0	0.0	-	-
" "	C	C	7.1	0.0	7.7	64.3	1.6	0.0	2.0	63.1
Small bowel resection; steatorrhoea	D	D	0.3	2.2	1.8	4.5	0.1	1.4	0.5	1.4
Malabsorption syndrome ?cause	D	N	16.1	19.4	21.5	49.0	17.6	15.6	17.7	38.3
"	CD	C	21.6	33.3	33.7	45.0	14.6	16.1	34.6	22.4
"	C	C	22.1	49.5	45.6	-	17.4	64.6	53.3	-
Idiopathic steatorrhoea	D	N	0.6	9.2	33.5	48.5	0.1	9.4	41.1	68.1
Partial gastrectomy	N	N	9.5	13.1	24.9	31.2	13.1	10.8	18.8	31.0
"	D	N	33.6	42.5	32.6	53.1	13.7	16.8	18.1	47.0
"	N	N	8.4	3.1	-	-	3.0	1.0	-	-
"	N	N	14.7	6.7	23.1	32.9	20.5	8.8	60.0	112.6
Hyperthyroidism	N	N	40.1	17.2	36.2	-	29.7	11.3	28.9	-
Hypothyroidism (untreated)	C	C	0.0	1.0	18.6	-	0.0	0.3	8.1	-
"	C	C	3.2	1.6	2.8	31.4	1.5	0.6	0.5	39.2
Hypothyroidism (treated)	C	N	13.0	-	11.8	25.7	9.6	-	8.6	27.9

continued

TABLE XII - continued

Diagnosis	Bowel Habit*		Motor Activity (%)				Motility Index			
	Usual	At study	Rest	Emotion	Food	Prostig-mine	Rest	Emotion	Food	Prostig-mine
Diverticulitis of the colon	D	N	16.7	47.9	18.8	38.9	8.1	23.4	9.2	29.5
"	CD	N	20.2	54.5	39.3	-	9.3	36.3	24.6	-
Chronic purgation	CD	D	3.9	2.1	7.4	48.1	0.9	0.5	1.7	18.6
Uretero-colic anastomosis	D	D	4.3	14.1	18.7	61.3	1.1	7.6	9.7	69.2
Alcoholism, peripheral neuropathy	D	D	2.9	12.3	5.3	8.1	2.0	6.4	4.2	3.2
Systemic mastocytosis	D	D	0.4	-	2.0	10.5	0.1	-	0.3	10.6
"	D	D	0.0	-	0.4	5.7	0.0	-	0.1	2.9
Gastric ulcer	N	N	0.0	0.0	0.0	21.9	0.0	0.0	0.0	15.3
Scleroderma	N	N	3.2	10.5	18.1	22.5	1.7	6.2	16.3	11.8
Infective diarrhoea	N	D	2.8	12.6	16.7	-	1.2	4.5	7.6	-
Acquired megacolon	C	C	0.0	2.1	0.8	22.3	0.0	0.5	0.2	5.3
"	C	C	0.3	-	3.2	15.1	0.1	-	0.8	4.3
Diabetic diarrhoea	D	D	0.3	14.0	7.3	25.0	0.1	3.3	1.9	16.2
Aperient-induced diarrhoea	N	D	3.6	8.0	16.9	-	0.9	5.1	5.5	-

*Symbols: C = constipation

D = diarrhoea

N = normal bowel habit

CD = alternating constipation and diarrhoea

TABLE XII - continued

Case	Mean Amplitude (mm. Hg.)				Mean Duration (seconds)			
	Rest	Emotion	Food	Prostigmine	Rest	Emotion	Food	Prostigmine
33	5.7	4.9	3.4	8.3	16.5	12.8	13.5	18.7
68	3.7	8.2	5.7	5.9	15.5	14.0	13.8	16.1
69	8.8	13.1	13.0	24.0	17.2	19.3	19.1	20.5
70	0.0	0.0	-	-	0.0	0.0	-	-
71	4.0	0.0	4.3	15.2	20.5	0.0	21.0	22.4
72	3.0	10.4	4.7	4.1	9.0	17.2	14.4	13.4
73	13.1	12.3	13.2	12.6	16.9	19.0	17.2	17.1
74	9.5	7.8	12.9	7.0	24.6	25.2	26.8	15.6
75	11.6	17.4	16.3	-	19.1	18.6	20.7	-
76	2.3	15.5	16.4	21.2	10.3	41.6	21.6	17.8
8	17.8	13.9	11.0	14.6	19.7	21.2	16.8	19.9
9	7.0	7.0	8.2	19.1	17.8	18.1	18.2	20.7
13	5.5	7.3	-	-	10.5	12.6	-	-
26	24.0	22.3	39.8	52.6	17.6	18.8	18.1	16.6
77	11.0	10.5	11.7	-	13.8	14.3	14.0	-
78	0.0	5.0	5.3	-	0.0	17.5	17.0	-
79	7.4	4.7	2.8	17.1	21.9	13.3	11.5	20.4
"	8.7	-	9.5	15.0	13.0	-	12.3	15.3

TABLE XII - continued

Case	Mean Amplitude (mm. Hg.) Rest	Emotion	Food	Prostigmine	Mean Duration (seconds) Rest	Emotion	Food	Prostigmine
34	6.6	7.9	7.8	10.3	14.0	15.6	14.7	17.0
80	7.7	10.8	9.6	-	14.8	19.0	19.3	-
30	3.8	3.7	3.6	6.1	14.0	12.5	16.1	14.0
81	3.3	8.4	7.5	14.3	14.3	19.4	22.6	21.6
82	7.8	9.4	11.2	5.6	15.9	20.5	16.8	15.4
83	2.5	-	2.7	13.4	7.0	-	8.4	7.3
"	0.0	-	3.0	8.0	0.0	-	20.0	9.2
84	0.0	0.0	0.0	9.4	0.0	0.0	0.0	18.1
85	10.5	10.3	13.2	7.4	19.3	16.8	12.5	13.5
86	11.1	6.2	8.1	-	14.8	18.9	19.1	-
87	0.0	4.3	4.3	5.2	0.0	25.0	14.3	24.7
"	3.0	-	3.9	4.3	15.0	-	13.5	19.2
88	2.8	5.0	3.8	6.7	5.8	18.8	12.2	14.9
89	4.2	8.4	5.6	-	15.0	17.2	19.3	-

TABLE XIII - Comparison of the percentage motor activity and motility index in control subjects, patients with functional diarrhoea and patients with diarrhoea due to organic alimentary disease

	Organic Diarrhoea (10 studies)		Functional Diarrhoea (13 studies)		Control (27 studies)	
	Mean	(range)	Mean	(range)	Mean	(range)
Motor Activity (%)						
Rest	1.6	(0.0 - 4.3)	5.7	(0.0 - 16.1)	13.2	(0.9 - 55.6)
Emotion	8.2	(0.0 - 14.1)	9.6	(0.0 - 16.0)	19.9	(2.5 - 60.0)
Food	8.5	(0.4 - 18.7)	9.7	(0.2 - 19.2)	15.4	(0.9 - 62.0)
Prostigmine	23.3	(4.5 - 61.3)	23.1	(2.7 - 50.4)	32.1	(2.2 - 60.4)
Motility Index						
Rest	0.6	(0.0 - 2.0)	2.4	(0.0 - 8.9)	8.6	(0.2 - 38.7)
Emotion	3.6	(0.0 - 7.6)	5.9	(0.0 - 13.8)	18.4	(1.1 - 77.0)
Food	3.5	(0.1 - 9.7)	5.3	(0.0 - 11.6)	15.0	(0.2 - 74.7)
Prostigmine	17.4	(1.4 - 69.2)	17.8	(0.7 - 46.3)	34.0	(0.6 - 94.6)

basis of duration was approximately equal in all three groups of subjects although patients with functional diarrhoea tended to have fewer waves of all durations than either the control subjects or patients with the spastic colon (Figure 35).

Patients with miscellaneous disorders affecting the alimentary tract

The composition of the miscellaneous group is shown in Table II. The majority of the patients had had either constipation or diarrhoea as a result of organic disease, although many of them had normal bowel habits at the time of the present study.

Nine patients in the miscellaneous group had diarrhoea at the time of the intraluminal pressure recording. Table XII shows that these patients had low values for the percentage motor activity and motility index. Table XIII illustrates the values for these two parameters of motility in control subjects, patients with functional diarrhoea and patients with diarrhoea due to various organic alimentary disorders. It can be seen that the motility of the large intestine was reduced to very similar levels in the two latter groups.

Five of the nine patients with organic alimentary disease and diarrhoea at the time of recording had noted definite aggravation of the diarrhoea by emotional tension. The following case history illustrates this point:

> Case 76 was a 36 year old woman whose presenting symptoms were those of colicky, low abdominal pain and intermittent

diarrhoea. Although these symptoms had been present for some years she had lost no weight and was in good general health. She attributed her attacks of diarrhoea to emotional stress, having noticed that even minor degrees of nervous tension would precipitate an attack of diarrhoea. This caused her social embarrassment and led her to seek medical advice. Although she had an aversion for milk, eggs and acid fruits, none of these foods apparently aggravated the diarrhoea.

Physical examination revealed no abnormality and the blood picture, sedimentation rate and barium studies of the small and large intestine were all normal. She was therefore initially thought to be suffering from functional diarrhoea, particularly as psychogenic factors appeared to be important in producing her symptoms. However, three-day collections of faeces showed definite steatorrhoea, the fat excretion being 32 grammes in three days, and 23 grammes in three days on two separate occasions. The absorption of labelled vitamin B_{12} was subnormal as was the absorption of d-xylose. A jejunal biopsy specimen showed subtotal villous atrophy of the mucosa compatible with the diagnosis of idiopathic steatorrhoea.

The motility of the large intestine was studied shortly

Figure 36: The large intestine: the resting pattern of motility (top panel) and response to the emotive interview (lower panel) in a patient with idiopathic steatorrhoea (case 76). Paper speed 0.5 mm. per second. Thus one small square equals ten seconds.

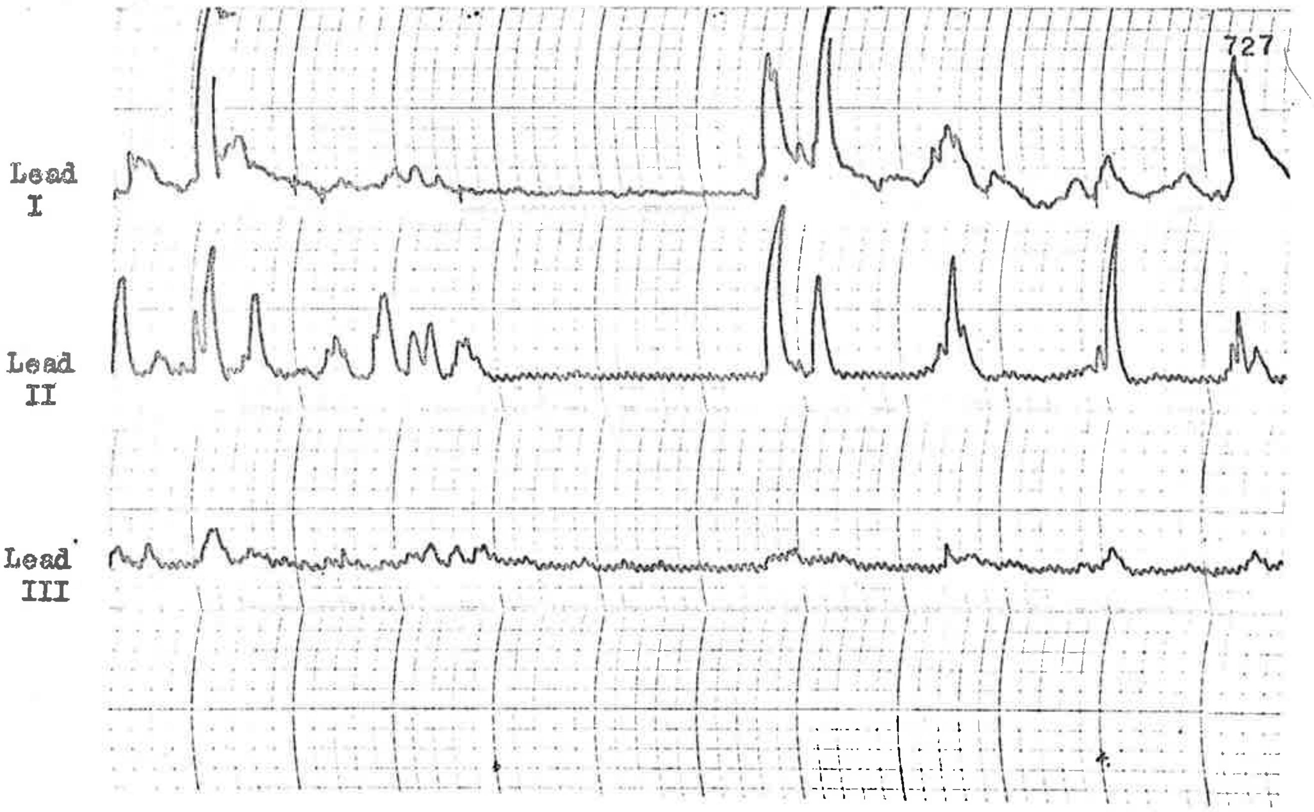


Figure 37: The large intestine: the response to food in the same patient with idiopathic steatorrhoea (case 76). Paper speed 0.5 mm. per second. Thus one small square equals ten seconds.

after an attack of diarrhoea had subsided. The resting pattern of motility (Figure 36) showed few intraluminal pressure changes. During the interview, pressure waves were seen, but their appearance did not correlate well with discussion of any particular topics (Figure 36). The standard meal induced marked motor activity in leads I and II, while lead III, closest to the anus, remained relatively inactive (Figure 37).

Case 81, who had had a uretero-colic anastomosis, provides another example of the absence of intraluminal pressure changes associated with the passage of loose stools. This 48 year old woman had had recurrent papillomata of the bladder with repeated attacks of haematuria. The bladder tumours were fulgurated on 16 separate occasions but kept recurring and finally a total cystectomy with implantation of both ureters into the sigmoid colon was carried out, ten months before the motility tests were done. Immediately after the operation she began to have 20 to 30 semi-solid stools mixed with urine every 24 hours. The frequency of the bowel actions had not diminished by the time she was referred for motility studies. Before the operation her bowels had been normal.
At sigmoidoscopy the ureteric orifices were not seen but the mucosa of the large bowel was hyperaemic and showed

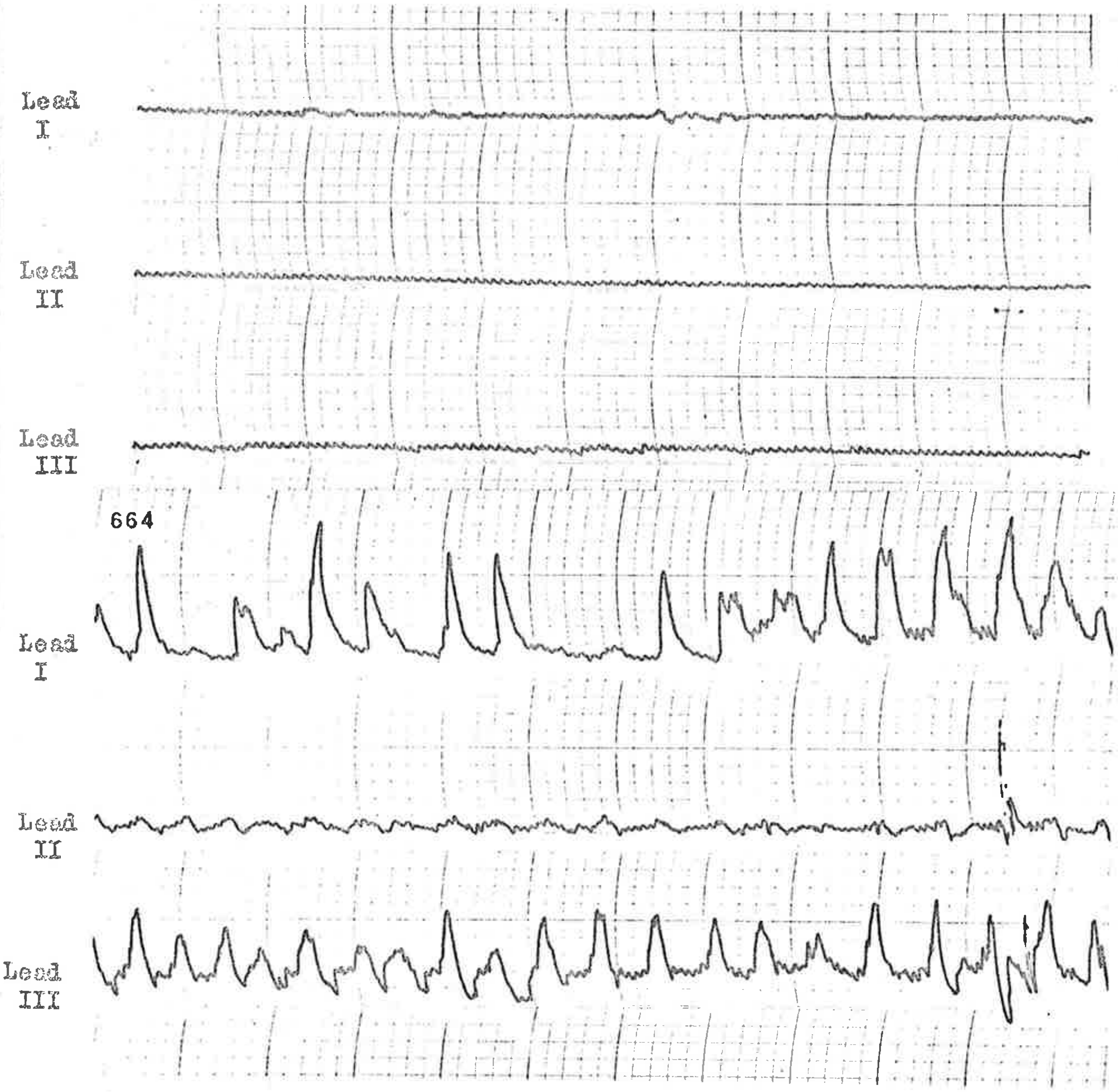


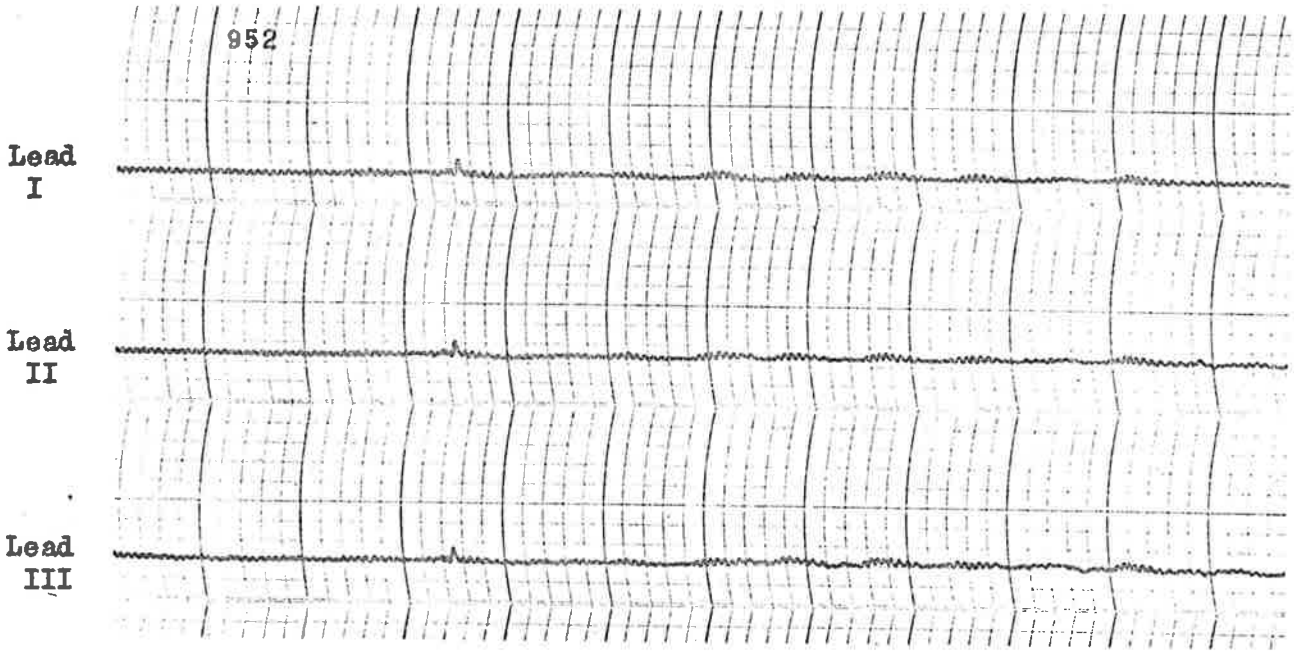
Figure 38: The large intestine: the resting pattern of motility (top panel) and the response to Prostigmine (lower panel) in the patient with implantation of both ureters into the sigmoid colon (case 81). Paper speed 0.5 mm. per second; thus one small square equals ten seconds.

a fine stippled pigmentation. The rectum contained a small amount of mucus, semi-solid faeces and urine. Figure 38 shows the motility tracings done during the resting phase and after Prostigmine. There was almost complete inactivity in all three leads during the resting phase. Prostigmine, however, caused marked motor activity in leads I and III while only small changes in intraluminal pressure were recorded in lead II. The presence of respiratory waves in lead II shows that the middle catheter was not blocked.

Of the patients with organic diarrhoea, this woman had the highest percentage motor activity and motility index during all phases of the recording with the exception of the resting phase (Table XIII). Thus in the patients with diarrhoea from various causes, the closest approximation to normal was found in the patient in whom the passage of loose stools was the result of admixture of faeces with urine.

Three patients with thyroid disorders were studied. Two patients had hypothyroidism and one had hyperthyroidism.

Case 78, with a diagnosis of myxoedema, was a woman of 70 years who gave a twelve month history of fatigue and intolerance to cold. She had also noticed that her face had become puffy and her voice deep and hoarse. She complained of loss of hair and of severe constipation; the latter symptom was the one which had caused her to



<u>Figure 39</u>: The large intestine: the resting pattern of motility in a patient with untreated myxoedema (case 78). Paper speed 0.5 mm. per second. Thus one small square equals ten seconds.

> seek medical advice. She also had chest pain typical of ischaemic heart disease. The myxoedematous facies and the cold, dry, rough skin were striking and the serum level of protein bound iodine was 0.5 µg. per 100 ml. The motility recording was done before treatment with l-thyroxine had been commenced and showed inactivity of the distal large intestine during the resting phase and the interview (Figure 39, Table XII). The response to food was within normal and no Prostigmine was given in view of the symptoms of myocardial ischaemia.

The second patient with hypothyroidism was studied both before and after treatment:

> This patient (case 79) was a 40 year old woman who had undergone a partial thyroidectomy in 1946 for hyperthyroidism. In 1959 the recurrence of symptoms led to treatment with radio-active iodine. Following this treatment the patient developed symptoms of hypothyroidism and replacement therapy was begun. However, five months before the motility tests were done, she moved interstate and ceased taking the thyroid tablets. She then noticed a gradual onset of lethargy, constipation and a feeling of coldness as well as a coarsening of her skin and hair. Physical examination revealed the features of hypothyroidism and the

serum level of protein bound iodine was 2.1 μg. per 100 ml. Motility tracings were done and repeated after seven months of replacement therapy by which stage the patient was clinically euthyroid. In particular, she had regained the normal use of her bowels. The values for the percentage motor activity and motility index are set out below:

Motor activity (%)	Before treatment	After treatment
Rest	3.2	13.0
Emotion	1.6	-
Food	2.8	11.8
Prostigmine	31.4	25.7
Motility index		
Rest	1.5	9.6
Emotion	0.6	-
Food	0.5	8.6
Prostigmine	39.2	27.9

The figures for the resting phase and the response to food show that the return to a euthyroid state was associated with an increase in motility towards normal. The response to Prostigmine, which before treatment had been of the magnitude seen in control subjects, changed little.

A striking contrast to the motility patterns of the two patients with hypothyroidism was seen in the patient with hyperthyroidism (case 77).

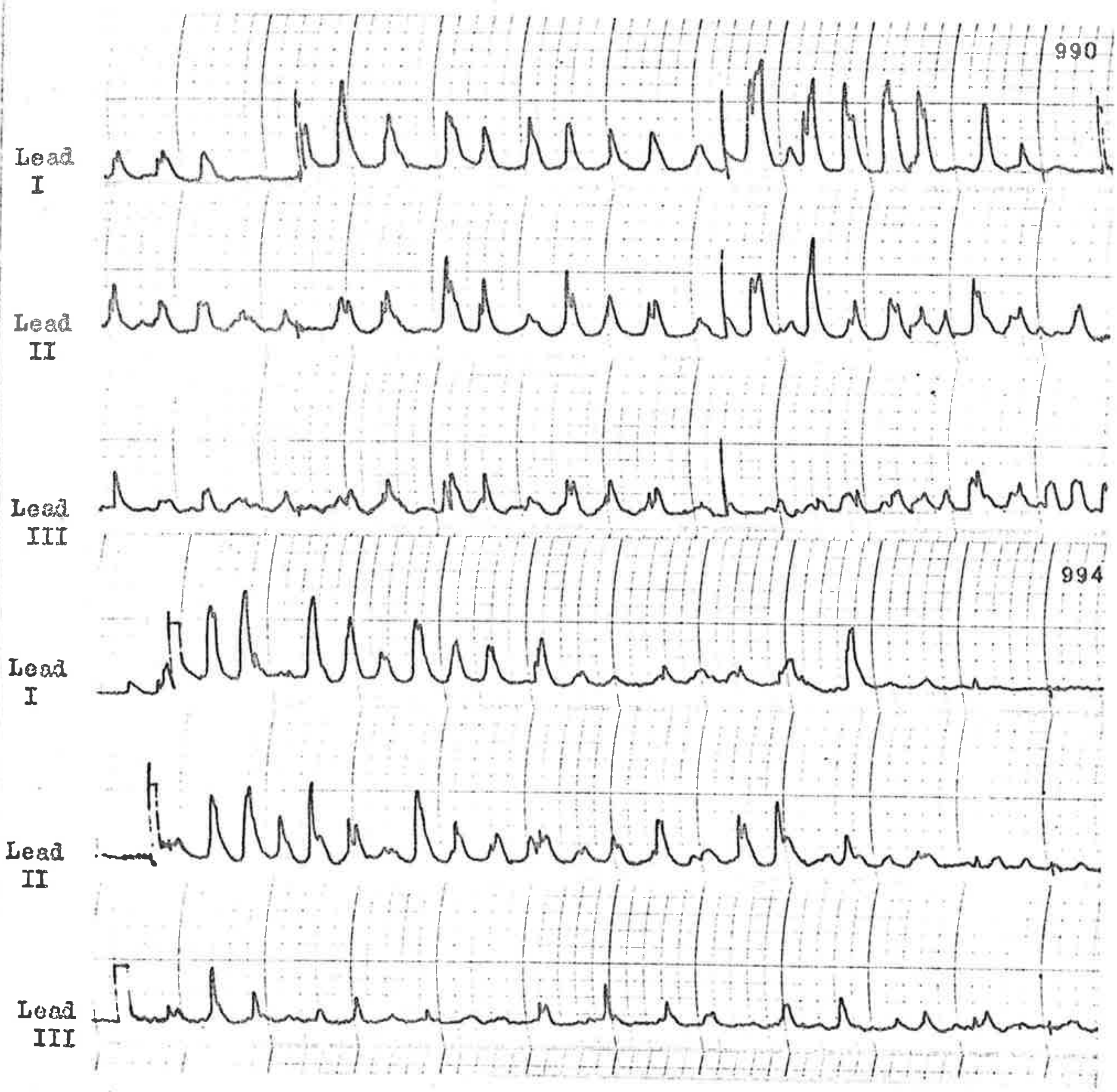


Figure 40: The large intestine: the resting pattern of motility (top panel) and response to food (lower panel) in the patient with untreated hyperthyroidism (case 77). Paper speed 0.5 mm. per second (one small square equals ten seconds).

Case 77 was a 74 year old woman whose presenting symptoms were those of irritability, trembling, muscular weakness and weight loss. Her bowel habits had not altered and she was passing two formed stools a day. When examined she had warm, moist palms, slight tremor of the fingers and tachycardia. There was no exophthalmos or lid retraction and the thyroid gland was not enlarged. Two of her sisters had had toxic goitre. The serum level of protein bound iodine was 11.2 µg. per 100 ml. and radio-active iodine uptake studies confirmed the diagnosis of hyperthyroidism. Figure 40 shows the extremely active pattern of motility during the resting phase. Food did not augment the motor activity.

The effect of treatment in a young boy with acquired megacolon was assessed by repeated motility studies:

Case 87 was a lad of 13 years of age when he was first studied. During a sea voyage from England to Australia at the age of 11 he had become severely constipated. Thereafter he had daily liquid bowel actions with faecal incontinence. A barium enema and a sigmoidoscopy both showed a greatly dilated rectum and sigmoid colon without any narrowed segment to suggest a diagnosis of Hirschsprung's disease. He was unable to appreciate moderate distension of the rectum with air during the sigmoidoscopy.

The effect of daily bowel wash-outs over a period of nine months was negligible:

Motor activity (%)	Before treatment	After treatment
Rest	0.0	0.3
Emotion	2.1	-
Food	0.8	3.2
Prostigmine	22.3	15.1
Motility index		
Rest	0.0	0.1
Emotion	0.5	-
Food	0.2	0.8
Prostigmine	5.3	4.3

During the sigmoidoscopic examination at the second study it was noted that rectal sensation was still deficient and that the large bowel appeared to be as dilated as it had been nine months previously.

Radiotelemetering from the intestine

The radiotelemetering capsule was used in 14 separate studies. Use was made of the radio pill mainly to obtain pressure tracings from the caecum and right colon while simultaneous recordings of the motility of the distal colon and rectum were being made with open ended catheters. Thus the capsule and the catheters were used together in 13 of the 14

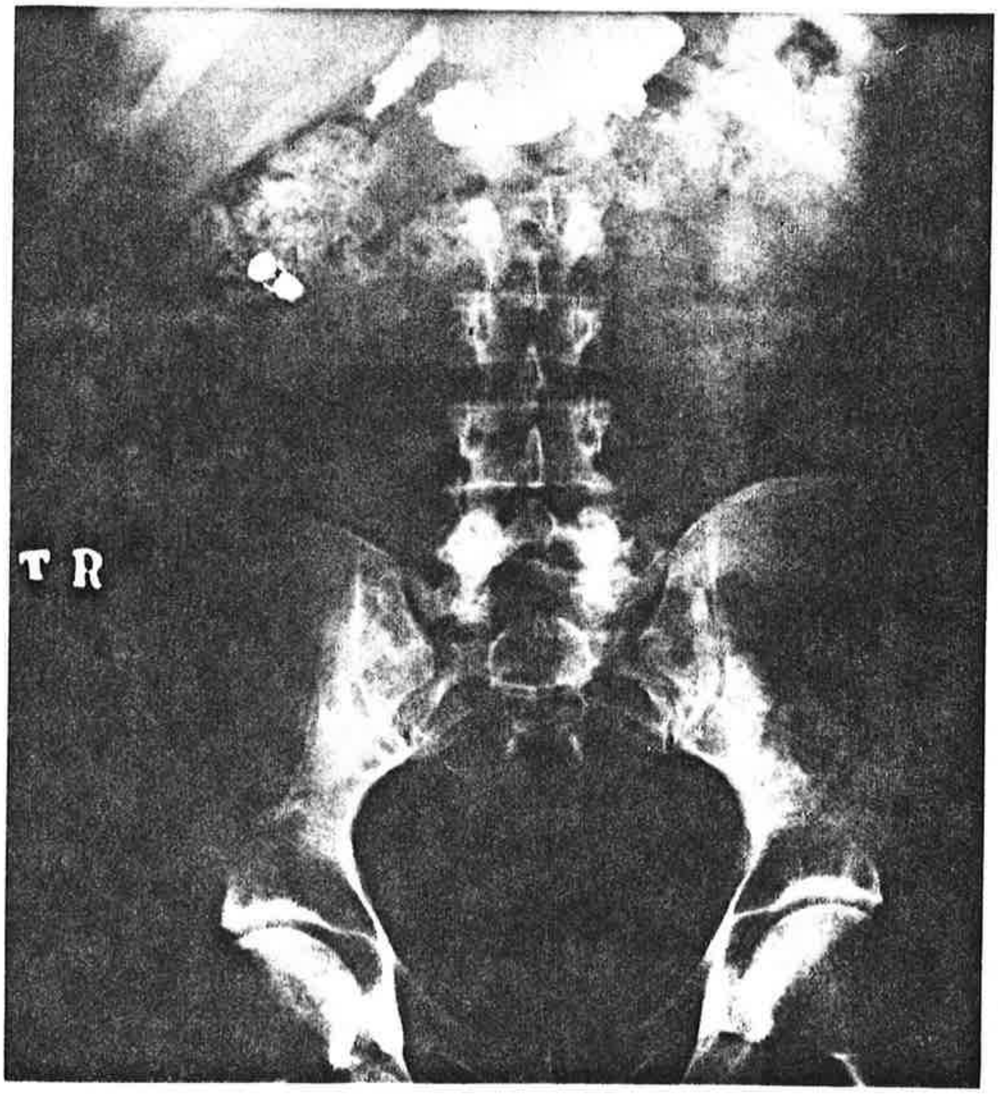


Figure 41 (case 45): The stomach and ascending colon are outlined by barium markers. The radiotelemetering capsule is at the hepatic flexure of the colon.

radiotelemetering studies.

In some cases the patients swallowed the capsule which had been attached to 13 feet of surgical silk. This length of silk was usually found to arrest the pill in the caecum or proximal colon. At other times the pill was swallowed "free" and its progress was followed by intermittent fluoroscopy. A radiograph of the abdomen was taken before the recording was begun to show the position of the capsule in relation to barium markers outlining the stomach and the ileo-caecal region. Figure 41 shows the capsule in the proximal colon.

Radiotelemetering was performed from the following parts of the intestine:

Site	Number of studies
Proximal small intestine	2
Terminal ileum	2
Caecum and proximal colon	6
Distal colon	4

In normal subjects the transit time for the unattached capsule varied from 24 hours to 40 hours. The shortest time of 10 hours occurred in a patient with diarrhoea (case 83). Loss of contact was often observed when the capsule was in the upper small intestine, but it did not occur sufficiently often in the colon to warrant continuous recording of signal strength.

The tracings made with the capsule were in no way different from those obtained with catheters from corresponding parts of the intestine. Radiotelemetered records from the small intestine showed examples of

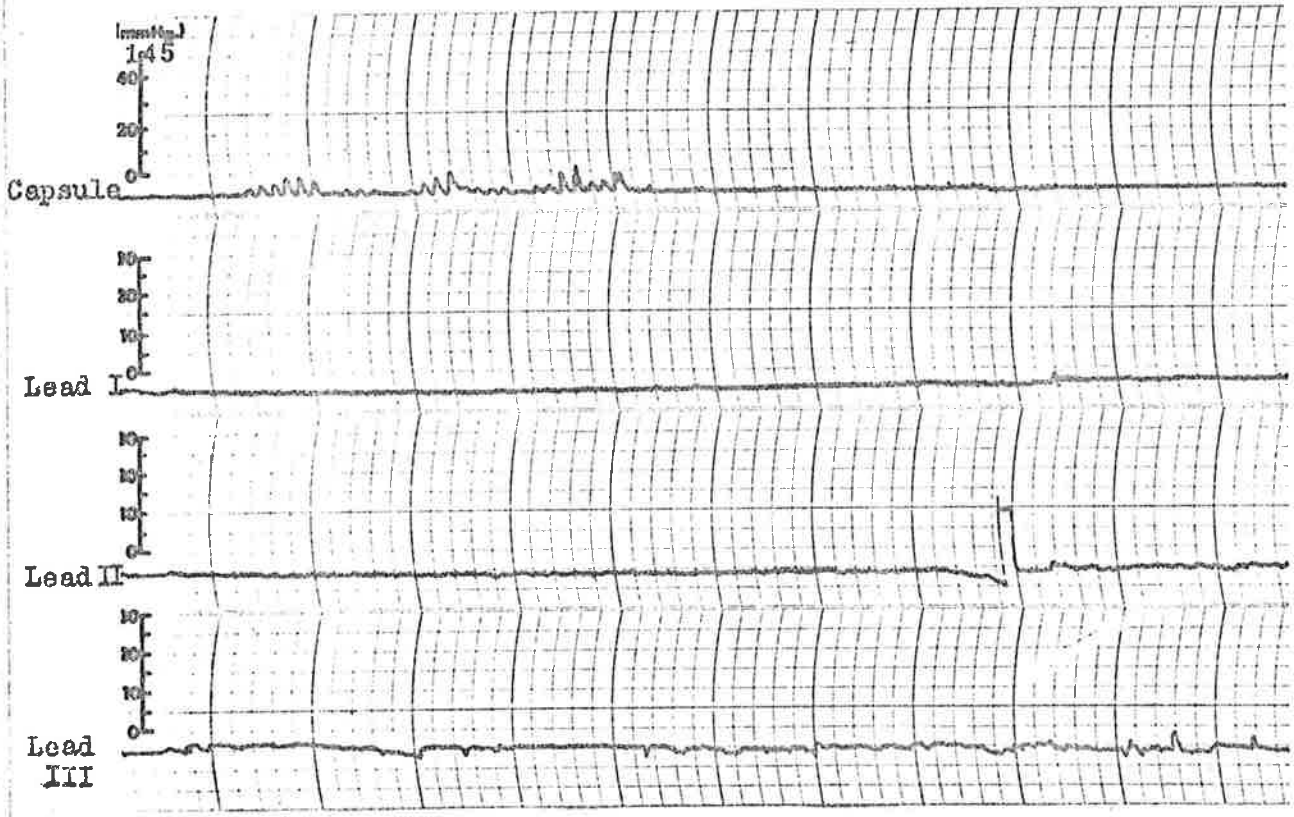


Figure 42: The gastro-colic reflex. Intraluminal pressure changes from the proximal colon (top trace) and sigmoid colon and rectum (three lower traces) recorded simultaneously with the radio-telemetering capsule and catheters. Standard meal given at the beginning of the panel. Re-study of a patient with systemic mastocytosis and diarrhoea (case 83). Note inactivity of distal large intestine characteristic of diarrhoeal states. Paper speed 0.5 mm. per second (one small square equals 10 seconds).

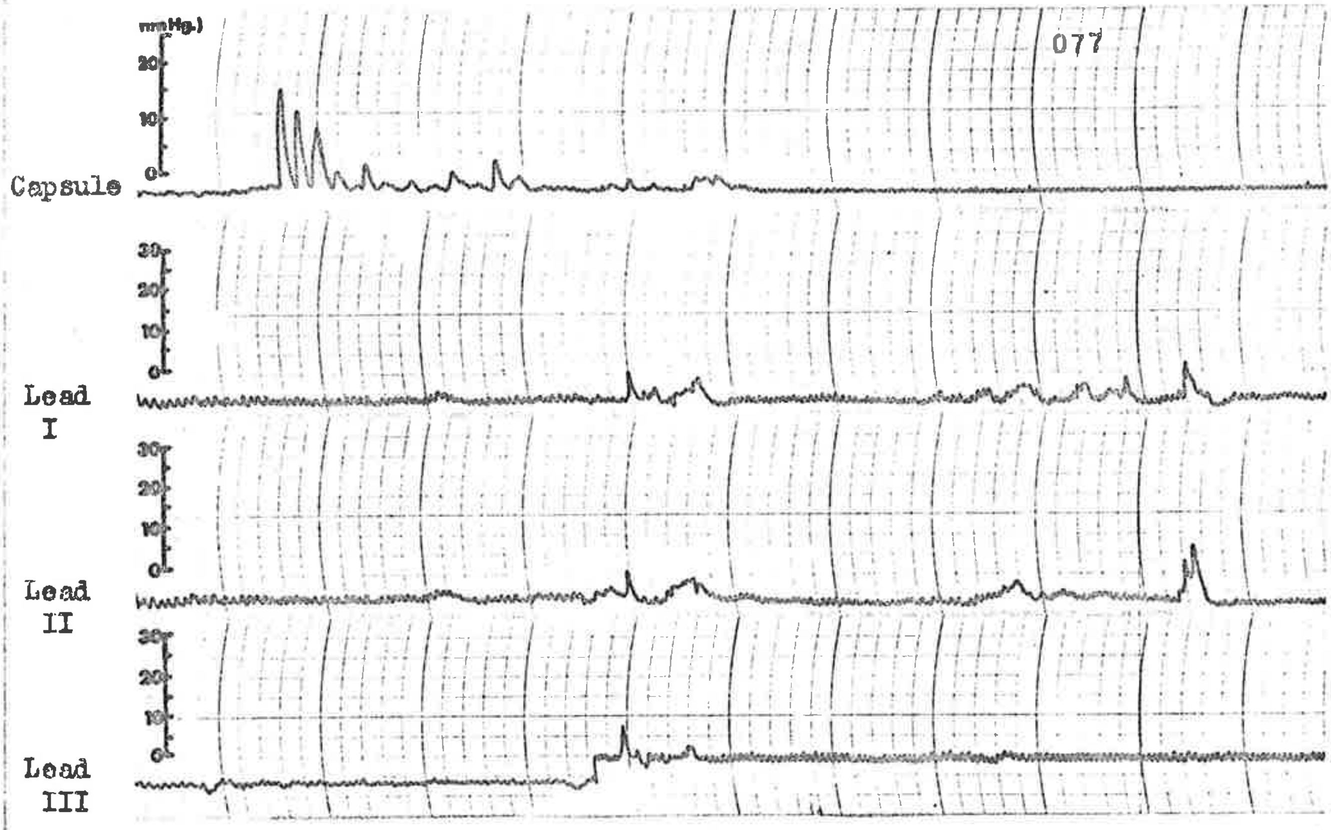


Figure 43: The gastro-colic reflex in a control subject (case 38). Position of radio-pill and catheters as in Figure 42. Standard meal given at beginning of panel. Paper speed 0.5 mm. per second (one small square equals ten seconds).

Table XIV - The percentage motor activity and motility index in 14 radiotelemetering studies

te of psule	Case and (study)	Diagnosis	Bowels at study*	Motor Activity (%) Radio pill (catheters) Rest	Emotion	Food	Prostigmine
oximal mall intestine	67	Functional diarrhoea	D	-	-	-	20.5 (14.4)
"	83 (1)	Systemic mastocytosis	D	8.8 (0.4)	-	18.5 (2.0)	57.1 (10.5)
rminal ileum	35 (1)	Control	N	2.4 (9.3)	3.8 (3.0)	4.6 (2.9	12.9 (11.9)
"	38 (1)	"	N	1.3 (6.2)	2.1 (10.3)	3.3 (15.2)	7.1 (18.1)
oximal colon	35 (2)	"	N	1.7 (0.7)	-	10.1 (8.6)	9.4 (7.8)
"	38 (2)	"	N	5.1 (5.4)	-	7.5 (3.7)	67.4 (2.2)
"	43	"	N	12.6 (25.3)	-	-	-
"	45	"	N	1.1 (55.6)	-	-	-
"	74	Steatorrhoea	C	3.2 (21.6)	1.3 (33.3)	3.3 (33.7)	15.6 (45.0)
"	83 (2)	Systemic mastocytosis	D	1.7 (0.0)	-	6.7 (0.4)	14.8 (5.7)
stal colon	35 (3)	Control	N	13.8 (3.7)	-	17.9 (8.6)	43.8 (11.9)
"	44 (1)	"	N	21.3 (21.0)	33.8 (9.7)	18.1 (10.5)	55.7 (60.4)
"	44 (2)	"	N	26.0	-	-	-
"	51	"	N	16.2 (0.9)	-	-	-

*Symbols: N = normal

C = constipation

D = diarrhoea

continued

TABLE XIV - continued

Site of Capsule	Case and (Study)	Diagnosis	Bowels at study*	Motility Index Radio pill (catheters) Rest	Emotion	Food	Prostigmine
Proximal small intestine	67	Functional diarrhoea	D	-	-	-	7.5 (9.7)
"	83 (1)	Systemic mastocytosis	D	9.8 (0.1)	-	11.7 (0.3)	46.3 (10.6)
Terminal ileum	35 (1)	Control	N	0.9 (4.0)	1.7 (1.8)	2.5 (0.3)	7.3 (7.8)
"	38 (1)	"	N	0.3 (2.4)	0.4 (3.4)	0.7 (5.8)	1.3 (7.8)
Proximal colon	35 (2)	"	N	0.4 (12.7)	-	1.5 (2.3)	7.3 (7.1)
"	38 (2)	"	N	1.6 (1.7)	-	4.1 (1.4)	25.4 (0.6)
"	43	"	N	5.3 (20.7)	-	-	-
"	45	"	N	0.6 (38.7)	-	-	-
"	74	Steatorrhoea	C	1.0 (14.6)	0.4 (16.1)	1.1 (34.6)	3.7 (22.4)
"	83 (2)	Systemic mastocytosis	D	1.5 (0.0)	-	2.2 (0.1)	11.5 (2.9)
Distal colon	35 (3)	Control	N	9.7 (1.0)	-	14.5 (4.1)	69.8 (6.7)
"	44 (1)	"	N	16.2 (15.7)	27.8 (4.7)	9.7 (5.2)	44.5 (40.4)
"	44 (2)	"	N	21.9	-	-	-
"	51	"	N	41.9 (0.2)	-	-	-

type I and type III waves; waves of types I and II were seen in tracings from the colon and rectum. Pressure waves from the caecum and proximal colon were usually of shorter duration than those observed in the distal large intestine. The mean duration of the pressure waves from the caecum and right colon in four control subjects during the resting phase was 10.1 seconds, the corresponding figure for the distal colon and rectum being 19.3 seconds. After food and Prostigmine there was no appreciable difference in the duration of the waves from these sites, the values being 17.8 seconds and 20.2 seconds for the proximal large intestine and 17.3 seconds and 18.3 seconds for the left colon and rectum.

The gastro-colic reflex which had not been recognised in the catheter traces was seen in recordings from the proximal colon (Figures 42 and 43).

Table XIV lists the results of the radiotelemetering studies. The figures in brackets under the headings of "motor activity (%)" and "motility index" represent the results of simultaneous catheter studies of the distal large intestine. Judged by the motility index the control subjects had more activity in the distal colon than the proximal colon during the resting phase while the reverse was true after food and after Prostigmine (studies 35 (2), 38 (2), 43 and 45). In the patient with constipation (case 74) the distal large intestine was more active throughout the recording. By contrast, the patient who had diarrhoea at the time of study (study 83 (2)) had more activity in the proximal

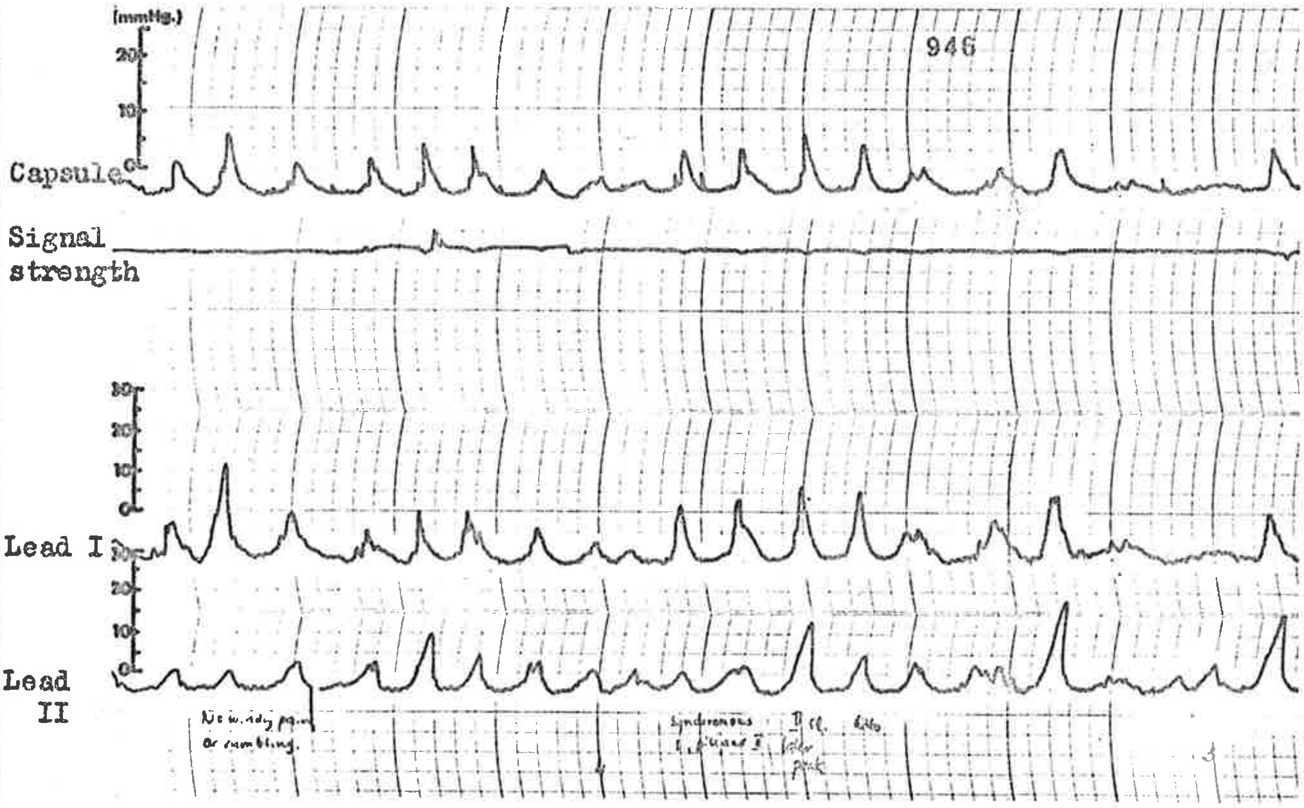


Figure 44: The large intestine: the effect of Prostigmine in a control subject (case 44). Radiotelemetering capsule (first trace) attached to catheter assembly 2.5 cm. below the highest recording tip (third trace) and 4.5 cm. above the intermediate recording tip (fourth trace). Lead I and the trace from capsule are qualitatively similar. The second trace represents the signal strength which remains steady apart from small fluctuations coinciding with the pressure waves. Paper speed 0.5 mm. per second (one small square equals 10 seconds).

TABLE XV - The effect of 5-hydroxytryptamine on the motility of the large intestine in three control subjects

	Motor Activity (%) Radio pill	(catheters)	Motility Index Radio pill	(catheters)
Case 45. Capsule in ascending colon.				
Resting phase I: 30 minutes	1.1	(55.6)	0.6	(38.7)
Resting phase II: "	5.1	(56.7)	2.1	(49.7
5-hydroxytryptamine I: 0* to 20 minutes	33.1	(10.0)	12.6	(6.6)
5-hydroxytryptamine II: 20 to 40 minutes	24.8	(30.0)	12.7	(19.7)
Case 43. Capsule in caecum.				
Resting phase = 48 minutes	12.6	(25.3)	5.3	(20.7)
5-hydroxytryptamine : 0 to 14 minutes	8.5	(22.3)	3.3	(13.7)
Case 51. Capsule in left transverse colon.				
Resting phase: 30 minutes	16.2	(0.9)	41.9	(0.2)
5-hydroxytryptamine: 0 to 12 minutes	0.0	(0.0)	0.0	(0.0)

* "O" denotes start of infusion.

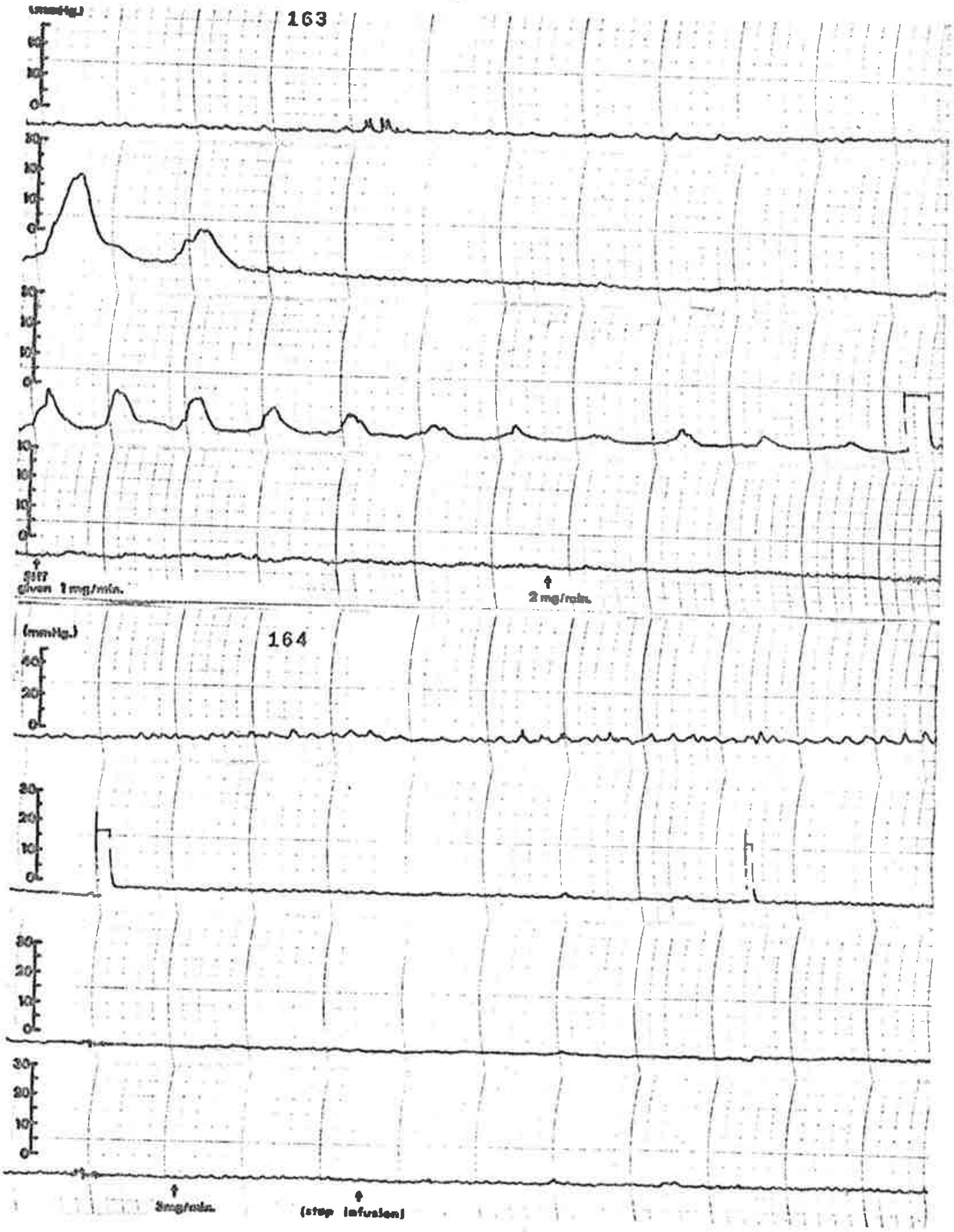


Figure 45: The large intestine: the effect of 5-hydroxytryptamine in a control subject (case 45). Paper speed 1 mm. per second (one small square equals five seconds. Tracing continued in Figure 46.

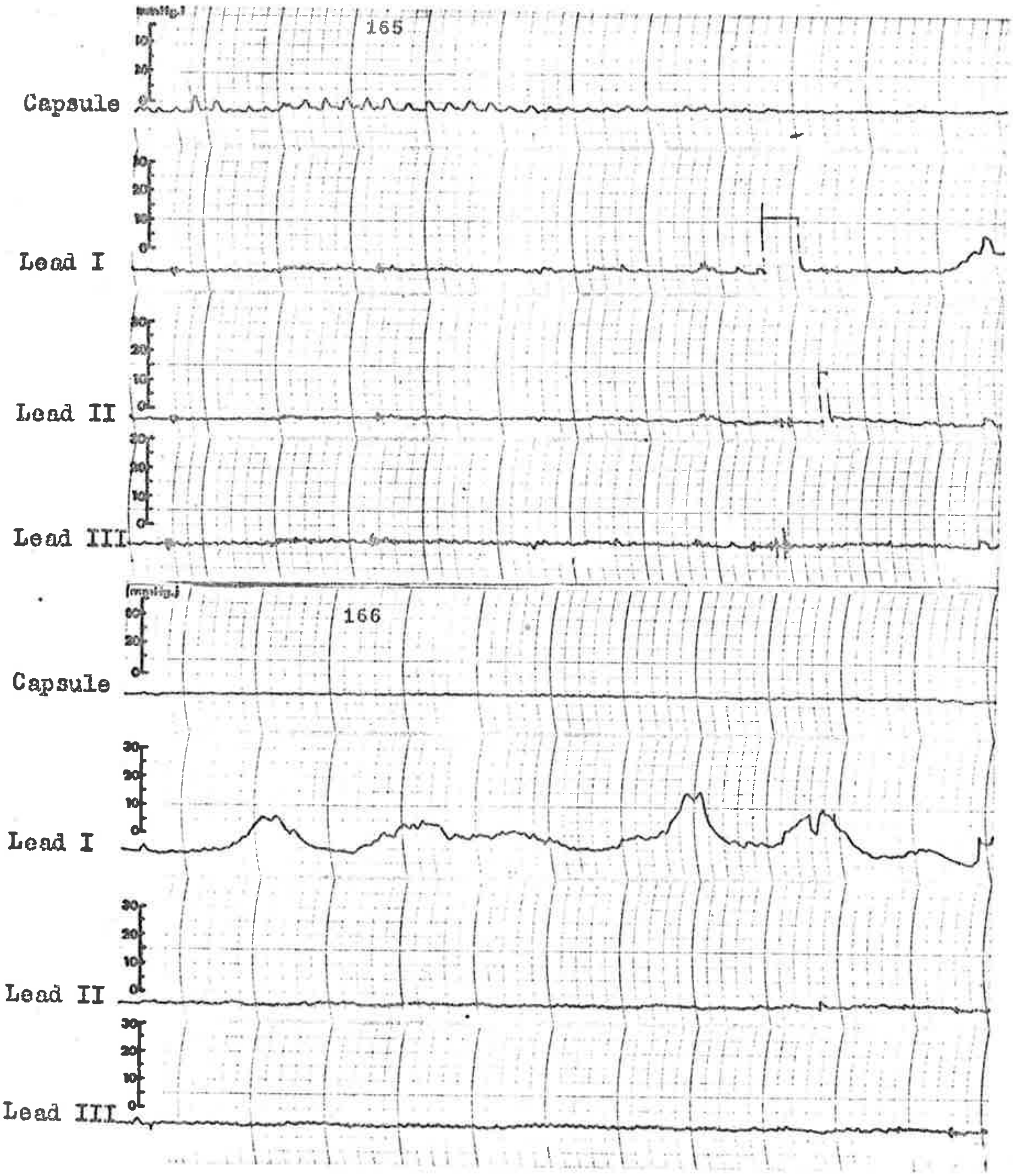


Figure 46: The large intestine: the effect of 5-hydroxytryptamine in a control subject (case 45). Tracing continued from Figure 45. Paper speed 1 mm. per second (one small square equals five seconds).

colon than in the distal colon and rectum.

A comparison of the traces obtained with the pill and the catheters was made in study 44 (1). The pill was tied to the catheter assembly 2.5 cm. below the highest recording tip. The resultant tracing showed that the wave forms in lead I and in the trace from the capsule were identical (Figure 44). However, the waves recorded by the capsule were not as high as those in lead I although they were higher than those in lead II.

The effect of systemic 5-hydroxytryptamine on the motility of the large intestine was investigated in three studies (cases 43, 45 and 51) (Table XV). The resting pattern of motility was first recorded and after an intravenous injection of normal saline 5-hydroxytryptamine was infused at the rates of 1 mg. per minute for three minutes, 2 mg. per minute for two minutes and 3 mg. per minute for one minute. Table XV shows that case 45, in whom the unattached capsule remained in the proximal large intestine throughout the experiment, responded to the drug with augmented motility of the proximal colon and diminished motility of the distal colon and rectum. Figures 45 and 46 show that in this subject the effect of 5-hydroxytryptamine on the distal large intestine began almost immediately and lasted for approximately seven and one-half minutes after the infusion had been stopped. The response of the proximal colon appeared later but lasted for the same length of time. The subject experienced a feeling of warmth in the arm used for the infusion but had no other symptoms.

Case 43 complained of faintness and became pale with a rapid "thready" pulse as soon as 0.5 mg. of the drug had been administered. There were no abdominal symptoms. Two further attempts produced the same reaction and the experiment was abandoned. Table XV shows that the dose of 5-hydroxytryptamine used had no definite effect on motility.

In the third subject (case 51) the capsule was initially in the ascending colon and its position was verified radiologically. However, shortly after the recording of the resting pattern had commenced the capsule moved to the left side of the transverse colon and remained there until the conclusion of the experiment. In this subject, as expected, the activity recorded both by the capsule and by the catheters decreased in response to 5-hydroxytryptamine administered at the same rate as in case 45 (Table XV).

Thus the motility of the distal large intestine was reduced or abolished in both the experiments in which a total dose of 10 mg. of 5-hydroxytryptamine was infused over a time of 5 minutes. The proximal large intestine responded by augmented motility in one technically satisfactory study.

Cineradiography of the Intestine

Cineradiographic studies were performed on 41 patients and combined with simultaneous manometric recordings in all but 2 instances. The results of the cine films were more difficult to express than the results of manometric studies as they could not be quantatively analysed. Static pictures are not well suited to express a dynamic process such as the movements of the small intestine. However, an attempt was made to overcome this problem by arranging serial cine frames to illustrate a particular event. Nevertheless, it is appreciated that this procedure does not adequately communicate the rapidity and complexity of the events in the small intestine.

It would not be possible to describe each cineradiographic study separately. Therefore, the results will be given in the form of general comments and as a more detailed description of representative studies.

General remarks

The alternation of activity and quiescence which was a feature of pressure tracings from the small and the large intestine was reflected in the cineradiographic appearances. The inactivity was particularly marked in the distal large intestine which at times had to be stimulated with Prostigmine so that combined manometric and X-ray studies could be performed. The small intestine was rarely quiescent for more than two or three minutes at a time.

In the small intestine it was not possible on the radiographic appearances to distinguish waves of type III from a series of type I waves. In particular, the presence or absence of propulsion did not serve to separate these two wave types from each other. However, single type I waves could be recognised because they were of shorter duration and caused less propulsion than waves of type III. The segmenting movements (type I waves) were almost invariably associated with some degree of transport of the contrast medium which was usually propelled 3 to 5 centimetres in either direction. However, since the segmenting contractions were generally most frequent in the upper small intestine the net movement of the contrast medium was in an aborad direction. On occasions the contrast medium was seen to move 10 to 20 centimetres in a distal direction in one second. At such speeds the velocity effect would not be sufficiently great to impair the accuracy of the intraluminal pressure recordings from the catheters*. Classical peristalsis consisting of a wave of relaxation preceding a slowly progressive contraction was not observed.

Gastric emptying appeared to be largely governed by gravity in patients who had had the Polya operation. No obvious differences were

---

*The velocity effect resulting from the flow of intestinal contents would depend on the rate of the flow and on the orientation of the recording ports in relation to the direction of the flow. The maximum positive or negative effect on a single port could not exceed a full pressure head ($\frac{v^2}{2g}$, where v = velocity of flow). The accuracy of the pressure recordings from the small intestine would therefore not be significantly impaired as each recording tip had three separate ports. (R. Culver, personal communication.)

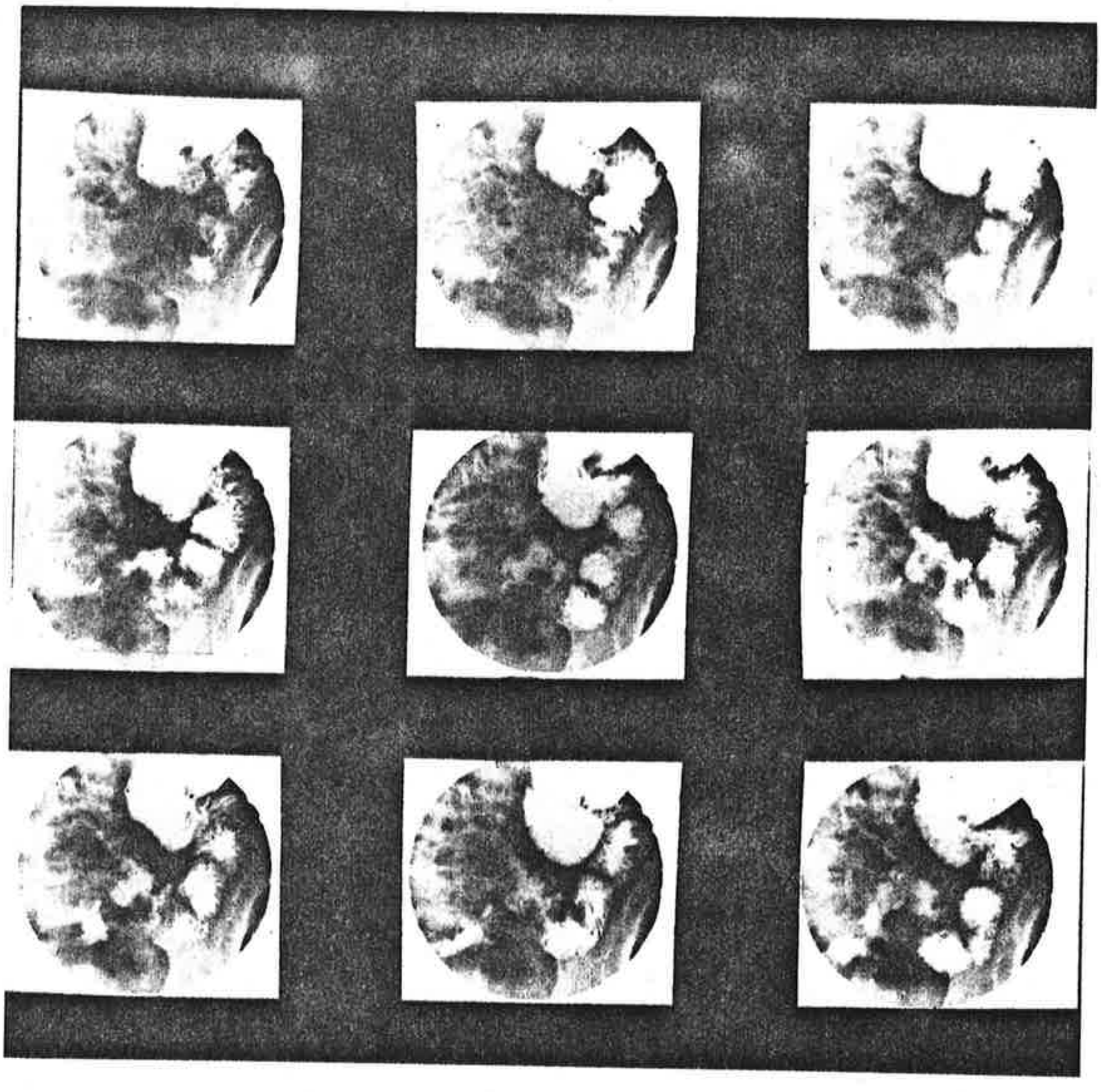
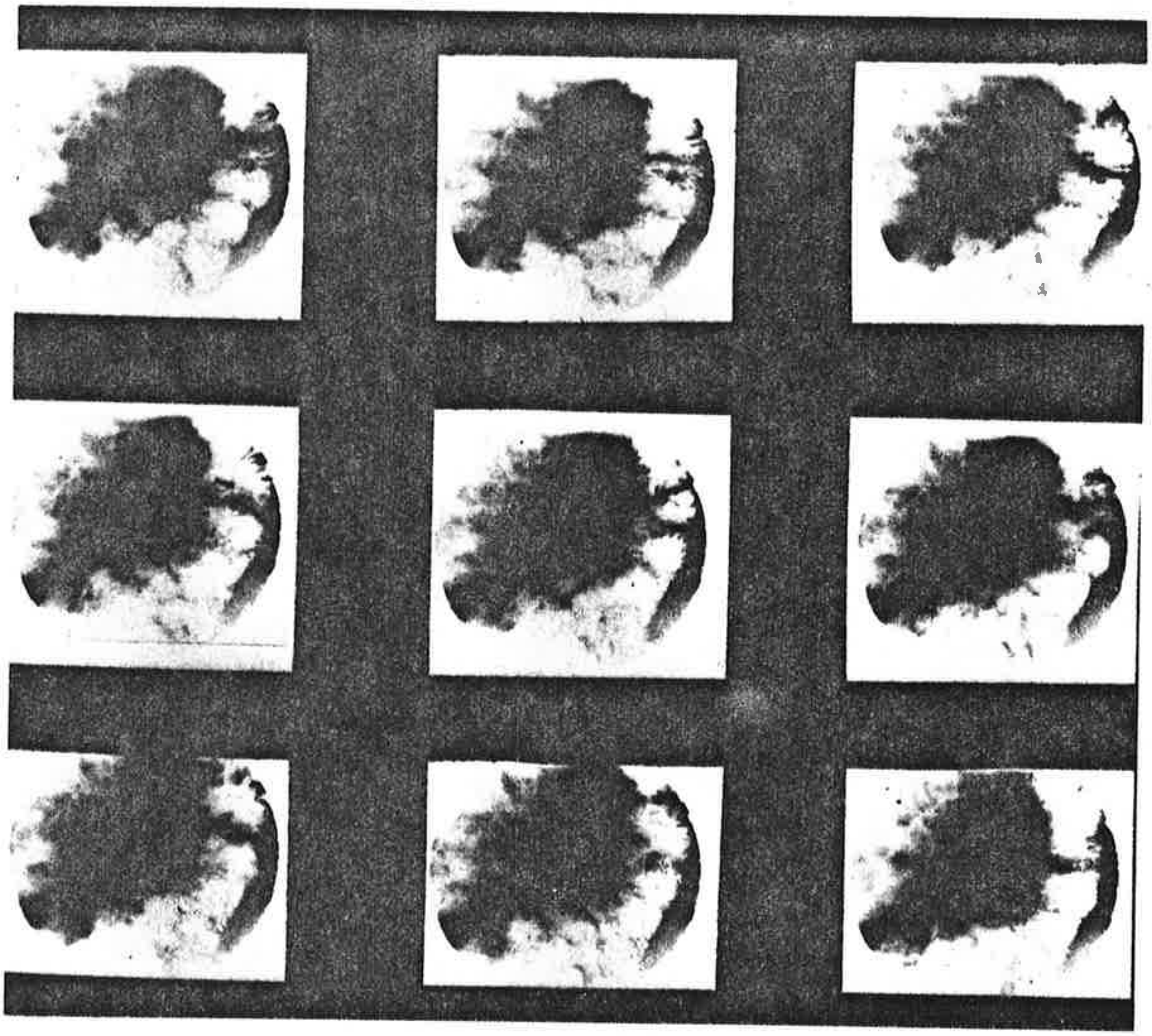


Figure 47: The small intestine. Frames taken at four-second intervals from the cine film from a patient who had undergone a Polya type partial gastrectomy and in whom symptoms of "dumping" were not induced (case 19). In this and in all subsequent reproductions of the cine films the sequence begins in the top left hand corner and should be read from left to right in the same manner as printed text.
The gastric remnant and the efferent loop are outlined. There is rapid progress of the contrast medium through the upper small intestine; the afferent loop has not filled.



<u>Figure 48</u>: The small intestine. Frames taken at four-second intervals from the cine film from a patient who had had a Polya type partial gastrectomy (case 12). In this patient the standard meal provoked an attack of "dumping". The film was exposed at the end of the attack when the symptoms had subsided largely but not completely. Only the efferent loop is shown. Motor activity is present although not to the same extent as in Figure 47, the small intestine appears dilated and its markings are indistinct.

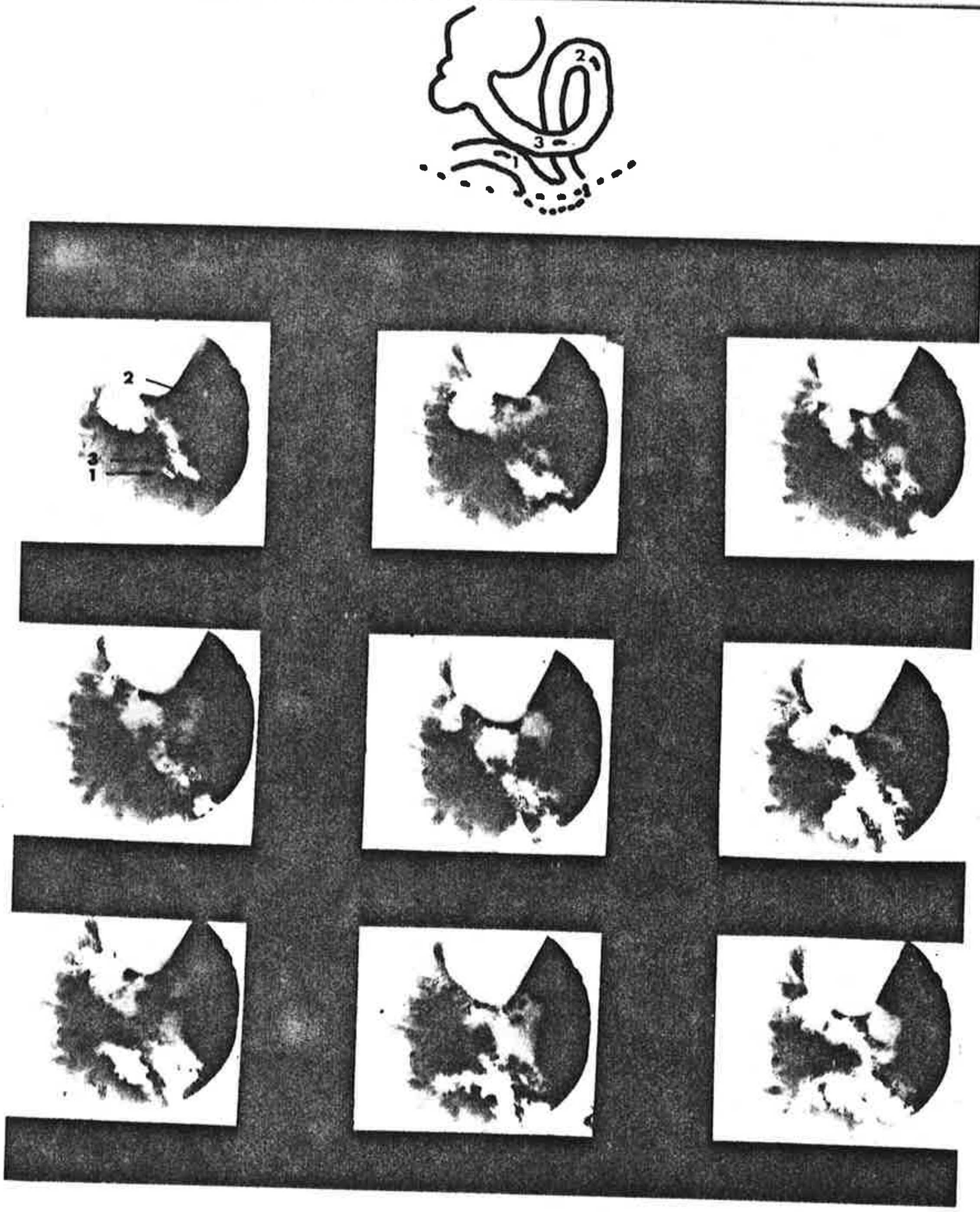
observed between the appearances of the contractions of the small intestine in the control subjects and in the patients after partial gastrectomy. However, in the absence of symptoms of "dumping" the movements of the small intestine were more pronounced in the patients after gastrectomy than in the control subjects. Patients with a Polya type of anastomosis appeared to have more activity in the cine films than patients who had undergone the Billroth I operation. When cineradiography was performed during symptoms of "dumping" contractions of the small intestine were few. In one instance virtually complete quiescence and "pooling" of the contrast in the small intestine occurred. Figure 47 illustrates the radiological appearances in one patient with the Polya type of anastomosis who did not have the dumping syndrome. Figure 48 is a sequence from one patient after the Polya operation in whom the cine film was exposed at the end of an attack of "dumping"; the degree of motor activity is obviously less than in the first patient. However, amongst the patients with the Polya anastomosis no difference in the radiological appearances of the small intestine was evident between patients who had not experienced the dumping syndrome and those who had, as long as symptoms of "dumping" were not actually present when the film was exposed.

With regard to the colon and rectum, the observed contractions were far more infrequent than was the case in the upper small intestine. The movements were also slower and did not cause major alterations in the outline of the viscus. The presence of propulsion was difficult to judge because the contrast medium when injected through the catheter furthest away from the anus tended to run down and fill the rectum. Thus the viscus very quickly became completely outlined by the barium suspension so that analward propulsion could not be distinguished. Nevertheless, the impression gained was that contractions of the rectum and lower sigmoid colon caused little movement of the contrast medium.

Correlation of pressure traces and cine films from the small intestine

All major movements which were observed in the cine films in the vicinity of the recording tips were represented by pressure waves in the corresponding leads of the manometric tracings. The reverse was also true; all pressure waves had their radiological counterparts. However, because of the complexity of the radiologically observed movements and because of the frequent overlapping of loops of the small intestine minor alterations in the outline of the viscus could have escaped detection. These minor contractions could have occurred while the pressure trace remained inactive and thus it would not be correct to state that there was complete agreement between the manometric and the cineradiographic representations of motility.

The height of the intraluminal pressure during a contraction did not necessarily correlate with the degree of narrowing of the lumen of the small intestine. However, high pressure waves were associated with more marked transport of the contrast medium than waves of low amplitude.



<u>Figure 49</u>: The small intestine. Frames taken at one-second and two-second intervals from the cine film from a patient without the dumping syndrome after the Polya type partial gastrectomy (case 20). The line drawing and the arrows in frame 1 show the position of the recording tips in the upper small intestine.
The corresponding pressure tracing is illustrated in Figure 50 and the correlative analysis is detailed in the text.

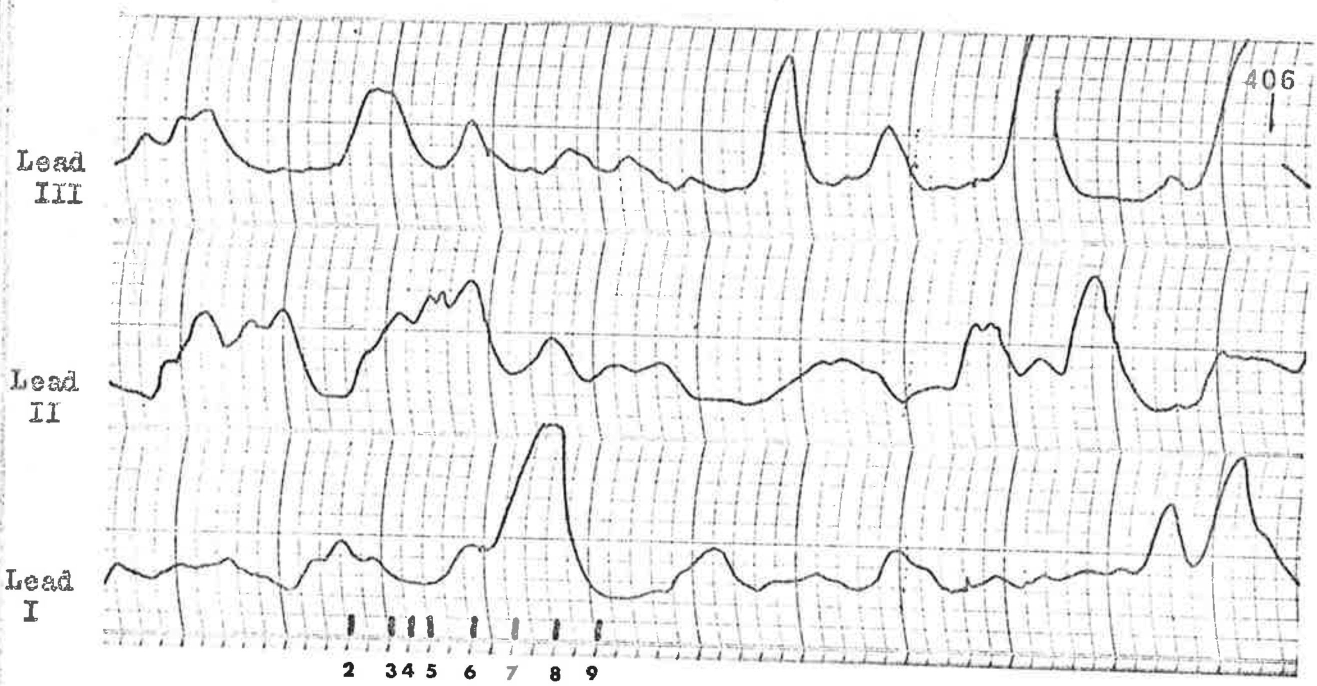


Figure 50: The small intestine. The pressure tracing recorded simultaneously with the cine sequence in Figure 49. The numbers beneath the panel indicate the position of the cine frames in relation to the pressure tracing. Frame 1 is not represented on this panel as it was taken from the beginning of the cine film to show the location of the recording tips. The correlation of the pressure record and cine sequence is described in the text. Paper speed 5 mm. per second (one small square equals one second).

Propulsion of intestinal contents was observed both in association with type I activity occurring independently in one lead and with waves appearing in two or more leads with a progressive delay. Figures 49 and 50 illustrate the latter phenomenon. The events are as follows:

frame 1 shows the location of the recording tips and is not represented in the pressure record;

frames 2 and 3 show a small amount of contrast medium being transported from the third to the second recording tip; this movement coincides with a wave in lead III;

frames 4, 5 and 6 show that the movement of contrast continues and the bolus is swept past the second recording tip; a wave is recorded in lead II; in frame 5 another bolus is entering the lower part of the field and travels towards the first recording tip in frame 6; the intraluminal pressure begins to rise in lead I;

frames 7 and 8 show a contraction with a change in the outline of the intestine over the first recording tip corresponding to the peak of the wave in lead I;

in frame 9 part of the contrast medium has passed the first recording tip and the intestine has relaxed; the wave in lead I is complete.

However, a progressive delay in the appearance of the pressure waves did not necessarily imply propulsion of intestinal contents.

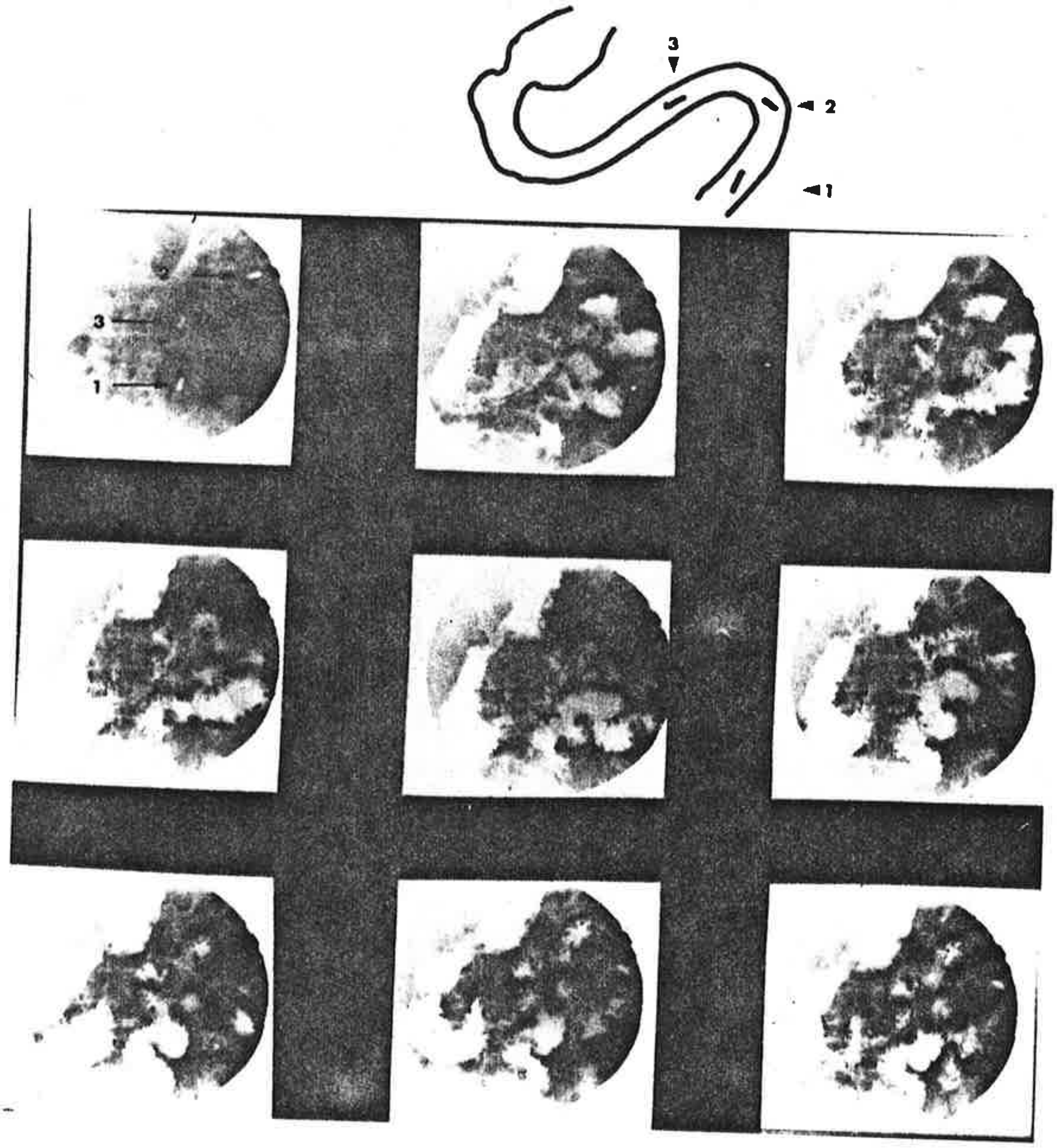


Figure 51: The small intestine. Frames taken at one-second and two-second intervals from the cine film from a patient with the dumping syndrome after the Billroth I type partial gastrectomy (case 10). This patient had recovered completely from an attack of "dumping" by the time the film was exposed. The line drawing and the arrows in frame 1 show the position of the recording tips in the upper small intestine.
This figure corresponds in time to the first series of numbers beneath the pressure tracing illustrated in Figure 52. The correlative analysis is detailed in the text.

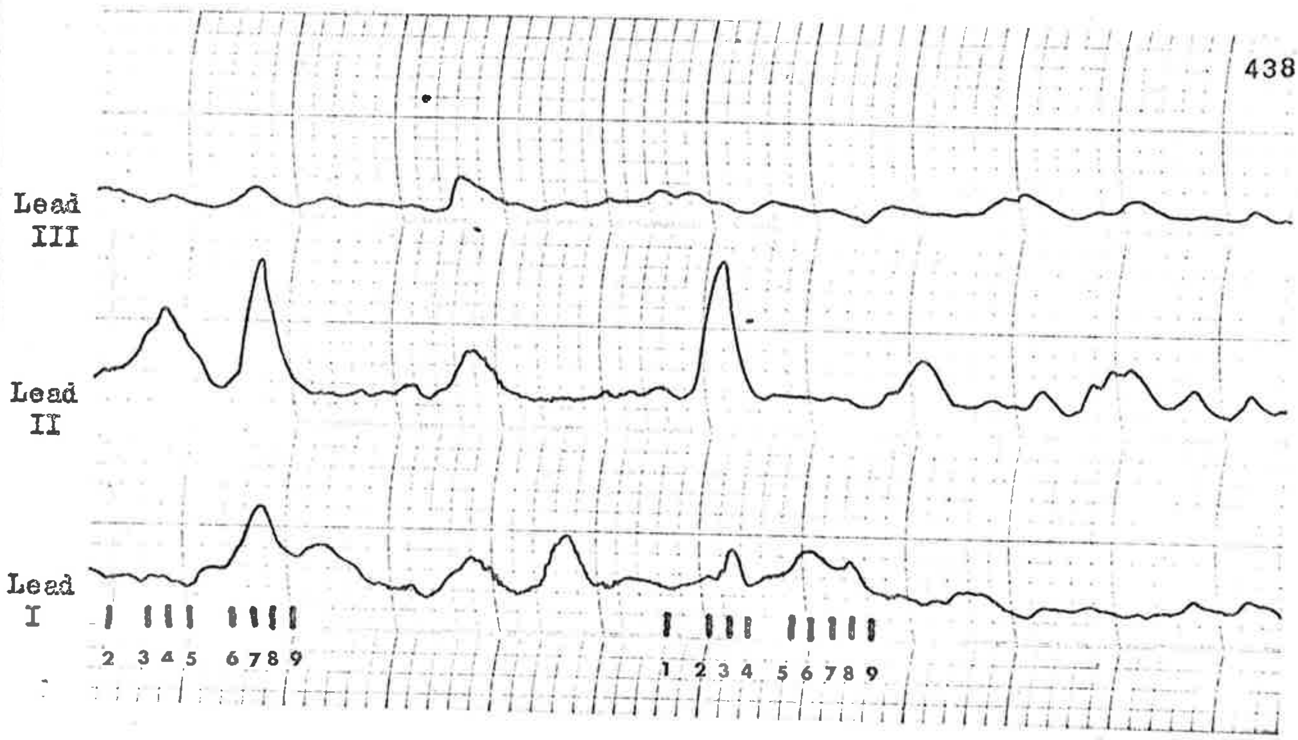
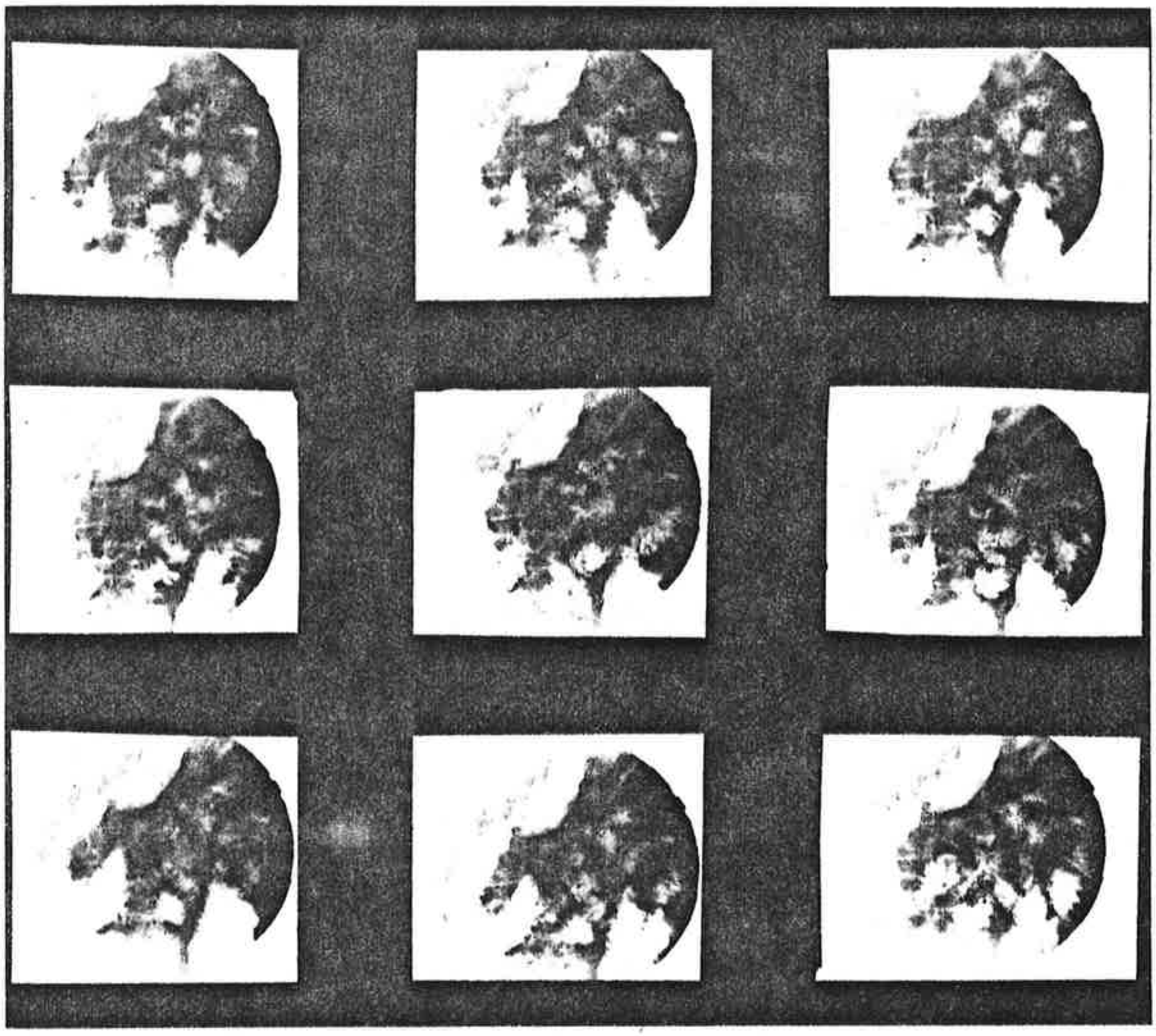


Figure 52: The small intestine. Pressure tracing done during the exposure of the cine film in a patient after partial gastrectomy (case 10).
The first series of numbers beneath the panel indicate the position of the cine frames of Figure 51 in relation to the pressure tracing. Frame 1 was taken to show the location of the recording tips and is not represented on this panel.
The second series of numbers indicate the position of the cine frames of Figure 53 in relation to the pressure tracing.
Paper speed 5 mm. per second (one small square equals one second).



<u>Figure 53</u>: The small intestine. Frames taken at one second and two-second intervals from the same patient as in the two preceding figures (case 10).
This figure corresponds in time to the second series of numbers beneath the pressure tracing illustrated in Figure 52. The correlation of the cine sequence and the pressure record is described in the text.

Figures 51 and 52 illustrate this point:

frame 1 shows the location of the three recording tips and is not represented in the pressure tracing - in fact the second recording tip was slightly lower when the cine film was exposed as shown in frame 9;

there is little activity in the vicinity of the third recording tip in frames 2 to 9 and, correspondingly, no pressure waves in lead III;

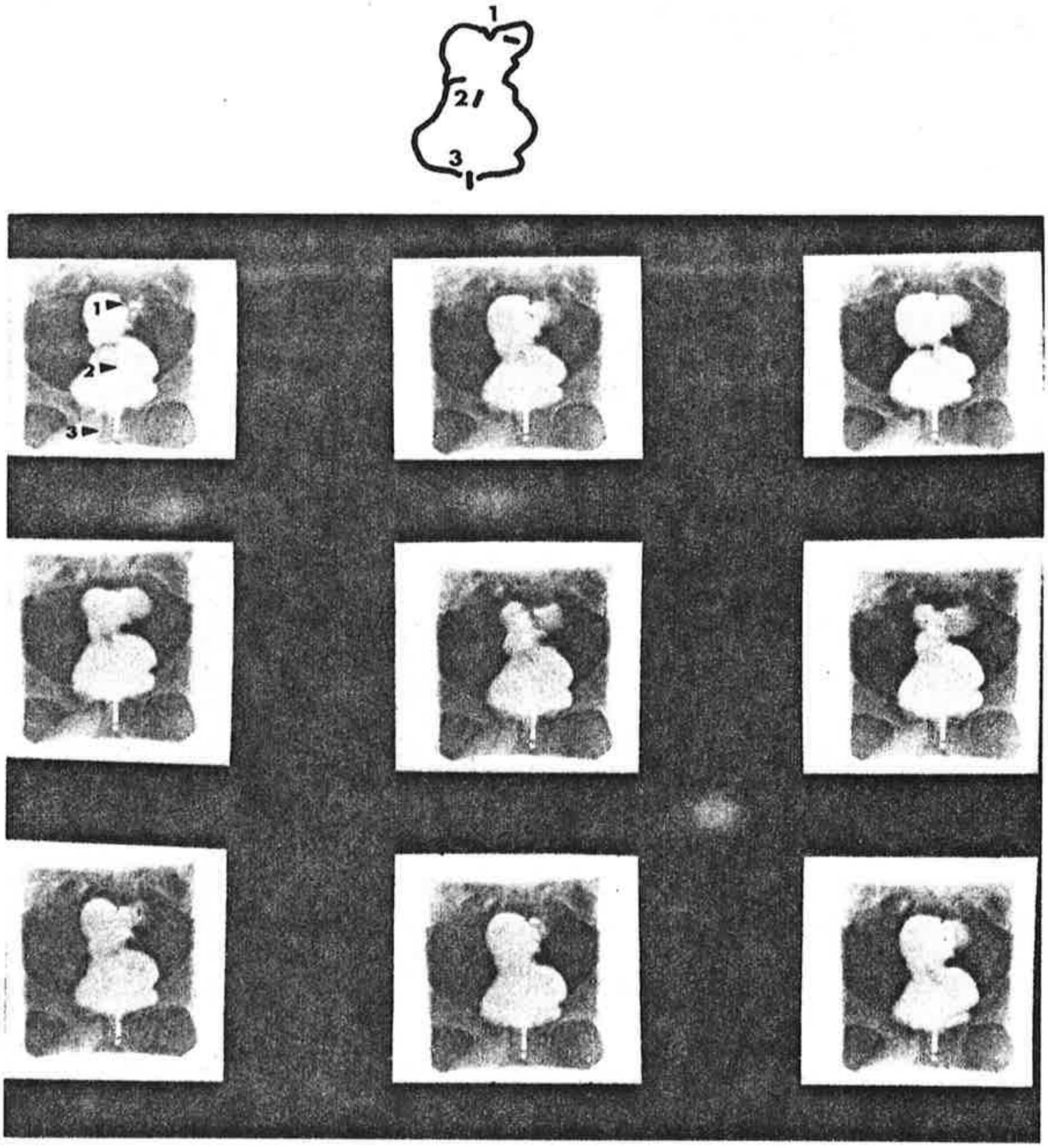
in frames 2 and 3 a contraction develops over the second recording tip and propulsion of barium occurs in frames 2 to 6; there is activity in lead II;

frames 7, 8 and 9 show retrograde transport of contrast medium from the first to the second recording tip - this transport coincides with the latter part of the pressure wave in lead I.

Thus progressive delay in the appearance of a wave in two or more leads, often referred to as a "propulsive wave pattern", could in fact represent to and fro movements of the intestinal contents. Figures 52 and 53 show another example of activity of this nature:

throughout the cine sequence the small intestine remains quiescent over the third recording tip and lead III of the pressure tracing remains inactive;

between frames 3 and 4 forward transport of a small amount of contrast medium from the second recording tip has occurred



<u>Figure 54</u>: The large intestine. Frames taken at eight-second intervals from the cine film from a patient with functional diarrhoea (case 65). The line drawing and the arrows in frame 1 show the position of the recording tips in the distal large intestine. The frames of this figure correspond in time to the first series of numbers beneath the panel illustrated in Figure 55. The correlative analysis is detailed in the text.

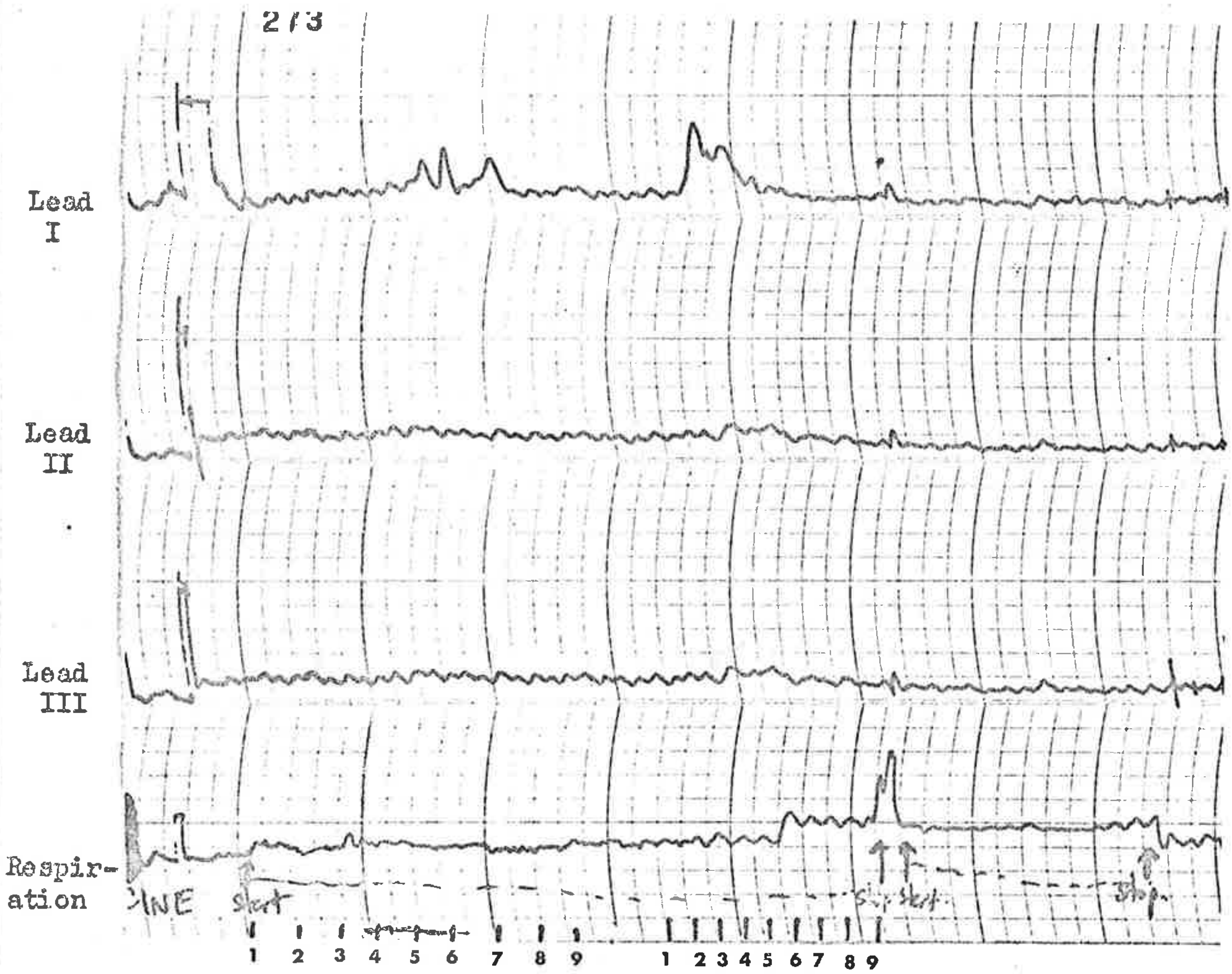


Figure 55: The large intestine. Pressure tracing done during the exposure of the cine film in a patient with functional diarrhoea (case 65).
The first series of numbers beneath the panel indicate the position of the cine frames of Figure 54 in relation to the pressure tracing and the second series of numbers indicate the position of the frames of Figure 56 relative to the tracing.
Paper speed 1 mm. per second (one small square equals five seconds).

corresponding to the latter part of the pressure wave recorded in lead II;

retrograde transport from the first to the second recording tip takes place in frames 5 to 9 with a return to the initial appearances; during this time a pressure wave is recorded in lead I.

Whether the rise in intraluminal pressure preceded the visible contraction or coincided with it could not be determined in this study. The cine camera and the chart-drive of the polygraph were started manually by two separate persons on a given command and a delay of up to one second could have occurred in either procedure.

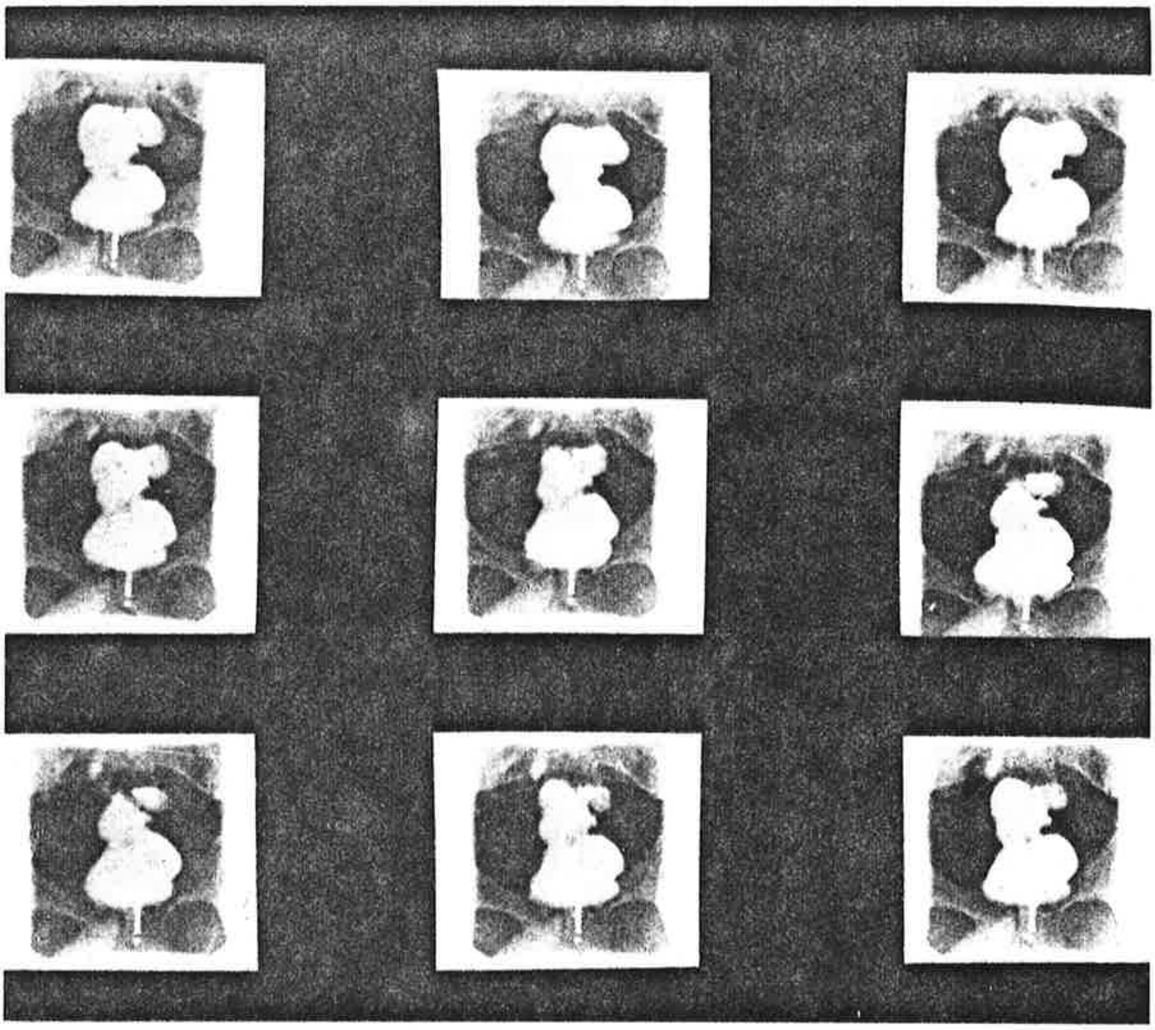
Correlation of pressure traces and cine films from the large intestine

With regard to the large intestine, not all radiologically observed movements had manometric counterparts. Furthermore, when pressure waves and contractions of the viscus occurred together the temporal correlation between the two was not constant.

A close correlation was sometimes observed between the cine appearance and the pressure trace in respect of the onset of a contraction (Figures 54 and 55, from a patient with functional diarrhoea:

frames 1 to 4 show filling of the rectum over the first recording tip;

a contraction with displacement of the contrast medium follows



<u>Figure 56</u>: The large intestine. Frames taken at intervals of 5.4 seconds from the cine film from a patient with functional diarrhoea (case 65). The frames correspond in time to the second series of numbers beneath the panel illustrated in Figure 55. The correlation of the cine sequence and the pressure record is described in the text.
The arrangement of the recording tips is the same as that in Figure 54.

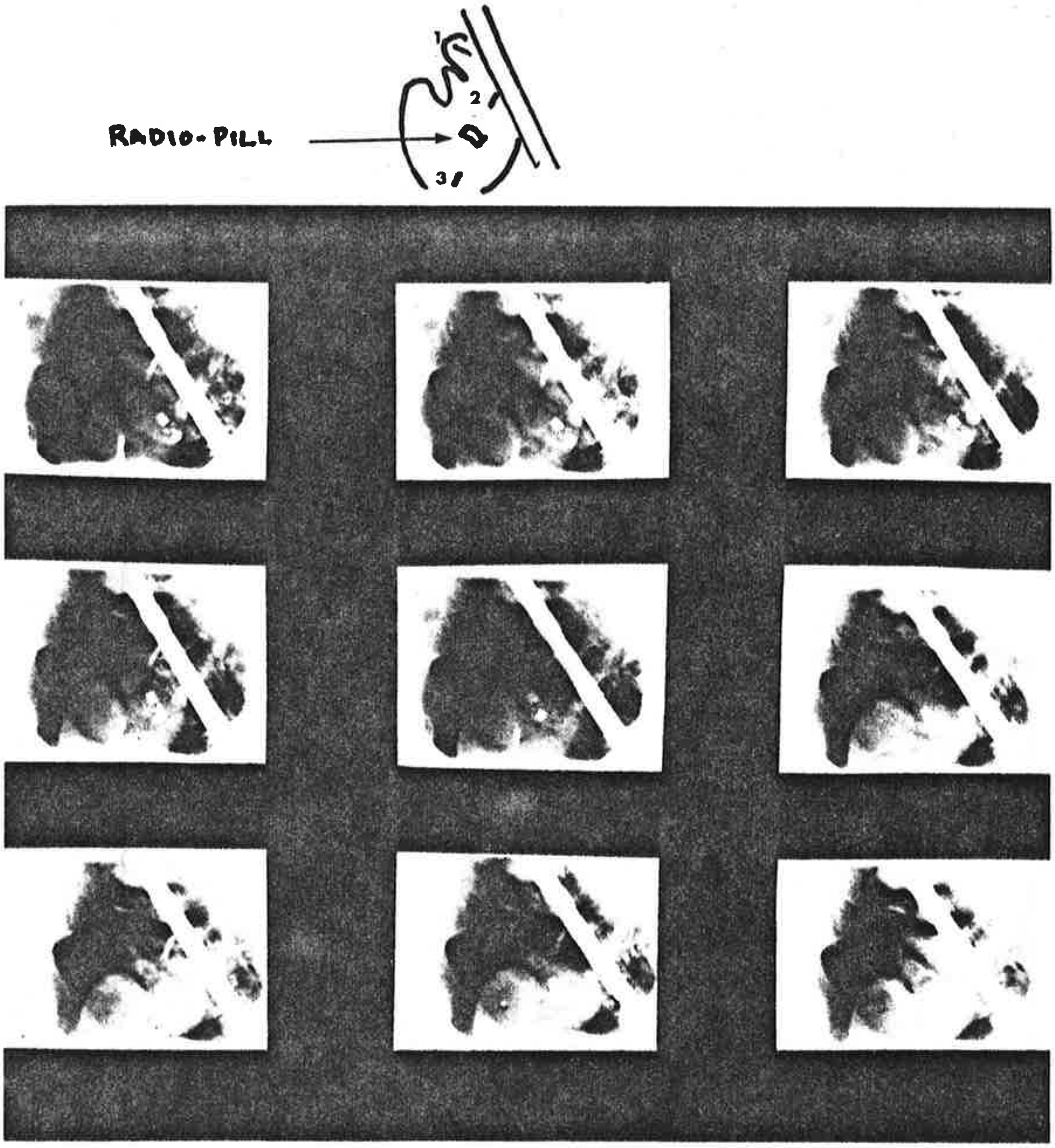


Figure 57: The large intestine. Frames taken at intervals of 3.7 seconds from the cine film from a control subject (case 35). The frames correspond in time to the numbers beneath the lower panel of Figure 58. The arrangement of the recording devices is shown in the line drawing. The diagonal rod in the frames is the aerial for the radio pill.

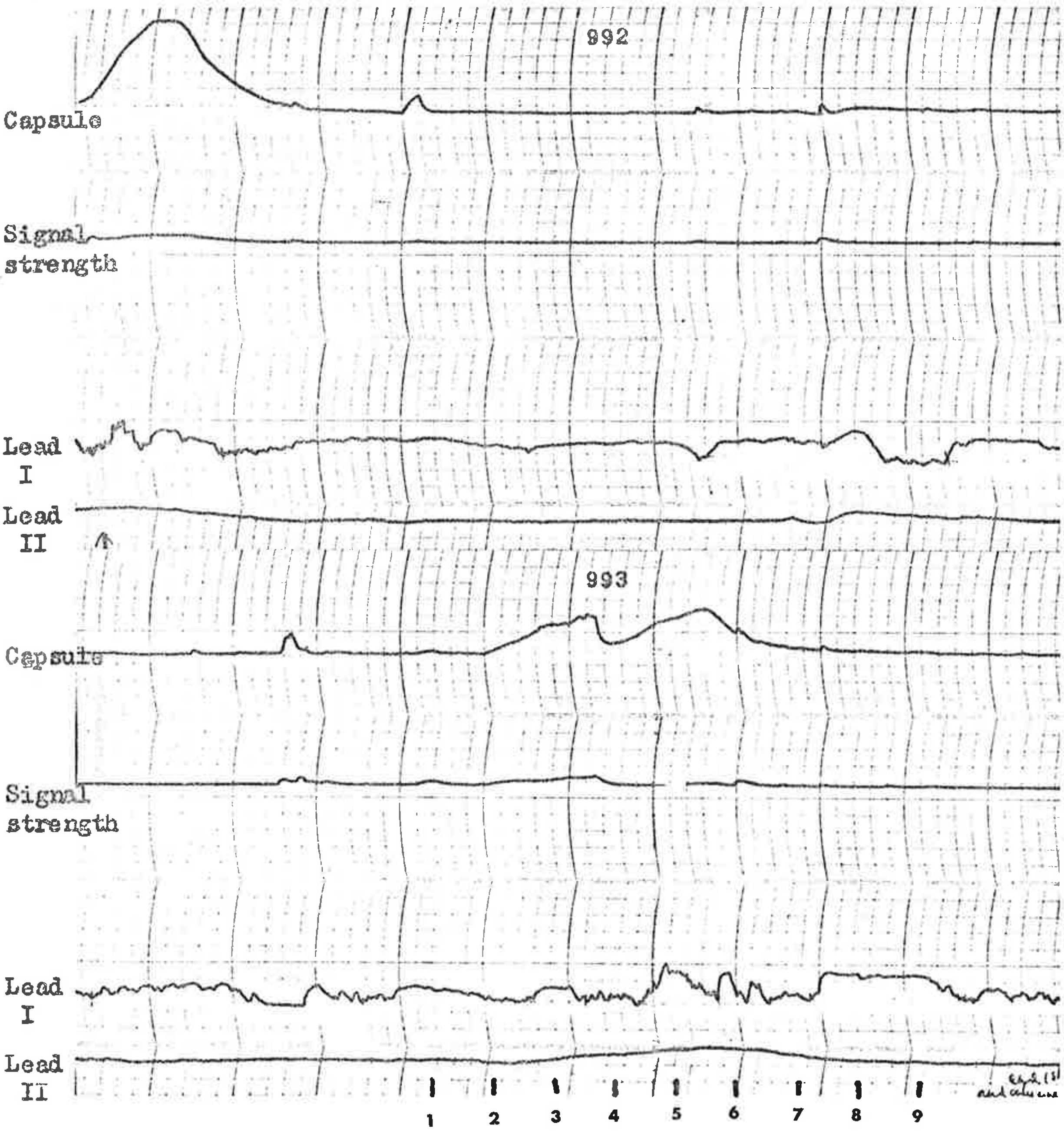


Figure 58: The large intestine. Pressure tracing done during the exposure of the cine film in a control subject (case 35). The numbers beneath the lower panel indicate the position of the cine frames of Figure 57 in relation to the tracing. Paper speed 5 mm. per second (one small square equals one second).

in frames 5 to 8;

the pressure trace shows that the visible contraction commenced simultaneously with the rise in intraluminal pressure recorded in lead I but lasted longer than did the pressure wave.

At other times no rise in intraluminal pressure accompanied a visible contraction (Figures 54 and 55, from the same patient):

a deep ring-like contraction develops between frames 2 and 3 and constricts the mid-rectum over the second recording tip;

no pressure wave appears in lead II which remains completely inactive.

Finally, visible contractions were seen to occur after the cessation of a pressure wave (Figures 55 and 56):

frames 4 to 9 show a contraction taking place over the first recording tip; the contraction has not subsided at the end of the cine sequence;

lead I shows that the pressure wave in fact precedes the visible contraction which occurs while only basal pressure is being recorded.

Figures 57 and 58 show that the delay in the appearance of a visible contraction was not restricted to patients with diarrhoea. The sequence in Figure 57 came from a control subject in whom the radiotelemetering capsule was used:

frames 1 to 3 show the capsule stationary at the left hand margin of the rectum but a small pressure wave is being registered in the trace from the capsule;

frames 4 and 5 show the radio pill beginning to move in from the margin of the rectum and this movement coincides with the initial part of the second pressure wave in the trace from the capsule.

CHAPTER V

DISCUSSION

The main aim of the present investigation was to study intestinal motility in man by the techniques of intraluminal pressure recording and cineradiography, separately and together, employing qualitative, quantitative and correlative analysis of the motility recordings. The following aspects of motility were studied by this approach:

the range of motor activity of the small and large intestine in normal subjects and the effects on motility of emotion, food and Prostigmine;

the behaviour of the small intestine in patients who have undergone partial gastrectomy with particular reference to changes in motility during the dumping syndrome;

the motor activity of the distal large intestine in patients with the irritable colon syndrome;

the motor activity of the proximal colon in relation to the mechanisms of constipation and diarrhoea;

the functional significance of the wave forms which represent intraluminal pressure changes.

In the study a quantitative assessment of motility was achieved by measuring all waves of the intraluminal pressure tracings and calculating as parameters of motility the percentage motor activity, the motility index, the mean amplitude of waves, the mean duration of waves and the distribution of waves on the basis of amplitude and duration. When motility was defined in these terms the following results emerged:

there was a considerable individual variation in the motor activity of the small and large intestine in normal subjects; however, motility was clearly augmented by Prostigmine and less markedly by emotion and food;

compared with normal subjects, patients who had undergone partial gastrectomy had higher levels of activity during the resting phase and after Prostigmine; they also had a more marked late response to food;

the dumping syndrome was associated with a reduction in the motility of the small intestine;

patients with functional diarrhoea had significantly less motor activity of the distal large intestine than patients with the spastic colon;

patients with diarrhoea due to miscellaneous alimentary disorders had patterns of motility strikingly similar to those of patients with functional diarrhoea;

in the small number of studies in which the motility of the proximal and the distal colon was recorded simultaneously the resting pattern of motility in normal subjects and in constipated patients showed more activity in the distal colon than in the proximal colon;

similar studies in patients with diarrhoea at the time of study showed the reverse situation with a pressure gradient directed towards the distal colon;

correlation of the intraluminal pressure recordings from the small intestine with their cineradiographic counterparts did not support the hitherto maintained separation of type I and type III waves on the basis of propulsive function.

In the present work motility was assessed by measurements of intraluminal pressures with open ended catheters and radiotelemetering capsules and by cineradiography. Open ended saline filled catheters have previously been found to provide an accurate and sensitive method for pressure measurements (Davidson et alii, 1956b; Chaudhary and Truelove, 1961a). Ingestible telemetering capsules were employed mainly to study the proximal large intestine. Cineradiography was combined with manometric studies in an attempt to correlate the waves of the pressure tracings with the visually observed movements of the intestine.

Open ended catheters are generally held to be superior to balloons (Quigley and Brody, 1952; Code et alii, 1952; Chaudhary and Truelove, 1961a). Unlike balloons they record true intraluminal pressures and the sensitivity and dynamic response of fluid filled catheters connected to the type of pressure transducer used in the present work has been found satisfactory (Quigley and Brody, 1952).

In this investigation, the recording system was sufficiently sensitive to show that the rhythmic waves of type I which constitute the basic rhythm of the small intestine and which have previously been assumed to be simple and monophasic (Code et alii, 1952) were in fact complex. Catheters have the additional advantage over balloons of not distending the intestine or interfering with the flow of its contents

(Chaudhary and Truelove, 1961a). In the present study a mercury bag was used to facilitate the passage of the catheters through the small intestine, but since the bag was small and situated eight centimetres distal to the first recording tip, it is unlikely that it modified intestinal motility to any extent.

However, there are some disadvantages in the use of catheters. In spite of the fact that intestinal contents are said not to be forced into a catheter of 1 mm. bore at pressures of less than 155 cm. of water (Rowlands et alii, 1953), the open ends may become blocked by mucosal folds, food or mucus. This may be overcome by using constantly perfused catheters (Lorber and Shay, 1954; Davidson et alii, 1956b). However, in this study the presence of a block was easily detected by inspection of the pressure trace and remedied by gentle syringing.

The main disadvantages of catheters are attached to their use in the small intestine. Placing the catheters in the jejunum may be a time consuming process and carries a certain failure rate. Roth and Beams (1959) in a study of the motility of the small intestine in patients after gastric surgery failed to place the recording balloon in the desired position in 20 of their 34 patients. This is an unusually high rate of failure and with practice better results can be obtained. In the present study the first 3 attempts did not succeed; thereafter only 3 further failures occurred in 36 consecutive patients. It appeared that success was least likely to be met with in patients with active peptic ulceration.

It should be realised that catheters may influence the motor activity of the small intestine but that this is more likely to be due to their presence in the oropharynx than to a direct effect on the intestine. Therefore in the present study every effort was made to relax and reassure the patient both before and during the experiment. Furthermore, partial pharyngeal anaesthesia was maintained by the use of topical lignocaine or local anaesthetic lozenges until the catheters were in situ.

The advantages of the radiotelemetering capsule are obvious. The capsule offers the most physiological method at present available for measurements of intraluminal pressures as well as a means of recording from parts of the intestine which for practical purposes are inaccessible to study with catheters. However, most workers who have had experience with gastro-intestinal radiotelemetering, emphasise the technical problems attached to the use of the radio pill. The directional nature of the signal emitted by the capsule has led to the development of complex systems of aerial loops (Smith and Ridgway, 1962) and omni-directional aerials (Connell et alii, 1963). In this work the capsule was used chiefly to record from the proximal large intestine where positional changes occur but infrequently and hence the phenomenon of loss of contact created few difficulties. It may not be possible to localise the transducer exactly in the upper small intestine even with radiological aid. However, in this study determination of the site of the strongest signal combined with contrast radiography made the assessment of the position of the capsule in the large intestine a relatively simple matter.

One of the main disadvantages of the radio pill is the fact that at least in the upper small intestine prolonged studies cannot be made of one particular segment as the pill rapidly travels downstream (Connell et alii, 1963). This can be obviated by anchoring the pill by means of a thin thread. However, in this work such a procedure was found to cause even more discomfort to the patient than that which the presence of the catheters evoked. In the large intestine anchoring is unnecessary once the capsule has reached the desired position although on occasions, as happened in case 51 of this study, unexpected progress of the pill may defeat the object of the experiment.

The telemetering capsule compares unfavourably with open ended catheters on another point. Whereas with catheters three or more simultaneous recordings can be made from different levels of the intestine, only a single pressure trace is obtained from the radio pill. This introduces the risk of a sampling error as it has been shown that there may be considerable variation in the activity of closely adjacent segments of the intestine (Chaudhary and Truelove, 1961b, c, d). However, it may be possible to overcome this difficulty by the simultaneous use of two capsules transmitting on different radio frequencies (Watson et alii, 1962).

The sensitivity of the radio pill to changes in environmental temperature, the necessity for separate calibration of each pill and the increasing complexity and cost of the equipment are all factors which have prevented a widespread acceptance of gastro-intestinal telemetering. Nevertheless, selected aspects of motility can be studied with the relatively simple equipment which was adequate for the purpose of the present investigation. The qualitative response of the radio pill was good as shown by the close similarity of the telemetered record and the pressure trace resulting from a catheter recording tip in juxtaposition to the capsule (Figure 44). Similar findings were reported by Connell and Rowlands (1960). Judged by the experiments in which the capsule could be recovered before its power supply was exhausted the stability of calibration was satisfactory. The experience gained in this study strongly supported the opinion of Connell et alii (1963) that catheters and telemetering should be regarded as complementary techniques. Furthermore, it was felt that certain aspects of motility, such as the mechanism of diarrhoea, could only be investigated by a method in which simultaneous use was made of both devices.

In this study a single observer measured the amplitude and the duration of the pressure waves in the motility tracings. This procedure was adopted because it was found that although there was good agreement between different observers in regard to the amplitude of a pressure wave, measurements of wave duration were subject to greater interpretative error. By constantly using the same observer, inter-observer error was eliminated and quantitative comparison of the various groups of patients investigated could be made with greater validity. However, it is appreciated that inter-observer differences still exist in the comparison of the results of this study with those of other workers.

It was felt that a quantitative way of expressing the results was necessary in studies of intestinal motility. Therefore in the present work motility was defined in terms of five parameters, namely the percentage motor activity, motility index, mean amplitude of waves, mean duration of waves and the distribution of waves on the basis of amplitude and duration. Davidson et alii (1956b), Connell (1959), Chaudhary and Truelove (1961b) and Kim and Barbero (1963) calculated the percentage activity by adding the periods during which waves occurred and expressing the sum as a percentage of the recorded time. However, it is felt that this method is not satisfactory as considerable difficulty may exist in deciding what constitutes a period of activity when the pressure waves occur at irregular intervals. A preferable alternative is to express the total sum of the wave durations as a percentage of the recorded time as was done in the present study.

The quantitative analysis of the intraluminal pressure tracings was found to be extremely time-consuming. Electronic analysis of the pressure changes would be of great value in dealing with large numbers of tracings. This could possibly be accomplished by connecting a computer to the output of the amplifier used in the recording procedure or by programming a computer to "process" the pressure tracings.

In the present work cineradiography was of substantial aid in providing information on the function of the pressure patterns observed in the small intestine. In addition an outline of the difficulties which were experienced may be of aid in future studies.

When the small intestine is studied by a combination of cineradiography and manometry the exposure of the film should begin when the first portion of the contrast medium is approaching the pressure recording devices. Interpretation of the film is difficult when the contrast has progressed well beyond the site of pressure recording and superimposition of intestinal loops has occurred.

Perfect synchronization of pressure tracing and cine film is a prerequisite for judging the temporal relationship of the commencement of a rise in intraluminal pressure and the beginning of radiologically observed movement. This could be done by superimposing an oscilloscope tracing of the pressure changes on the lens of the cine camera (Texter, 1961). In addition, simultaneous projection of the pressure tracing and the cine film would facilitate correlative analysis. This could be accomplished either by Texter's (1961) method mentioned above or by arranging for the pressure trace to be carried along with the film by a special "synchronizer" connected to the film projector (Caroli et alii, 1960). The X-ray viewing table used in the present study was not well suited for correlative analysis; a 16 mm. analysing projector would have been preferable.

The film speeds used in this investigation, though allowing detailed observation of the movements of the intestine, were unnecessarily high. Speeds of six to eight frames per second and two to three frames per second would probably be adequate for correlative studies of the small and the large intestine respectively. Finally, even with the use of closed circuit television image intensification the radiation hazard limits the length of exposure. Further advances in X-ray physics are needed to allow longer periods of study with minimal risk to the patient.

Many findings reported by earlier workers were confirmed in this study. Examples of type I and type III waves were recognised but the type II waves of Adler et alii (1941) and Posey et alii (1948) could not be identified in pressure tracings from the small intestine. This accords with the experience of Foulk et alii (1954), Barbero et alii (1958) and Connell (1961a). Bursts of rhythmic type I waves constituting the basic rhythm of the small intestine (Foulk et alii, 1954) were observed; the negative pressure deflection which often occurred as a continuation of the downstroke of a wave may have been due to a vacuum effect in the rapidly relaxing intestine. A remarkably constant rate of the basic rhythm of 11 to 12 waves per minute was noted in this study and has been previously reported by Foulk et alii (1954), and Connell (1961a). This lends support to the suggestion of Milton and Smith (1956) that the slow electrical potentials of the electromyographic record from the small intestine govern the rate of the basic rhythm. Furthermore, at least in this study the basic rhythm represented the fastest rate of contraction of which the small intestine was capable.

It was found that the nature of the pressure waves was not a reliable index of propulsion. This opinion was based on the correlative analysis of intraluminal pressure tracings and cineradiographic films which showed that it was not possible to distinguish a series of type I waves from a wave of type III on the basis of the radiological appearances. Propulsion was seen to take place with both wave types. However, type III waves were more strongly propulsive than single waves of type I. Furthermore, a progressive delay in the appearance of a wave in two or more leads did not invariably indicate propulsion because to and fro movement of the contrast medium was also noted with this type of activity.

Thus the results of the present study do not support the previous assignment of propulsive activity to type III waves alone (Posey et alii, 1948; Rowlands et alii, 1950a; Chapman et alii, 1952). Chapman and Palazzo (1949) combining pressure recording and fluoroscopy stated that waves of type I were not propulsive whereas type III waves were. However, they did not encounter any type III waves during the fluoroscopic observations and their opinion was thus not substantiated by factual evidence. It is also of interest that Ingelfinger and Moss (1943) who studied two patients with sprue found that transport of the recording balloons was only slightly slower than normal when no waves of type III were present.

It is believed therefore, that in respect of propulsion there is no qualitative difference between type I and type III waves, any distinction being of a quantitative nature. Furthermore, classical peristalsis is not responsible for propulsion and finally, waves with progressive delay may or may not indicate propulsion. It is suggested that aborad transport of the intestinal contents is the result of a pressure gradient between proximal and distal segments of the small intestine and that this gradient is due to the high levels of activity present in the upper small intestine with a progressive decrease at lower levels. Ridgway and Smith (1962) showed that progressively less motor activity was recorded by the radio pill as it travelled down the small intestine and in the present study the highest levels of motility were recorded through the most proximal recording tip. The suggestion that a pressure gradient rather than any particular wave form is responsible for propulsion receives support from Connell's observation that there was little or no correlation between individual pressure waves and movement of the radio pill (Connell, McCall, Misiewicz and Rowlands, 1963).

In the present work no attempt was made to measure intraluminal basal pressures or intestinal "tone". The basal pressure in the small intestine which has been estimated at between 6 and 10 cm. of water (Kewenter and Kock, 1960) is largely determined by the weight of the tissues surrounding the abdominal viscera, being the same in living subjects and cadavers (Edwards and Rowlands, 1961). There is at present no satisfactory method of measuring the resistance of the intestine to distension (Lipkin, Almy and Bell, 1962).

There are few quantitative studies similar to the present one in terms of technique and analysis and hence a comparison with the results of other workers is rendered difficult. Of the parameters of motility the percentage motor activity is most easily calculated and should therefore be best suited for purposes of comparison. However, as mentioned both by Connell (1961a) and in the present work, different investigators have used different ways of computing the percentage activity. Fink (1959) calculating the percentage activity as it was done in this study found that in fasting patients the upper small intestine was active for 15 per cent. of the recorded time, compared to 32.1 per cent. in the present study. However, the method which Fink (1959) used did not permit multiple simultaneous recordings to be made from different levels of the small intestine as in the present study. Barbero et alii (1958) reported a mean activity of 23 per cent. in the duodenum of children up to the age of 14 years. However, apart from the age difference between the control subjects in the present study and the children investigated by Barbero's (1958) group the routine use of sedation in the latter weakens the comparison between the two studies. Barbero and her co-workers (1958) found that milk augmented the activity from 23 to 50 per cent. in the first 10 minutes; the activity decreased to 44 per cent. and 41 per cent. during the next two 10 minute periods. These values are rather similar to the 40 per cent. in the first 10 minutes and 38.2 per cent. in the next 20 minutes found in this study.

According to Connell (1961a) the differences in the reported values for percentage motor activity may in part be due to variations in the length of fast imposed on the patient before the study. In the present investigation this interval was kept constant at six hours.

Prostigmine, as expected, augmented the percentage activity, motility index and mean amplitude of the waves in the control subjects of this study. This stimulation of the small intestine has been reported by many observers (McMahon, Code, Sauer and Bargen, 1949; Liljedahl et alii, 1958; Kewenter and Kock, 1960) but not in quantitative terms. In the present study there was a marked individual variation in the response to Prostigmine. Although the dose of drug was not adjusted to the body weight of the subject this cannot explain the variation, since the magnitude of the response did not show an inverse relationship to body weight. It is more likely that, as suggested by Chaudhary and Truelove (1961c), individuals vary in their susceptibility to this drug.

It is appreciated that the motility of the small intestine was studied in only a small number of control subjects. It is therefore important that further studies should include control groups so that the normal motility of the small intestine may be more clearly delineated.

The qualitative features of pressure recordings from the large intestine are sufficiently well known not to require detailed discussion. The spontaneous variations in motor activity, the independent activity at different levels of the intestine and the wave types have been described previously (Connell, 1959; Chaudhary and Truelove, 1961b; Kim and Barbero, 1963) and were observed in the present study. Repeated studies performed in the same subjects showed that the level of motility was fairly constant in each individual when the recordings were done in identical circumstances; a similar opinion was expressed by Connell (1959).

There was a considerable individual variation in the control group in respect of the percentage activity and motility index (Table VII). It is possible that the variation in motility during the resting phase was related to the amount of faeces in the rectum, as virtually flat pressure tracings were often obtained from subjects in whom the sigmoidoscopic examination showed the rectum to be empty. Kim and Barbero (1963) reported higher levels of activity in the large intestine in anxious children than in children who appeared relaxed but reported that the majority of the pressure waves recorded were of an amplitude of 2 cm. of water. In the present study, the respiratory fluctuations often exceeded this amplitude and it is therefore difficult to assess the accuracy of Kim and Barbero's (1963) estimate of percentage activity. Nevertheless, it is possible that in some of the control subjects the anticipation of the experiment may have created a degree of apprehension which, though not obvious to the observer, may have influenced motility. If this were so, a particularly obvious response to the emotive interview could perhaps have been expected in those subjects in whom the levels of activity were at the extremes of the normal range during the resting phase; however, this was not the case.

The response to the emotive interview was not constant amongst the control subjects. The mean values of percentage activity and motility index for the group did rise but an increase to more than 200 per cent. of the resting value was noted only 8 times of 15 during the initial emotive interview. Chaudhary and Truelove (1961d) reported colonic hyperactivity during a stressful interview in 4 of 16 control subjects but did not state their criteria for judging the presence of hyperactivity.

In the present study food augmented the motility of both the proximal and the distal large intestine; however, in the latter the increase was not as marked as that observed during the interview and did not reach a level of statistical significance. Prostigmine, however, caused a highly significant rise in both the percentage activity and motility index ($p < 0.001$). The augmentation of colonic motility by Prostigmine has been reported many times (Adler et alii, 1942; Atkinson et alii, 1943; McMahon et alii, 1949; Chaudhary and Truelove, 1961c) but has not previously been proved statistically significant.

Studies of the motility of the small intestine were performed on patients who had undergone partial gastrectomy because changes in motility may be responsible for some of the undesirable results of this operation. There can be no doubt that gastric surgery, and in particular partial gastrectomy, has been the decisive factor in reducing the mortality and morbidity of peptic ulceration and that the majority of surgically treated patients derive benefit from the operation. However, it should also be recognised that partial gastrectomy is associated with a mortality of approximately 4 per cent (Brookes, Waterhouse and Thorn, 1960) and that peptic ulceration recurs in 1.5 per cent. of patients after the Polya operation (Capper and Welbourn, 1955) and in a greater proportion after the Billroth I operation. In addition about 10 per cent. of patients develop one or more of the delayed sequelae of partial gastrectomy (Illingworth, 1960).

Chief amongst the late complications of gastric surgery are the dumping syndrome; anaemia due to a deficiency of either iron, vitamin B_{12} or folic acid or a combination of these; recurrent or anastomotic ulceration; the afferent loop syndrome, steatorrhoea and impaired nutrition. Perhaps less common but by no means unimportant are the late hypoglycaemic syndrome; osteoporosis and osteomalacia (Deller, 1963); the malabsorption syndrome due to bacterial invasion of the afferent loop or to gastro-jejuno-colic fistula; food bolus obstruction and carcinoma of the gastric remnant. Diarrhoea may or may not be part of a malabsorption syndrome and may occur both after vagal resection and when the vagus has been spared. The two late complications of gastric surgery in which the motility of the small intestine is of particular interest are the dumping syndrome and diarrhoea.

In this study patients who had undergone gastric surgery had pressure tracings which were qualitatively similar to those obtained from the control group. A possible difference was the relative preponderance of type III waves in the resting pattern in patients after gastrectomy. Furthermore, these patients usually had more activity in lead II than in lead III, whereas in the control subjects the latter lead was the most active. Possibly the reason is that lead III was closest to the stoma of the Polya anastomosis which could act as an escape valve with rising intraluminal pressures. If this were so, it would have been expected that more activity would have been recorded in lead III than in the distal leads both in the patients who had had the Billroth I operation and in those patients in whom all three recording tips were well distal to the stoma of a Polya anastomosis. However, this was not the case.

There was little difference between the control subjects and patients after gastrectomy in respect of the percentage motor activity during the resting phase. Kewenter and Kock (1960) using a method very similar to the one employed in this study reported very little motor activity in fasting normal subjects and the same group (Christoffersson et alii, 1962) stated that patients who had had partial gastrectomy had equally low levels of activity. However, no quantitative assessment was attempted in either of these studies.

When the motility index was used for comparison of the groups both categories of patients after partial gastrectomy had higher resting values than the control subjects, but the difference was statistically significant only in the patients in whom symptoms of "dumping" were later induced. As a rule the interval between intubation and the beginning of the recording was shorter in the patients who had undergone partial gastrectomy than in the control subjects because some time was spent in negotiating the pylorus in the latter group. Accordingly, it is possible that the motility of the intestine was depressed by prolonged contact with the catheters. However, two of the six patients who constituted the group "partial gastrectomy with 'dumping'" had had the Billroth I type of anastomosis which was no more easily negotiated than the normal pylorus. Eleven of twelve patients without the dumping syndrome had the Polya anastomosis, and it would be expected that if the motility of the intestine were reduced by prolonged contact with the catheters, this group of patients should have had the highest motility index during the resting phase; this was not the case. The marked difference in the mean ages of the control subjects (28.7 years) and the patients after gastrectomy (58.7 years) may also be an explanation. However, the mean age of the patients with the dumping syndrome (55.5 years) was little different from those without this disturbance (59.8 years). There is at present no information on whether the motility of the small intestine bears a relationship to chronological age, and this aspect should be studied in future work. Nevertheless, it would be surprising to find an increase in motility with advancing age.

In this investigation the motility of the small intestine was studied after the administration of sweetened milk. In clinical practice warm, liquid and sweet foods are the usual precipitating causes of the dumping syndrome after gastrectomy. Experimentally the symptoms have been reproduced by distension of the jejunum with a balloon (Jordan et alii, 1957a) or by introduction into the small intestine of hypertonic glucose (Amdrup and Balslev-Jørgensen, 1957a), a fat suspension (Jordan et alii, 1957a) and dilute hydrochloric acid (Schmid, Heythaler, Schön and Henning, 1962). During the dumping syndrome there is reduction in the plasma volume, hyperglycaemia, impaired peripheral utilisation of glucose, hypokalaemia and electrocardiographic changes (Peddie, Jordan and DeBakey, 1957; Jordan et alii, 1957a; Morris, Greenfield, Jordan, Peddie, Gordon and DeBakey, 1959; Howe, Candy, Le Quesne, Hobsley and Spence, 1962).

In the present investigation a number of abnormalities in motility were demonstrated following the ingestion of food in the patients after operation. Compared with the corresponding values for the resting phase, the patients who experienced an attack of "dumping" showed a reduction in both the percentage motor activity and the motility index of the first ten minutes after the meal. In the individual tracings this was evident as reduced or absent motor activity after a few initial waves which often showed progressive delay. Although marked, the reduction in the percentage activity and the motility index was not statistically significant, possibly because of the small numbers involved and because one patient (case 25) had paradoxically marked motor activity during an attack of "dumping". It should also be noted that this patient was the only one in whom partial gastrectomy had been combined with vagal section. His values for the percentage activity and motility index during the resting phase and after food were the highest ones observed in the patients with the dumping syndrome.

The late response to food was qualitatively similar in both groups of patients after gastric surgery and consisted of strikingly increased motility. During this phase patients without the dumping syndrome had significantly higher values for percentage activity and motility index than the control subjects; the difference between the patients who experienced symptoms of "dumping" and the control group was not statistically significant.

There have been divergent reports of the motility of the small intestine during provoked attacks of "dumping". Most radiological studies have reported increased motility (Liljedahl et alii, 1959; Wallensten et alii, 1959; Duthie and McKellar, 1960; Mattsson and Perman, 1962). The radiological impression gained in the present work was one of decreased motility with distension of the small intestine and was thus similar to the findings of Cox and Allan (1960). Manometric studies have shown both decreased motility (Christoffersson et alii, 1962) as in the present work and hypermotility (Glazebrook and Welbourn, 1952; Jordan et alii, 1957a). However, Christoffersson and his colleagues (1962) were the only workers who used open ended catheters as in the present study.

According to the results of this study patients with and without provoked attacks of "dumping" differed only in their early response to food and both groups showed hypermotility of the small intestine after the first ten minutes following the meal. It seems therefore, that the conflicting results hitherto published may in part be due to a failure to distinguish between the immediate and late changes in motility during provoked attacks of "dumping". Thus the reports of hypermotility (Liljedahl et alii, 1959; Wallensten et alii, 1959) could be based on the observation of either the initial short period of activity which in this study preceded the reduction of motility or of the sustained hypermotility which followed it. Christoffersson et alii (1962) reported a similar sequence of changes in motility during provoked attacks of "dumping" to that observed in the present work although the initial motor activity lasted from two to eight minutes in their patients.

If it is accepted that changes in intestinal motility are seen during attacks of "dumping" their role in the production of symptoms of predominantly vasomotor nature has not been satisfactorily explained. It has been shown that there is a fall in the plasma volume when symptoms of "dumping" are provoked by instillation of hypertonic glucose into the small intestine (Amdrup and Balslev-Jørgensen, 1957a). Furthermore, in the experimental animal hypertonic solutions cause an influx of fluid into the lumen of the intestine, and the influx is directly proportional to the length of intestine in contact with the solution (Amdrup and Balslev-Jørgensen, 1957b). The rate of fluid diffusion into the lumen is greatest in the duodenum and smallest in the ileum (Amdrup and Balslev-Jørgensen, 1959) but it is not influenced by vagal section (Amdrup and Walbom-Jørgensen, 1962).

It has therefore been postulated that the well-documented initially rapid emptying of the gastric remnant (Liljedahl et alii, 1959; Duthie and McKellar, 1960) presents the proximal small intestine with a large amount of hyperosmolar solution. This leads to a shift of fluid from the extravascular compartment into the lumen of the intestine and hence to a loss of fluid from the intravascular compartment with a fall in the circulating plasma volume. This fall has been held responsible for the vasomotor symptoms. If this sequence of events were accepted it could be argued that the initial short-lived motor activity observed in this study in association with the provoked dumping syndrome could serve to bring the hypertonic solution into contact with the proximal small intestine. It could then be postulated that the subsequent hypomotility allowed the food to remain in the upper small intestine where the rate of fluid diffusion is greatest. A constantly high level of motor activity as demonstrated in the patients in whom the dumping syndrome did not follow the standard meal would serve to transport the food past the most vulnerable upper reaches of the small intestine.

However, although reductions in the plasma volume do occur, Webber, Bender and Moore (1957) have shown that there is no close correlation between the size of the reduction and the presence or absence of symptoms of "dumping". This fact led to the suggestion that symptoms develop in those patients who are particularly susceptible to hypovolaemia (Le Quesne, Hobsley and Hand, 1960). Alternatively it has been proposed that the symptoms are the result of an inherently abnormal response of the jejunum to food (Amdrup, 1961).

The vasomotor nature of the symptoms and their rapid onset has led many workers to believe that a humoral mechanism is responsible. Morris et alii (1959) studied the changes in the plasma volume, blood pressure, serum potassium levels, electrocardiogram, and renal function during provoked attacks of "dumping". This work led them to postulate that the release of a systemically circulating agent, possibly adrenaline, is responsible for the production of the dumping syndrome. It is of interest that on theoretical grounds adrenaline would be expected to diminish the motility of the small intestine although this effect has not been demonstrated with modern techniques and the early balloon studies gave inconclusive results (Ingelfinger, 1943). This aspect requires further study. Furthermore, although technically difficult, estimations of the blood levels of adrenaline during attacks of "dumping" would be of great interest.

Another humoral agent which has been considered to play a role in the dumping syndrome is 5-hydroxytryptamine. This substance, which is derived from the entero-chromaffin cells of the small intestine, is known to provoke hypermotility of the small intestine in animals after intravenous administration (Haverback, Hogben, Moran and Terry, 1957) and, in some species of animals, after intraluminal administration (Bülbring and Lin, 1958). 5-hydroxytryptamine has also been shown to augment jejunal motility in man when given intravenously (Hendrix, Atkinson, Clifton and Ingelfinger, 1957) but direct contact of the drug with the mucosal surface of the jejunum has no effect.

Spectrofluorometric estimations of the levels of 5-hydroxytryptamine in the portal and systemic venous blood in dogs have shown that the experimentally induced dumping syndrome is associated with hyperserotoninaemia (Drapanas, McDonald and Stewart, 1962). Furthermore, Johnson, Sloop, Jesseph and Harkins (1962) have shown that both in the dog and in man the increase in peripheral blood flow which accompanies the symptoms of "dumping" could be reduced or abolished by alpha-methyl dopa. This substance blocks the synthesis of 5-hydroxytryptamine by inhibiting the decarboxylation of 5-hydroxytryptophan (Irvine, O'Brien and North, 1962). Johnson et alii (1962) also claimed that alpha-methyl dopa and the 5-hydroxytryptamine antagonist cyproheptidine were effective in the clinical management of patients with the dumping syndrome.

It has therefore been suggested that the dumping syndrome could be due to a sudden release of 5-hydroxytryptamine from the stores in the small intestine into the portal circulation, and that the resulting high levels of the substance in the systemic circulation give rise to the vasomotor symptoms and the jejunal hypermotility. The release from the small intestine could be accounted for by the distension of the jejunum (Bülbring and Lin, 1958) caused by rapid gastric emptying.

However, there is by no means unanimity in regard to the role of 5-hydroxytryptamine in the production of the dumping syndrome. The results of Johnson et alii (1962) can be criticised on the grounds that no attempt was made to ascertain whether distension of the jejunum by an isotonic solution or by air without the production of symptoms of "dumping" was associated with hyperserotoninaemia. Furthermore, Schmid et alii (1962) estimated the urinary excretion of 5-hydroxy-indoleacetic acid (5-HIAA) in patients after partial gastrectomy and their results did not support the hypothesis that 5-hydroxytryptamine was involved in the pathogenesis of the dumping syndrome. They instilled alternatively hypertonic glucose, 0.1 N. hydrochloric acid and distilled water into the upper small intestine in three groups of patients after partial gastrectomy and found no evidence of increased excretion of 5-HIAA in the presence of symptoms of "dumping".

With regard to the present work, the diminished motility observed during attacks of dumping would not have been expected if 5-hydroxytryptamine was causally related to the dumping syndrome. The different responses to food which were observed in the control subjects and in the two groups of patients after gastrectomy in this study could be better explained by the following chain of events:

1. The normal rate of gastric emptying is exponential in that a fixed fraction of the gastric contents are presented to the small

intestine per unit of time (Hunt, 1958).

2. Partial gastrectomy leads to loss of gastric reservoir function and rapid emptying of the gastric remnant delivers an abnormally large volume of food to the proximal small intestine.

3. The intestine responds by hypermotility which continues in those patients who experience no symptoms of "dumping". However, if the dumping syndrome is precipitated, hypomotility sets in; almost immediately as in the present study or from two to eight minutes after the meal (Christoffersson et alii, 1962). With the cessation of the symptoms of dumping motor activity increases to approximately the levels observed in those patients after gastrectomy in whom food produced no disagreeable symptoms.

4. The decreased motility may be causally related to the dumping syndrome in that the small intestine is not capable of responding normally - that is by increased activity - to sudden distension or to contact with hypertonic solutions. However, a more likely alternative is that the hypomotility is a paraphenomenon being caused by the same, as yet unidentified, humoral substance which is responsible for the vasomotor changes. In either case hypomotility would allow prolonged contact between the hypertonic food and the mucosa of the upper small intestine and could thus be expected to augment the fall in plasma volume. In view of the results of the present study, a clinical trial of drugs which enhance motility should be made in the treatment of the dumping syndrome following gastric surgery.

The humoral agent is probably not 5-hydroxytryptamine (Schmid et alii, 1962) but may possibly be adrenaline (Morris et alii, 1959). It is therefore interesting that although the good effect of alpha-methyl dopa in the prevention of the dumping syndrome was attributed to its interference with the synthesis of 5-hydroxytryptamine (Johnson et alii, 1962) the drug also blocks the formation of adrenaline.

Prostigmine augmented the motility of the small intestine in both groups after gastrectomy, and more so in patients without the dumping syndrome. However, the difference between the two groups was not statistically significant, probably because only two of the patients in whom symptoms of "dumping" had been induced were given Prostigmine. Compared to the resting values, the increase in motility caused by Prostigmine was statistically significant in the patients without the dumping syndrome. The reason why patients after partial gastrectomy showed a greater response to the drug than did the control subjects is not clear, but it may be related to the presence of more food in the small intestine in the former group. Whether the amount of food in the intestine modifies the response to Prostigmine could profitably be investigated in future work.

Chaudhary and Truelove (1961c) in studies of the motility of the large intestine showed that patients with the irritable colon syndrome were more sensitive to Prostigmine than were normal subjects. By analogy, it would be interesting to know whether patients who have episodes of diarrhoea after gastric surgery are unduly responsive to cholinergic stimulation. The present study cannot answer this question because only three patients had unexplained episodic diarrhoea and the response to Prostigmine in these patients showed a random distribution. Further study on this matter is indicated.

Vagal resection is often performed as part of the surgical treatment of duodenal ulceration. The reported incidence of diarrhoea following vagotomy varies from 4 per cent. (Feggetter, 1959) to 30 per cent. (Burge, 1960). In man the motility of the small intestine after vagotomy has not been studied with modern techniques although Roth and Beams (1959) using balloons found that motility had not been basically affected by the operation. Muren (1956) showed that in dogs a reduction in motility was the immediate response to vagotomy, in the following three months hypermotility was observed and thereafter pre-operative levels of activity were restored. The investigation of intestinal motility after vagal resection in man is made difficult by the fact that the resection may be incomplete and regeneration of the vagal fibres may occur. The success of the operation can be judged by the gastric acid secretion after insulin-induced hypoglycaemia but a further complicating factor is the possibility that some of the para-sympathetic fibres may travel to the stomach in sympathetic nerves. Of the patients investigated in the present study only one had undergone vagal resection and although in his case the small intestine was extremely active after the standard meal he declined the injection of Prostigmine.

Diarrhoea is sometimes a troublesome complication of partial gastrectomy even when vagotomy has not been carried out. The precipitate gastric emptying and enhanced late response of the small intestine to food could obviously be of importance in production of this symptom. However, disturbances of motility were frequently present in this study in patients not suffering from diarrhoea.

Disturbed motility of the large intestine was demonstrated in patients with the irritable colon syndrome. In the present study patients with functional diarrhoea had marked inactivity and patients with the spastic colon had increased activity of the colon and rectum. Judged by the motility index the difference between these two subgroups of the irritable colon syndrome was statistically significant throughout all the phases of the recording. Furthermore, the patients with functional diarrhoea had a significantly lower percentage motor activity and motility index at rest than the control subjects.

It should be pointed out at this stage that, although the mean values for the percentage activity and motility index showed marked and often statistically significant differences between control subjects, patients with the spastic colon and patients with functional diarrhoea, there was considerable individual variation within each of these groups. Connell (1959) found that slightly more than one-half of the patients with functional bowel disorders had normal tracings. He also found that patients who had diarrhoea at the time of study had inactive tracings although he gave no detailed analysis of his results. Confirming this finding in a later report (Connell, 1962) he showed that patients with diarrhoea had significantly less "total activity" than control subjects. However, Connell (1962) calculated "total activity" as the product of the percentage activity and mean amplitude of waves, but used balloons which have been shown to be inaccurate in recording the amplitude of waves (Ritchie et alii, 1962). It is therefore difficult to assess the significance of his findings, particularly as he found little difference between normal subjects and patients with diarrhoea in terms of percentage activity. As mentioned previously, he calculated percentage activity in a way different from that used in the present work.

There have been other reports mentioning the relative inactivity of the colon in patients with diarrhoea (Spriggs et alii, 1951; Kern et alii, 1951; Chaudhary and Truelove, 1961b). However, until the present study it has not been shown with accurate techniques of pressure recording that diarrhoea is associated with a statistically significant reduction in the motility of the distal large intestine.

Most workers who have studied the subject agree that emotional stress may at times be associated with marked changes in the motor function and vascularity of the colon (Cannon, 1902; Weeks, 1946; Almy and Tulin, 1947; Almy et alii, 1949a,b; Almy et alii, 1950; Almy, 1951; Wener and Polonsky, 1950; Wener et alii, 1952; Welsh and Wolf, 1960; Chaudhary and Truelove, 1961d). It has also generally been conceded that a response to stress is not confined to patients with functional or organic disease of the colon but that such a response can be elicited in many normal subjects (Almy et alii,1949a,b; Chaudhary and Truelove, 1961d).

However, it is virtually impossible to compare the results of different groups of workers for two reasons. Firstly, it is difficult to judge when, and to what extent, stress has been induced; secondly, varying and arbitrary criteria of what constitutes a significant colonic response have been employed in the past. While it cannot be claimed that the first of these two difficulties has been eliminated in the present study, the emotive interview was conducted at a "level of intensity" which as far as could be judged was equal in all patients. Furthermore, quantitative criteria of an altered response of the large intestine were defined.

In this study only patients with functional diarrhoea had a significantly higher motility index during the emotive interview than during the resting phase. However, during the interview the motility indices of the two groups of patients with the irritable colon syndrome did not differ significantly from that of the control group. Furthermore, although the numbers were small, approximately equal proportions of control subjects and patients with the irritable colon syndrome had an enhanced response to the emotive interview. Chaudhary and Truelove (1961d) reported similar findings in that 25 per cent. of their control subjects and 26 per cent. of patients with the irritable colon syndrome showed colonic hyperactivity during the interview.

In the present investigation food augmented motility both in the control subjects and in the patients with the irritable colon syndrome. The increase in the motility index was statistically significant in patients with functional diarrhoea. However, in individual cases there was poor correlation between the response to the standard meal and the presence or absence of a history of intolerance to any of the constituents of the meal.

Prostigmine caused a statistically significant rise in the percentage motor activity and the motility index in control subjects as well as in patients with the irritable colon syndrome. After Prostigmine patients with the spastic colon had considerably more activity and patients with functional diarrhoea considerably less activity than patients in the control group although these differences were not statistically significant. Chaudhary and Truelove (1961c) also reported a more marked response to Prostigmine in patients with the spastic colon than in normal subjects.

Opinions vary as to whether the irritable colon syndrome has any distinctive radiological features. Kirsner and Palmer (1958) did not think so, whereas Kalser, Zion and Bockus (1956) reported radiological abnormalities of both the small and the large intestine in patients with this disorder. Lumsden and Truelove (1959) and Lumsden, Chaudhary and Truelove (1963) emphasised that contrast radiography of the large intestine could contribute to the diagnosis only if no irritant enemas and aperients were used to prepare the patient for radiography. In the present work the cineradiographic studies of the large intestine were too few in number to disclose possible differences between normal subjects and patients with disordered bowel habits. In view of the relative paucity of motor activity in the distal colon and rectum, prolonged cineradiographic exposures would be necessary to obtain representative records of the motility of the unstimulated large intestine. However, even with the increased margin of safety offered by closed circuit television image intensification, such exposures would entail a considerable amount of radiation. It is therefore considered that every effort should be made to devise non-radiological techniques capable of yielding similar information to that obtained by cineradiography. Ritchie et alii (1962) have devised a differential unit for recording intraluminal pressures which gives some information of this nature.

The following factors have been assumed to predispose to or to be of aetiological significance in the irritable colon syndrome: a past history of dysentery, abdominal operations, emotional stress, food intolerance, broad spectrum antibiotics and misuse of purgatives (Kalser et alii, 1956; Kirsner and Palmer, 1958; Chaudhary and Truelove, 1962). Each one of these factors except the last two mentioned was observed to have precipitated or aggravated the disorder in some of the patients of this study. However, there were eleven patients in whom no precipitating cause could be found. Only four patients stated that neither emotional stress nor specific foods initiated a relapse or aggravated already existing symptoms; these four patients all had the spastic colon.

In the present study particular emphasis was placed on the quantitative assessment of changes in the motility of the large intestine induced by emotions, food and cholinergic stimulation. It therefore seemed appropriate to consider in more detail the possible role of each of these three factors in the aetiology and pathogenesis of the irritable colon syndrome.

Clinically there was little doubt that emotional stress and the irritable colon syndrome were related. The onset of the disorder closely followed a major emotional crisis in three patients; in these and in a further nine patients nervous tension definitely aggravated pain or diarrhoea which were already present. Thus psychogenic factors appeared relevant in 12 of the 18 patients with the irritable colon syndrome. This proportion is only slightly smaller than the 79 per cent. reported by Chaudhary and Truelove (1962). Furthermore, the emotive interview performed in this study caused a statistically significant rise in the mean motility index of the patients with functional diarrhoea. Hence there was both clinical and experimental evidence favouring a close relationship between psychogenic factors and the irritable colon syndrome.

However, there is also evidence to suggest that the relationship between the psyche and the irritable colon may not be a causal one. Firstly, it is well known that emotional stress can induce changes in colonic motility in healthy control subjects as well as in patients with functional alimentary disorders (Almy and Tulin, 1947; Almy et alii, 1949b). Secondly, in the present work a response to the emotive interview was no more common amongst the patients with the irritable colon syndrome than in the control subjects; a positive response was observed in 8 of 18 patients with the irritable colon syndrome and 8 of 15 control subjects. Similar results were reported by Chaudhary and Truelove (1961d). Thirdly, in the present study no less than five of the nine patients who had miscellaneous organic alimentary disorders with diarrhoea at the time of the pressure recording stated that the diarrhoea was definitely aggravated by nervous tension. Of the 16 patients in the miscellaneous group who had a history of intermittent or continuous diarrhoea, regardless of whether the stools were loose at the time of study, 8 had noticed aggravation of the diarrhoea by emotional stress. Finally, the rise in the percentage motor activity and motility index during the emotive interview was no greater in the patients with functional diarrhoea than in those patients in whom the diarrhoea was caused by proven organic alimentary disease.

Intolerance to specific foods has previously been described in patients with the irritable colon syndrome, although true gastro-intestinal allergy appears to be rare (Kalser et alii, 1956; Kirsner and Palmer, 1958). Chaudhary and Truelove (1962) stated that 54 of their 130 patients noticed aggravation of the symptoms by particular items of food. In the present study 11 of the 18 patients with the irritable colon syndrome were considered to have intolerance to specific foods. However, there was no close correlation between a clinical history of intolerance to one or more of the ingredients of the standard meal on the one hand and the response of the large intestine to the meal on the other.

Although Almy and Kern (1952) reported inhibition of colonic motor activity by acetylcholine, it has been repeatedly shown that cholinergic stimulation augments the motility of the large intestine (Adler et alii, 1942; Atkinson et alii, 1943; Fink and Friedman, 1960; Chaudhary and Truelove (1961c). It has also been proposed by Chaudhary and Truelove (1961c) that increased sensitivity of the colon to parasympathetic stimulation is common to all patients with the irritable colon syndrome and may therefore be a factor in the pathogenesis of this disorder. However, these authors did not submit a statistical evaluation of the effect of Prostigmine observed in their study. The present work did not support the concept of heightened reactivity to parasympathetic stimulation. Although intramuscular Prostigmine caused a significant increase in motility both in control subjects and patients with the irritable colon syndrome, the differences between the response of the control subjects on one hand and the responses of patients with the spastic colon and with functional diarrhoea on the other were not statistically significant.

It seems likely that some of the currently accepted views of the irritable colon syndrome may need to be modified. Firstly, it has been generally held that psychogenic factors are of aetiological significance

(Kalser et alii, 1956; Kirsner and Palmer, 1958; Chaudhary and Truelove, 1961d). While this may be true in a proportion of the cases, the findings of the present study indicate that emotional stress may also aggravate diarrhoea due to organic alimentary disease. Furthermore, where a tendency to diarrhoea exists due to local disease of the small or the large intestine, nervous tension may precipitate an attack. In such cases the clinical history may lead to an erroneous initial diagnosis of functional alimentary disorder as happened in the present study. It is therefore suggested that the role of psychogenic factors in the irritable colon syndrome is a dual one: emotional stress may have aetiological significance in a proportion of the cases but more commonly it appears to play the role of an aggravating factor. The mechanism whereby emotions exert their influence on the intestine may be through increased susceptibility of the intestine to parasympathetic stimulation as suggested by Chaudhary and Truelove (1961c), although the findings of the present work do not support this hypothesis.

Secondly, there are some studies which suggest that the irritable colon syndrome may not be of purely colonic origin (Goin, 1952; Friedman, 1954; Horowitz and Farrar, 1962). The possible role of the small intestine in this disorder is as yet unknown, and the manometric studies of the small intestine in the present work were too few to permit valid conclusions. The problem is worth future investigation particularly with radiotelemetering techniques. Furthermore, although functional diarrhoea and the spastic colon are held to be variants of the same disorder, objective evidence to support this concept does as yet not exist.

It appears likely that future studies will disclose that organic disorders account for the symptoms of many patients who are at present considered to have the irritable colon syndrome. Recently some patients with diarrhoea and intolerance to specific sugars have been shown to have deficiencies of various intestinal mucosal disaccharidases (Auricchio, Rubino, Landolt, Semenza and Prader, 1963; Anderson, Messer, Townley and Freeman, 1963). Perhaps the food intolerance which is seen commonly in patients with the irritable colon syndrome is the result of genetic or acquired enzyme disturbances in the small intestine.

The mechanism of forward transport of intestinal contents has long been debated. It has been suggested that in the small intestine waves of type III are responsible for propulsion (Posey et alii, 1948; Chapman and Palazzo, 1949; Chapman et alii, 1950; Rowlands et alii, 1950b; Daniel et alii, 1959). Type I activity may also be concerned with propulsion in the small intestine because this activity has been recorded during the expulsion of faeces through enteric stomas (Daniel et alii, 1959). Propulsion in the large intestine has been attributed to waves of types I, II and III (Posey et alii, 1948, 1951). It has, however, been suggested that none of these wave forms are in themselves propulsive but that transport of the contents of the small and large intestine will take place only when two or more functional segments of the intestine contract synchronously (Adler et alii, 1941; Posey et alii, 1951). Finally, Kern et alii (1951) proposed that forward transport in the colon depended entirely on waves of type IV.

As mentioned earlier in this Chapter, correlation of the cine-radiographic and the manometric studies in the present investigation indicated that no single wave form was solely responsible for propulsion in the small intestine. It was therefore suggested that forward transport was due to the pressure gradient established by high levels of motor activity in the upper small intestine and a progressive decrease in activity in the lower jejunum and ileum. The relative inactivity of the terminal ileum in two control subjects was shown in Table XV (studies 35(1) and 38(1)).

The mechanism of transport in the large intestine remains to be considered. The results of the simultaneous pressure recordings from the proximal and distal large intestine (Table XIV) provided some information in this regard:

> Judged by the motility index all the control subjects had more motor activity in the distal colon than in the proximal colon during the resting phase;
>
> Prostigmine, and to a lesser extent, food, reversed the situation by inducing more activity in the proximal colon than in the sigmoid colon and rectum;
>
> One patient with constipation and steatorrhoea had

considerably more activity in the distal large intestine than in the right colon during all phases of the recording; Finally, in the patient with diarrhoea due to systemic mastocytosis the ascending colon was more active even during the resting phase than the distal large intestine and the difference became more marked after food and Prostigmine.

Although it is appreciated that the number of studies is small, these findings nevertheless suggest that a reversible pressure gradient exists in the large intestine. This gradient could be expected to effect a slow distalward movement of the contents of the large intestine as long as the proximal colon was more active than the sigmoid colon. Although no examples of type IV waves were seen in this study, it is possible that the slow analward transport could be augmented by infrequent but powerful waves of this type (Connell, 1962; Ritchie et alii, 1962).

Constipation could be expected to occur under three different sets of circumstances. Firstly, if the pressure gradient because of hypermotility of the sigmoid colon was predominantly directed away from the anus, filling of the rectum would be slow. Such hypermotility of the sigmoid colon and rectum has been shown to occur in patients with the spastic colon by Chaudhary and Truelove (1961b) and in the present study. Secondly, low levels of motor activity throughout the intestine as seen after prolonged misuse of cathartics (case 30) should result in constipation; hypothyroidism could have a similar effect on the intestine. This disturbance of motility may be the basis of what is commonly referred to as atonic constipation. In the third variety of constipation, sometimes referred to as simple dyschezia, intestinal motility may be normal in the early stages and the mechanism of constipation is probably the diminished sensitivity of the rectum to distension (Truelove and Reynell, 1963). The diminished sensitivty may be an accompaniment of the ageing process (Roth, Fein and Sturman, 1957) or it may be caused by repeated voluntary suppression of the defaecation reflex.

Accelerated transport of intestinal contents leading to diarrhoea would occur if the pressure gradient were constantly directed toward the anus instead of being directed away from the anus in the resting bowel. Such a constantly unidirectional pressure gradient would be the result of the diminished or abolished motility of the distal large intestine showed by Connell (1962) and by the present work to occur in diarrhoeal states. This concept is supported by the fact that the contractions of the sigmoid colon are now believed to delay rather than to accelerate the transport of faeces to the rectum (Connell, 1962; Ritchie et alii, 1962). The pressure gradient and thus transport could be further augmented by an increase in the motility of the small intestine or proximal colon. It may be significant that in the present study the standard meal induced marked hypermotility of the small intestine in two patients with functional diarrhoea and that both patients had noticed aggravation of the diarrhoea by the constituents of the meal.

The reason for the quiescence of the sigmoid colon and rectum and possibly the hypermotility of the small intestine and proximal colon in diarrhoea is unexplained. Simple parasympathetic stimulation is unlikely because Prostigmine augments the motility of the distal large intestine although it accelerates transport by the even more pronounced stimulation of the proximal colon shown by Fink and Friedman (1960). It is therefore of interest that 5-hydroxytryptamine which causes increased motility of the small intestine (Hendrix et alii, 1957) has been reported to augment motor activity in the proximal colon while abolishing the contractions of the distal large intestine (Fink and Friedman, 1960). These effects of 5-hydroxytryptamine were confirmed in the present study and would be well suited to accelerate transport through the intestine. Similar changes in motility are suggested as the motor component of diarrhoea. Diarrhoea may be one of the manifestations of the increased production of 5-hydroxytryptamine associated with metastatic carcinoid tumours. It is also of interest, that although the 24-hour excretion of 5-HIAA has been reported to be normal in the irritable colon syndrome (Kowlessar, Williams, Law and Sleisenger, 1958) there is evidence that short periods of excessive release of 5-hydroxytryptamine may not be reflected in the 24-hour excretion of the metabolite (Peltola and Leppänen, 1963).

It is appreciated that the number of simultaneous pressure recordings from the proximal and distal colon was small. There is thus ample scope for future work and it is felt that an approach along the following lines would provide important information:

simultaneous studies should be made of the motility of the proximal and distal colon in normal subjects and patients with diarrhoea to confirm or refute the small number of experiments in the present study;

the *in vivo* effect of 5-hydroxytryptamine on the large intestine should be confirmed in view of the report by Fishlock and Parks (1963) that this substance inhibits the contractions of isolated muscle strips from all parts of the colon;

the effect on motility of drugs which antagonise the action of 5-hydroxytryptamine could well be studied in patients with diarrhoea;

if one of the drugs tested was found to reverse the changes in motility associated with diarrhoea it should be subjected to a clinical trial;

finally, estimation of the excretion of 5-HIAA in repeated two-hour specimens of urine from patients with the irritable colon syndrome should demonstrate whether intermittent hyperserotoninaemia is responsible for the diarrhoea which is a feature of this disorder.

CHAPTER VI

SUMMARY

The motor activity of the digestive tract in man has previously been investigated by a large number of methods. Valuable information on the motility of the small and the large intestine has been obtained by means of direct observation, balloons, open ended catheters, radio-telemetering capsules, electromyography and radiography. Studies have been made of the effects on motility of emotion, food and drugs and of the behaviour of the intestine in peptic ulceration, the irritable colon syndrome, ulcerative colitis and other alimentary disorders.

However, progress in the field of motility has been retarded by a number of factors. By necessity, many of the early studies were made with equipment which was only capable of providing information of a purely qualitative nature. Even in later work quantitative analysis of the records has often been neglected and statistical evaluation of the results has rarely been performed. Furthermore, the range of motility of the small intestine in normal subjects has not hitherto been defined. Finally, the interpretation of the function of the various wave forms encountered in motility tracings has been largely speculative. With regard to the large intestine, this deficiency has been partly rectified by recent correlative manometric and cineradiographic studies. However, in respect of the small intestine, the function of the waves has not been adequately studied.

Intestinal motility is necessary for the processes of transport, mixing, absorption and excretion which are the chief functions of the digestive tract. Moreover, disturbances of motility may be of importance in a number of disorders affecting the alimentary tract. The post-prandial distress following gastric surgery is of considerable practical importance because of the frequency with which it occurs and because of the adverse effect it may have on the maintenance of adequate nutrition. The motor behaviour of the small intestine has been reported to be abnormal in the dumping syndrome but there is disagreement on the nature of the abnormality and its role in the production of symptoms.

Changes in the motility of the large intestine in patients with the irritable colon syndrome have been demonstrated with modern techniques in one previous study. However, the results of this study have yet to be confirmed. Moreover, no statistical comparison has been made of the differences in motility between normal subjects and patients with the irritable colon syndrome.

It was therefore decided to apply the techniques of intraluminal pressure recording and cineradiography, separately and together, to the study of a number of aspects of intestinal motility. Chief of these were: the range of motor activity of the small and the large intestine in normal subjects and the effects on motility of emotion, food and Prostigmine; the behaviour of the small intestine in patients after partial gastrectomy with particular reference to changes in motility during the dumping syndrome; the motor activity of the large intestine in patients with the irritable colon syndrome; the activity of proximal and distal colon in patients with miscellaneous organic alimentary disorders with reference to the motor mechanism of constipation and diarrhoea; and finally, the correlation of intraluminal pressure tracings with the appearances of the intestine at cineradiography.

In the present investigation changes in intraluminal pressure were recorded mainly with open ended saline filled catheters connected to pressure transducers. In a small number of experiments the radio-telemetering capsule was used to record intraluminal pressures. Cine-radiographic studies were carried out using closed circuit television image intensification. The pressure tracings were subjected to qualitative inspection. In addition quantitative analysis was performed by measuring the amplitude and duration of each pressure wave and calculating the following parameters of motility: the percentage motor activity, the motility index, the mean amplitude of the waves, the mean duration of the waves and the distribution of the waves on the basis of amplitude and duration. The cine films were analysed by correlating the radiographic appearances of the intestine with the pressure waves of the manometric record.

Intestinal motility was investigated in 114 studies performed on eighty-nine subjects. The resting pattern of motility and the effects of food and Prostigmine on the small intestine were recorded in normal subjects, in patients with and without the dumping syndrome after partial gastrectomy and in patients with miscellaneous alimentary disorders. The motor activity in the resting large intestine and the effects on motility of emotion, food and Prostigmine were studied in a control group, in a group of patients with the irritable colon syndrome and in a miscellaneous group of patients with organic disorders affecting the alimentary tract. In addition, the effect of 5-hydroxytryptamine on the large intestine was investigated in a few control subjects.

The present investigation showed that in the control group there was considerable variation in the activity of closely adjacent segments both in the small intestine and the large intestine. There was more activity in the proximal than in the distal segments of the intestine. Furthermore, there was often a marked variation in motility between different subjects. However, when prolonged or repeated studies were made in the same subject there was a reasonable degree of reproducibility. Type I and type III waves were recognised in pressure tracings from the small intestine and waves of types I, II and III in recordings from the large intestine. Type IV waves were not observed. Correlation of the manometric records and the cine films from the small intestine showed that both type I and type III waves had propulsive function: thus forward transport of the contents of the intestine could not be attributed solely to waves of type III. Moreover, the progressive delay in the appearance of a wave in the leads of the pressure record did not necessarily indicate propulsion as to and fro movement of the barium contrast medium was also observed with this type of activity.

In the normal controls Prostigmine, but not food, enhanced the motility of the small intestine. With regard to the large intestine, emotion, food and Prostigmine all augmented the motor activity. In a small number of experiments, 5-hydroxytryptamine reduced or abolished the motility of the distal large intestine but augmented the activity of the proximal colon.

In the patients after partial gastrectomy the pressure tracings from the small intestine were qualitatively similar to those obtained from the control subjects. However, quantitative analysis revealed a number of differences:

The patients who had undergone gastric surgery generally had less activity in the proximal lead than in the more distal leads;

The patients with the dumping syndrome had a significantly higher resting level of activity than the control subjects;

The early response to food was one of reduced motility in those patients in whom attacks of "dumping" were provoked;

As the symptoms of "dumping" abated, the motility increased to levels above those of the resting phase;

By contrast the early response to food was increased motor activity of the small intestine in patients in whom the standard meal did not induce disagreeable symptoms;

Both groups of patients after gastrectomy had a more marked late response to food than did the control subjects and the difference between the patients without the dumping syndrome and the control group was statistically significant;

Prostigmine enhanced motility both in the control subjects and in the patients after gastric surgery.

It was considered that the hypomotility of the small intestine observed during induced attacks of "dumping" was not the cause of the symptoms but rather an accompanying phenomenon. However, it is likely that the motor behaviour of the small intestine during provoked attacks of "dumping" would enhance the influx of fluid into the lumen of the intestine and thus contribute to the severity of the vasomotor symptoms. The increased motility which constituted the late response to food in both groups of patients after gastrectomy, was considered to be due to rapid emptying of the gastric remnant.

The pressure tracings from the large intestine of patients with the irritable colon syndrome were qualitatively similar to tracings from normal subjects. However, there were quantitative differences:

Patients with the spastic colon had significantly higher levels of motility than patients with functional diarrhoea during all phases of the experiment;

Patients with the spastic colon had a more active resting pattern of motility than did the control subjects;

By contrast, during the resting phase patients with functional diarrhoea had significantly less motor activity than did the control subjects;

The emotive interview enhanced motility both in the control subjects and in the patients with the irritable colon syndrome;

Furthermore, a marked response of the colon was no more common in the patients with the irritable colon syndrome than in the normal controls;

Food augmented motility in all groups of subjects; however, amongst the patients with the irritable colon syndrome there was no close correlation between intolerance to any of the ingredients of the standard meal and the motor response of the colon;

Prostigmine significantly enhanced motor activity in all study groups;

Compared to the control subjects, patients with the spastic colon had a more marked response to Prostigmine and patients with functional diarrhoea had a less marked response.

Catheter studies performed on patients with diarrhoea due to organic alimentary disease showed that in these patients the motor activity of the colon was in all respects similar to that of patients with functional diarrhoea. In particular, a marked motor response of the colon to the emotive interview was equally common in both groups. It was therefore felt that in the irritable colon syndrome emotional stress played a role which was more often contributory than causative.

The results of a limited number of simultaneous recordings from the proximal and distal large intestine suggested the transport of the contents of the colon is attributable to a pressure gradient. This gradient was reversible in the control subjects, consistently directed away from the anus in the patient with constipation and constantly directed towards the anus in the patient with diarrhoea.

There are many aspects of intestinal motility which remain to be studied in future work. It would clearly be desirable to investigate further the motor activity of the small intestine in normal subjects and in patients with diarrhoea. The effect of drugs known to enhance motility could be assessed experimentally and clinically in patients with the dumping syndrome following partial gastrectomy. With regard to the large intestine, further work should be undertaken to confirm or refute the importance of a pressure gradient in the mechanism of constipation and diarrhoea. The effect of 5-hydroxytryptamine on the activity of the large intestine deserves further study. Moreover, the possibility of a relationship between intermittently excessive production of this substance and the irritable colon syndrome should be investigated. Finally, an experimental and clinical evaluation of drugs which antagonise the action of 5-hydroxytryptamine could lead to advances in the treatment of this disorder which continues to present a diagnostic and therapeutic problem.

APPENDICES

Appendix A

Date | U.R.

DEPARTMENT OF MEDICINE

INTESTINAL MOTILITY RECORD SHEET

I.

Name
Address
Private doctor
Hospital unit
Age

Sex M F (A)
Phone
Occupation

II. Diagnosis and Conclusion

Control (B)
Postgastrectomy (C)

State condition
State operation
vagotomy

Functional Alimentary Disorders (D)
Pain (E)
Diarrhoea (F)
Constipation (G)

Organic Alimentary Disorders (H)
Duodenal Ulcer (I)
Ulcerative Colitis (J)
Malabsorption Syndrome (K)
Diverticulosis (L)
Postoperative Gut (M)

General Medical Disorders (Mc)
State condition

III. Studies Performed

Duodenum (N) Small bowel (O) Large bowel (P)

Recording technique: catheters (Q) internal diameter

number location

radio pill (R) recording from to

transit time

Order of experiments:

Resting pattern (S) time

Meal (T) composition

Emotions (U) occupation, ambition, income, childhood, family life, sex life, fear of disease

Prostigmine (V) dose onset before activity

side effects

Other experiments (W) specify

Cineradiography (X)

Specify experimental periods: Film speed

Comments:

Comments on studies:

History

Presenting symptom (note quality, duration, relation to pregnancy, emotion, food, etc.)

Abdominal pain (Y)

Constipation (Z)

Diarrhoea (a)

Food intolerance (e) milk, tomatoes, eggs, fish, onions, apples, cabbage, chocolate, cucumber

Relieving factors

Laxative habits: No Yes (i) duration
frequency
agent and dose
effects (?tolerance)

Weight Change

Appetite

Diet

Alcohol

Drugs (o) Tobacco

Postgastrectomy symptoms

Dumping syndrome (u) (mild, moderate, severe)

State symptoms:

Precipitating factors:

Late postprandial syndrome (1)

Bilious vomiting (2)

Oesophageal reflux (3)

Past History

General medical illness - diagnosis, duration, treatment

G.I. operations (4) specify type
vagotomy
time interval
indication

Family history of G.I. illness or dysfunction:

Special Investigations

Haemoglobin: Occult blood:

Barium meal:

Barium enema:

Sigmoidoscopy:

Biopsy and other relevant investigations:

Total time of intubation:

Time of intubation from mouth to small intestine:

Total time of recording:

1. Distribution of Activity in Different Leads During Experimental Periods

		Rest	Emotion	Meal	Prostigmine	Others
Recorded time mins.						
Activity lead	I mins. (%)					
	lead II mins. (%)					
	lead III mins. (%)					
Mean activity $\left(\frac{I+II+III}{3}\right)$ mins.(%)						
Motility index	lead I					
	lead II					
	Lead III					
Mean motility index $\left(\frac{I+II+III}{3}\right)$						

2. Mean Amplitude and Mean Duration of the Intraluminal Waves During the Different Phases of the Experiment*

		Rest	Emotion	Meal	Prostigmine	Other
Amplitude (mm. Hg.)	range					
	mean					
Duration (sec.)	range					
	mean					
No. waves/unit time	range					
	mean					
Rhythmicity	Yes No					

*The values for each lead and the mean for the three leads were calculated separately for the different phases of the experiment.

3. Distribution of Waves on Amplitude-Duration Basis*

Duration (sec.)	0 - 5	6 - 10	11 - 15	16 - 30	31 - 60	61 - 120	131 - 300	> 300
Phase								
AMPLITUDE (mm.Hg.)								
0 - 5								
6 - 10								
11 - 15								
16 - 20								
21 - 25								
26 - 30								
31 - 35								
36 - 40								
41 - 45								
46 - 50								
51 - 55								

*The values for each lead and the mean for the three leads were calculated separately for the different phases of the experiment.

4. Distribution of Waves on the Basis of Duration*

Duration (sec.)	0 - 20	21 - 40	> 40
No. waves per hour			

*Calculated separately for the different phases of the experiment.

5. Distribution of Waves on the Basis of Amplitude*

Amplitude (mm. Hg.)	0 - 10	11 - 20	> 20
No. waves per hour			

*Calculated separately for the different phases of the experiment.

6. Percentage Increase (+) or Decrease (-) in Activity During Various Phases of Experiment Compared with Resting Pattern*

	Emotion	Meal	Prostigmine	Others
Activity lead I				
lead II				
lead III				
Lead I + II + III				

*Based on comparison of motility indices.

Appendix B

The names and unit numbers of subjects who underwent studies of intestinal motility

I. Control Subjects

	Name	Studies*	Hospital unit no.
1	Collins, J.	S L C	Yatala
2	Farmer, R.	S C	16935/62
3	Hammerstein, R.	S L C	Yatala
4	Herold, E.	S L C	Yatala
5	Howard, M.	S C	Yatala
6	Onofreiczuk, I.	S C	13503/62
7	Whenan, A.	C	Yatala
35	Ash, K.	L C R	Yatala
36	Brace, D.	L	Yatala
37	Bramley, M.	L	22882/62
38	Carson, L.	L C R	Yatala
39	Crispin, V.	L C	23656/62
40	Dunn, M.	L	Yatala
41	Edwards, M.	L	010829
42	Hepburn, A.	L	Yatala
43	Hilmi, L.	L R	018141
44	Josephs, K.	L C R	Yatala
45	McNeish, W.	L R	Yatala
46	Pritchard, C.	L	Yatala
47	Richardson, J.	L C	19485/62

*Abbreviations:
S = catheter studies of the small intestine
L = catheter studies of the large intestine
C = cineradiography
R = radiotelemetering

48	Stewart, J.	L		16545/62
49	Wilson, J.	L		Yatala
50	Wright, W.	L		Yatala
51	Yates, R.	L	R	Yatala
52	Yeing, G.	L	C	Yatala

II. Patients who had undergone partial gastrectomy

	Name	Type of operation	Time since operation	Studies		Hospital unit no.
8	Francis, C.	Billroth I	4 years	S	C	1473/62
9	Martin, W.*	Billroth I	1 year	S	C	015192
10	Spercu, P.*	Billroth I	8 years	S	C	25265/62
11	Ball, D.	Polya	5 years	S		19224/62
12	Barrett, S.*	Polya	16 years	S	C	23399/62
13	Buffett, W.	Polya	6 years	S	C	16478/62
14	Childs, E.	Polya	13 years	S	C	15710/62
15	Cooper, P.	Polya	11 years	S	C	26435/62
16	Dillon, C.*	Polya	10 years	S	C	25667/62
17	Galvin, P.*	Polya	14 years	S	C	22348/62
18	Heyen, H.	Polya	5 years		C	23060/62
19	Hutchins, L.	Polya	14 years	S	C	24142/62
20	Lucieer, V.	Polya	6 years	S	C	24522/62
21	O'Malley, F.	Polya	8 years	S	C	24892/62
22	Slater, H.	Polya	17 years	S	C	21186/62
23	Sloan, L.	Polya	7 years	S	C	19608/62
24	Smith, B.	Polya	6 years	S	C	19917/62
25	Stepanovic, M.*	Polya	2 years	S	C	26036/62
26	West, K.	Polya	11 years	S		18464/62

*An attack of "dumping" was induced in these patients.

III. Patients with the irritable colon syndrome

	Name	Studies	Hospital unit no.
27	Roberts, M.*	S L C	15593/62
28	Robertson, L.*	S L C	Yatala
29	Smith, G.	S L C	008741
53	Curgenven, M.	L	17238/62
54	Faulkner, J.	L	O.P.D.
55	Furler, D.	L	O.P.D.
56	Harmstorf, J.*	L	15440/62
57	Hutton, J.*	L C	O.P.D.
58	Johansen, A.	L	O.P.D.
59	Johns, E.*	L	O.P.D.
60	Kollias, S.	L	O.P.D.
61	Lane, E.*	L	O.P.D.
62	Lymberopoulos, A.*	L	O.P.D.
63	Neeb, H.*	L	O.P.D.
64	Parsons, C.	L	O.P.D.
65	Roder, R.*	L C	22438/62
66	Secker, M.*	L	O.P.D.
67	Valeiko, E.*	L R	O.P.D.

*The asterisked patients had functional diarrhoea; the remaining patients had the spastic colon.

IV. Patients with miscellaneous disorders*

	Name	Studies	Hospital unit no.
30	Catchpool, A.	S L C	009084
31	Evans, R.	S C	16992/62
32	Lockwood, R.	S C	18754/62
33	Veale, M.	S L C	13571/62
34	Walden, S.	S L C	12813/62
68	Lambert, V.	L	001428
69	McDonald, G.	L	21878/62
70	Murdoch, M.	L	21866/62
71	White, H.	L	18422/62
72	Dobbin, M.	L	013425
73	Cox, P.	L	012533
74	Bowyer, S.	L R	014809
75	Bannister	L	25365/62
76	Harley, E.	L	007334
77	Hudson, E.	L	O.P.D.
78	Martin, F.	L	18474/62
79	Morgan, M.	L	O.P.D.
80	Hatcher, C.	L	O.P.D.
81	Hagen, I.	L	Q.E.H. O.P.D.
82	Hall, M.	L	15090/62
83	Olafsen, H.	L R	016744
84	Poletti, G.	L	O.P.D.
85	Ryan, C.	L	15554/62
86	Sierp, E.	L	24009/62
87	Sumner, J.	L	Q.E.H. 026384
88	Tonkin, M.	L	O.P.D.
89	Wiles, L.	L C	20863/62

* The diagnoses in the patients in this group are presented on pp 87 to 88 and in Table II.

REFERENCES

Abbott, W.O., Hartline, H.K., Hervey, J.P., Ingelfinger, F.J., Rawson, A.J. and Zetzel, L. (1943), "Intubation studies of the human small intestine. XXI. A method for measuring intra-luminal pressures and its application to the digestive tract", J. clin. Invest., 22, 225.

Adler, H.F., Atkinson, A.J. and Ivy, A.C. (1941), "A study of the motility of the human colon: An explanation of dysynergia of the colon, or of the 'unstable colon'", Amer. J. dig. Dis., 8, 197.

Adler, H.F., Atkinson, A.J. and Ivy, A.C. (1942), "Supplementary and synergistic action of stimulating drugs on the motility of the human colon", Surg. Gynec. Obstet., 74, 809.

Almy, T.P. (1951), "Experimental studies on the irritable colon", Amer. J. Med., 10, 60.

Almy, T.P., Abbott, F.K. and Hinkle, L.E. (1950), "Alterations in colonic function in man under stress. IV. Hypomotility of the sigmoid colon, and its relationship to the mechanism of functional Diarrhoea", Gastroenterology, 15, 95.

Almy, T.P., Hinkle, L.E., Berle, B. and Kern, F. (1949b), "Alterations in colonic function in man under stress. III. Experimental production of sigmoid spasm in patients with spastic constipation", Gastroenterology, 12, 437.

Almy, T.P. and Kern, F. (Jr.) (1952), "The effects of acetylcholine and metacholine upon the human colon", J. clin. Invest., 31, 555.

Almy, T.P., Kern, F. and Tulin, M. (1949a), "Alterations in colonic function in man under stress. II. Experimental production of sigmoid spasm in healthy persons", Gastroenterology, 12, 425.

Almy, T.P. and Tulin, M. (1947), "Alterations in colonic function in man under stress: Experimental production of changes simulating the 'irritable colon'", Gastroenterology, 8, 616.

Alvarez, W.C. (1914), "Functional variations in contractions of different parts of the small intestine", Amer. J. Physiol., 35, 177.

Alvarez, W.C. (1919), "The metabolic gradient underlying peristalsis", J. Amer. med. Ass., 73, 1438.

Alvarez, W.C. (1924), "Intestinal autointoxication", Physiol. Rev., 4, 352.

Amdrup, E. (1961), "Variations in food tolerance after partial gastrectomy. The relationship between pathological findings at operation and type and intensity of postgastrectomy symptoms", Acta chir. scand., 120, 410.

Amdrup, E. and Balslev-Jørgensen, J. (1957a), "The influence of posture on the 'dumping' syndrome", Acta chir. scand., 113, 307.

Amdrup, E. and Balslev-Jørgensen, J. (1957b), "Fluid diffusion to the small intestine after intestinally injected hypertonic glucose solutions and its relationship to the dumping syndrome", Acta chir. scand., 113, 313.

Amdrup, E. and Balslev-Jørgensen, J. (1959), "Fluid diffusion and absorption in different parts of the small bowel and their relationship to postgastrectomy symptoms", Acta chir. scand., 116, 222.

Amdrup, E. and Walbom-Jørgensen, S. (1962), "Flow of fluid into the small intestine after intraintestinal injection of hypertonic glucose solutions as influenced by degree of peristalsis. Effect of vagotomy and various drugs", Acta chir. scand., 124, 333.

Anderson, C.M., Messer, M., Townley, R.R. and Freeman, M. (1963), "Intestinal sucrase and isomaltase deficiency in two siblings", Pediatrics, 31, 1003.

Andrew, R. (1954a), "Gastric and intestinal motility studies with morphine, atropine, hexamethonium bromide and 'banthine'", Aust. Ann. Med., 3, 305.

Andrew, R. (1954b), "Gastric, duodenal and jejunal motility in man; physiological studies by balloon-kymography", Aust. J. exp. Biol. med. Sci., 32, 479.

Atkinson, A.J., Adler, H.F. and Ivy, A.C. (1943), "Motility of the human colon. The normal pattern, dyskinesia and the effect of drugs", J. Amer. Med. Ass., 121, 646.

Auricchio, S., Rubino, A., Landolt, M., Semenza, G. and Prader, A. (1963), "Isolated intestinal lactase deficiency in the adult", Lancet, 2, 324.

Bachrach, W.H., Brody, M. and Drury, D.R. (1951), "The multiple simultaneous recording of gastrointestinal functions", Gastroenterology, 18, 609.

Bachrach, W.H., Rowen, B.R., Halsted, J.A., Schapiro, H., Holmström, W. and Price, P. (1954), "A critical analysis of the criteria for the clinical evaluation of anticholinergic and spasmolytic drugs in gastroenterology", Acta med. scand., supp. 288.

Bailey, N.T.J. Statistical Methods in Biology. The English Universities Press Ltd., London, 1959.

Baker, S.J. and Hughes, A. (1960), "Multiple-retrieving small-intestinal biopsy tube", Lancet, 2, 686.

Barbero, G.J., Ih Kim Chim, Davis, J. (1958), "Duodenal motility patterns in infants and children", Pediatrics, 22, 1054.

Bingham, J.R., Ingelfinger, F.J. and Smithwick, R.H. (1950), "The effects of sympathectomy on the motility of the human gastro-intestinal and biliary tracts", Gastroenterology, 15, 6.

Blankenthorn, D.H., Hirsch, J. and Ahrens, E.H. (1955), "Transintestinal intubation: Technic for measurement of gut length and physiologic sampling at known loci", Proc. Soc. exp. Biol. (N.Y.), 88, 356.

Brody, D.A. and Quigley, J.P. (1947), "Intralumen pressures of the stomach and duodenum in health and disease", Gastroenterology, 9, 570.

Brody, D.A., Werle, J.M., Meschan, I. and Quigley, J.P. (1940), "Intralumen pressures of the digestive tract, especially the pyloric region", Amer. J. Physiol., 130, 791.

Brookes, V.S., Waterhouse, J.A.H. and Thorn, P.A. (1960), "Partial gastrectomy for peptic ulcer", Gut, 1, 149.

Bülbring, E. and Lin, R.C.Y. (1958), "The effect of intraluminal application of 5-hydroxytryptamine and 5-hydroxytryptophan on peristalsis. The local production of 5-HT and its release in relation to intraluminal pressure and propulsive activity", J. Physiol., 140, 381.

Bülbring, E., Lin, R.Y.C. and Schofield, G. (1958), "An investigation of the peristaltic reflex in relation to anatomical observations", Quart. J. exp. Physiol., 43, 26.

Burge, H.W. (1960), "The surgery of peptic ulceration", Postgrad. Med. J., 36, 749.

Cannon, W.B. (1902), "The movements of the intestines studies by means of the Röntgen rays", Amer. J. Physiol., 6, 251.

Capper, W.M. and Welbourn, R.B. (1955), "Early post-cibal symptoms following gastrectomy. Aetiological factors, treatment and prevention", Brit. J. Surg., 43, 24.

Caroli, J., Porcher, P., Pequignot, G. and Delattre, M. (1960), "Contribution of cineradiography to study of the function of the human biliary tract", Amer. J. dig. Dis., 5, 677.

Chapman, W.P., French, A.B., Hoffman, P.S. and Jones, C.M. (1952), "Multiple balloon-kymograph recording of the effect of banthine, belladonna and placebos on upper-intestinal motility", New Engl. J. Med., 246, 435.

Chapman, W.P. and Palazzo, W.L. (1949), "Multiple-balloon-kymograph recording of intestinal motility in man with observations on the correlation of the tracing patterns with barium movements", J. Clin. Invest., 28, 1517.

Chapman, W.P., Rowlands, E.N., Taylor, A. and Jones, C.M. (1950), "Multiple balloon-kymographic recording of variations in motility of the upper small intestine in man during long observation periods before and after placebo administration", Gastroenterology, 15, 341.

Chaudhary, N.A. and Truelove, S.C. (1961a), "Colonic motility. A critical review of methods and results", Amer. J. Med., 31, 86.

Chaudhary, N.A. and Truelove, S.C. (1961b), "Human colonic motility: A comparative study of normal subjects, patients with ulcerative colitis, and patients with the irritable colon syndrome. I. Resting patterns of motility", Gastroenterology, 40, 1.

Chaudhary, N.A. and Truelove, S.C. (1961c), Part II "The effect of Prostigmin", Gastroenterology, 40, 19.

Chaudhary, N.A. and Truelove, S.C. (1961d), Part III "Effects of emotions", Gastroenterology, 40, 27.

Chaudhary, N.A. and Truelove, S.C. (1962), "The irritable colon syndrome", Quart. J. Med., 21, 307.

Christoffersson, E., Kewenter, J. and Kock, N.G. (1962), "Intestinal motility during provoked dumping reaction", Acta chir. scand., 123,405.

Code, C.F., Hightower, N.C. Jr., and Morlock, C.D. (1952), "Motility of the alimentary canal in man. Review of recent studies", Amer. J. Med., 13, 328.

Code, C.F., Rogers, A.G., Schlegel, J., Hightower, N.C. and Bargen, J.A. (1957), "Motility patterns in the terminal ileum: Studies on two patients with ulcerative colitis and ileac stomas", Gastroenterology, 32, 651.

Colcher, H., Goodman, E.N. and Katz, G.M. (1959), "Gastrointestinal mechanical and electrical activities after gastrectomy", Amer. J. Gastroent., 31, 408.

Connell, A.M. (1959), "Intraluminal Pressures in the pelvic colon", Proc. roy. Soc. Med., 52, 69.

Connell, A.M. (1961a), "The motility of the small intestine", Postgrad. Med. J., 37, 703.

Connell, A.M. (1961b), "Colonic motility in megacolon", Proc. roy. Soc. Med., 54, 1040.

Connell, A.M. (1961c), "The motility of the pelvic colon. I. Motility in normals and in patients with asymptomatic duodenal ulcer", Gut, 2, 175.

Connell, A.M. (1962), "The motility of the pelvic colon. Part II. Paradoxical motility in diarrhoea and constipation", Gut, 3, 342.

Connell, A.M., McCall, J., Misiewicz, J.J. and Rowlands, E.N. (1963), "Observations on the clinical use of radio pills", Brit. med. J., 2, 771.

Connell, A.M. and Rowlands, E.N. (1960), "Wireless telemetering from the digestive tract", Gut, 1, 266.

Cox, H.T. and Allan, W.R. (1960), "The dumping syndrome. Clinical and radiological aspects", Lancet, 2, 1261.

Crosby, W.H. and Kugler, H.W. (1957), "Intraluminal biopsy of the small intestine. The intestinal biopsy capsule", Amer. J. dig. Dis., 2, 236.

Cummins, A.J. and Almy, T.P. (1953), "Studies on the relationship between motility and absorption in the human small intestine", Gastroenterology, 23, 179.

Daniel, E.E., Carlow, D.R., Wachter, B.T., Sutherland, W.H. and Bogoch, A. (1959), "Electrical activity of the small intestine", Gastroenterology, 37, 268.

Daniel, E.E., Honour, A.J. and Bogoch, A. (1960), "Antagonism of serotonin-induced contraction and electrical activity in the ileum", Gastroenterology, 39, 62.

Daniel, E.E., Sutherland, W.H. and Bogoch, A. (1959), "Effects of morphine and other drugs on motility of the terminal ileum", Gastroenterology, 36, 510.

Davidson, M. and Bauer, C.H. (1958), "Studies on distal colonic motility in children. IV. Achalasia of the distal rectal segment despite the presence of ganglia in the myenteric plexuses of this area", Pediatrics, 21, 746.

Davidson, M. Sleisenger, M.H., Almy, T.P. and Levine, S.Z. (1956a), "Studies of distal colonic activity in children. II. Propulsive activity in diarrhoeal states", Pediatrics, 17, 820.

Davidson, M. Sleisenger, M.H., Almy, T.P. and Levine, S.Z. (1956b), "Studies of distal colonic activity in children. I. Non-propulsive patterns in normal children", Pediatrics, 17, 807.

Davidson, M. Sleisenger, M.H., Steinberg, H. and Almy, T.P. (1955), "Studies on distal colonic motility in children. III. The pathologic physiology of contenital megacolon - (Hirschsprung's disease)", Gastroenterology, 29, 803.

Deller, D.J. (1963), "Metabolic Effects of Partial Gastrectomy with Special Reference to Calcium, Folic Acid and Vitamin B_{12}". M.D. Thesis, University of Adelaide.

Drapanas, T., McDonald, J.C. and Stewart, J.D. (1962), "Serotonin release following instillation of hypertonic glucose into the proximal intestine", Ann. Surg., 156, 528.

Duthie, H.L. and McKellar, N.J. (1960), "Radiological appearances in the post-gastrectomy dumping syndrome", Brit. J. Radiol., 33, 171.

Edwards, D.A.W. and Rowlands, E.N. (1961), quoted by Connell, A.M. 1961a), Postgrad. Med. J., 37, 703.

Faik, S., Grindlay, J.H. and Mann, F.C. (1950), "Effect of vagotomy on intestinal activity", Surgery, 28, 546.

Farrar, J.T. (1961) in W.I. Card (Ed.) "Modern Trends in Gastro-enterology". Volume 3, p. 223-233 "Telemetering of Gastro-Intestinal Motility". Butterworths, London.

Farrar, J.T. and Bernstein, J.S. (1958), "Recording of Intraluminal gastrointestinal pressures by a radiotelemetering capsule", Gastroenterology, 35, 603.

Farrar, J.T. and Ingelfinger, F.J. (1955), "Gastrointestinal motility as revealed by study of abdominal sounds", Gastroenterology, 29, 789.

Farrar, J.T., Zworykin, V.K. and Baum, J. (1957), "Pressure-sensitive telemetering capsule for study of gastrointestinal motility", Science, 126, 975.

Feggetter, G.Y. (1959), "Treatment of chronic duodenal ulcer by vagotomy and posterior gastro-enterostomy", Proc. roy. Soc. Med., 52, 838.

Fetter, D., Barron, L. and Carlson, A.J. (1932), "The effect of induced hyperthyroidism on the gastrointestinal motility of vagotomized dogs", Amer. J. Physiol., 101, 605.

Fetter, D., and Carlson, (1932), "The effect of experimental hyper-thyroidism on gastro-intestinal motility", Amer. J. Physiol., 101,598.

Fink, S. (1959), "The intraluminal pressures in the intact human intestine", Gastroenterology, 36, 661.

Fink, S. and Friedman, G. (1960), "The differential effect of drugs on the proximal and distal colon", Amer. J. Med., 28, 534.

Fishlock, D.J. and Parks, A.G. (1963), "A study of human colonic muscle in vitro", Brit. med. J., 2, 666.

Foulk, W.T., Code, C.F., Morlock, C.G. and Bargen, J.A. (1954), "A study of the motility patterns and the basic rhythm in the duodenum and upper part of the jejunum of human beings", Gastroenterology, 26, 601.

Friedman, J. (1954) "Roentgen studies of the effects on the small intestine from emotional disturbances", Amer. J. Roentgenol., 72,367.

Gianturco, C. and Alvarez, W.C. (1932), "Roentgen ray motion pictures of the stomach", Proc. Mayo Clin., 7, 669.

Glazebrook, A.J. and Welbourn, R.B. (1952), "Some observations on the function of the small intestine after gastrectomy", Brit. J. Surg., 40, 111.

Goin, L.S. (1952), "Some obscure factors in the production of unusual small bowel patterns", Radiology, 59, 177.

Groisser, V.W. and Farrar, J.T. (1962), "Effect of intestinal motility on the absorption of sodium in man", Amer. J. dig. Dis., 1, 57.

Harper, A.A., Kidd, C. and Scratcherd, T. (1959), "Vaso-vagal reflex effects on gastric and pancreatic secretion and gastro-intestinal

Grützner (1898) quoted by Cannon, W.B. (1902) Amer. J. Physiol., 6, 251.

motility", J. Physiol., 148, 417.

Haverback, B.J., Hogben, A.M., Moran, N.C. and Terry, L.L. (1957), "Effect of serotonin (5 hydroxytryptamine) and related compounds on gastric secretion and intestinal motility in dog", Gastroenterology, 32, 1058.

Hedenstedt, S., Liljedahl, S.-O. and Mattsson, O. (1961), "Motility of the gastrointestinal tract after partial gastrectomy with special reference to operations with jejunal transposition", Acta chir. scand., 121, 448.

Helm, J.D., Kramer, P., MacDonald, R.M. and Ingelfinger, F.J. (1948), "Changes in motility of the human small intestine during sleep", Gastroenterology, 10, 135.

Hendrix, T.R., Atkinson, M., Clifton, J.A. and Ingelfinger, F.J. (1957), "The effect of 5-hydroxytryptamine on intestinal motor function in man", Amer. J. Med., 23, 886.

Higgins, J.A., Code, C.F. and Orvis, A.L. (1956), "The influence of motility on the rate of absorption of sodium and water from the small intestine of healthy persons", Gastroenterology, 31, 708.

Hightower, N.C. Jr. (1952), "Comparison of intraluminal pressures and motility patterns in the gastrointestinal tract of human beings when recorded by balloon and direct (electrical transducer) pressure systems", Fed. Proc., 11, 69.

Hightower, N.C., Code, C.F. and Maher, F.T. (1949), "A method for the study of gastrointestinal motor activity in human beings", Proc. Mayo Clin., 24, 453.

Hines, L.E., Lueth, H.C. and Ivy, A.C. (1929), "Motility of the rectum in normal and in constipated subjects", Arch. intern. Med., 44, 147.

Holaday, D.C., Volk, H. and Mandell, J. (1958), "Electrical activity of the small intestine with special reference to the origin of rhythymicity", Amer. J. Physiol., 195, 505.

Horowitz, L. and Farrar, J.T. (1962), "Intraluminal small intestinal pressures in normal patients and in patients with functional gastro-intestinal disorders", Gastroenterology, 42, 455.

Howe, C.T., Candy, J. Le Quesne, L.P., Hobsley, M. and Spence, M.P. (1962), "Effect of insulin on the dumping syndrome", Brit. med. J., 2, 1504.

Hunt, J.N. in Avery Jones E. (Ed.) "Modern Trends in Gastro-enterology", Butterworth & Co. London, 1958.

Illingworth, C.F.W. (1960), "Post-gastrectomy syndromes: A review", Gut, 1, 183.

Ingelfinger, F.J. (1943), "The modification of intestinal motility by drugs", New Engl. J. Med., 229, 114.

Ingelfinger, F.J. and Moss, R.E. (1943), "The motility of the small intestine in sprue", J. clin. Invest., 22, 345.

Irvine, R.O.H., O'Brien, K.P. and North, J.D.K. (1962), "Alpha methyl dopa in treatment of hypertension", Lancet, 1, 300.

Johnson, L.P., Sloop, R.D., Jesseph, J.E. and Harkins, H.N. (1962), "Serotonin antagonists in experimental and clinical 'dumping'", Ann. Surg., 156, 537.

Jordan, G.L., Barton, H.L. and Williamson, W.A. (1957b), "A study of motility in the gastric remnant following subtotal gastrectomy", Surg. Gynec. Obstet., 104, 257.

Jordan, G.L., Overton, R.C. and DeBakey, M.E. (1957a), "The post-gastrectomy syndrome. Studies on pathogenesis", Ann. Surg., 145, 471.

Kalser, M.H., Zion, D.E. and Bockus, H.L. (1956), "Functional Diarrhoea: an analysis of the clinical and Roentgen manifestations", Gastroenterology, 31, 629.

Kern, F., Almy, T.P., Abbot F.K. and Bogdonoff, M.D. (1951), "The motility of the distal colon in nonspecific ulcerative colitis", Gastroenterology, 19, 492.

Kewenter, J. and Kock, N.G. (1960), "Motility of the human small intestine. A method for continuous recording of intra-luminal pressure variations", Acta chir. scand., 119, 430.

Kewenter, J. and Kock, N.G. (1963), "Studies on intestinal motility during the first few days after partial gastrectomy and after cholecystectomy. II. Response to Prostigmine with and without jejunal feeding", Acta chir. scand., 125, 248.

Kewenter, J., Kock, N.G., Pompeius R. and Scheller, S. (1962), "A clinical and experimental study of palerol comp., a new spasmo-analgetic compound", Acta chir. scand., 123, 396.

Kim, I.C. and Barbero, G.J. (1963), "The pattern of rectosigmoid motility in children", Gastroenterology, 45, 57.

Kirsh, I.E. (1956), "Motility of the small intestine with non-flocculating medium. A review of 173 Roentgen examinations", Gastroenterology, 31, 251.

Kirsner, J.B. and Palmer, W.L. (1958), "The irritable colon", Gastroenterology, 34, 491.

Kock, N.G. (1963) "Studies on intestinal motility during the first few days after partial gastrectomy. I. Response to jejunal feeding", Acta chir. scand., 125, 241.

Koelle, G.B., Koelle, E.S. and Friedenwald, J.S. (1950), "The effect of inhibition of specific and non-specific cholinesterase on the motility of the isolated ileum", J. Pharmacol. exp. Therap., 100, 180.

Kowlessar, O.D., Williams, R.C., Law, D.H. and Sleisenger, M.H. (1958), "Urinary excretion of 5-hydroxyindoleacetic acid in diarrhoeal states, with special reference to nontropical sprue", New Engl. J. Med., 259, 340.

Legros and Onimus (1869), "Recherches experimentales sur les mouvements de l'intestin", Journal de l'anatomie et de la physiologie normales et pathologiques de l'homme et des animaux, 6, 37.

Le Quesne, L.P., Hobsley, M. and Hand, B.H. (1960), "The dumping syndrome. I. Factors responsible for the symptoms", Brit. med. J., 1, 141.

Liljedahl, S.O. Mattsson, D. and Pernow, B. (1958), "Cineroentgenography of the intestine with special reference to the effect of stimulating agents upon motility", Acta Radiol., 49, 348.

Liljedahl, S.O., Mattsson, O., Pernow, B. and Wallensten, S. (1959), "Cineroentgenographic studies of gastrointestinal motility in healthy subjects and in patients with gastric or duodenal ulcer. With special reference to various methods of gastrectomy and the dumping syndrome", Acta chir. scand., 117, 206.

Lipkin, M., Almy, T., and Bell, B.M. (1962), "Pressure-volume characteristics of the human colon", J. clin. Invest., 41, 1831.

Lorber, S.H. and Shay, H. (1954), "Technical and physiological considerations in measuring gastrointestinal pressures in man", Gastroenterology, 27, 478.

Lumsden, K., Chaudhary, N.A. and Truelove, S.C. (1963), "The irritable colon syndrome", Clin. Radiol., 14, 54.

Lumsden, K. and Truelove, S.C. (1959), "Intravenous pro-banthine in diagnostic radiology of the gastro-intestinal tract", Brit. J. Radiol., 32, 517.

Mackay, R.S. (1961), "Radio telemetering from within the body", Science, 134, 1196.

Mackay, R.S. and Jacobson, B. (1957), "Endoradiosonde", Nature, 179 (2), 1239.

McMahon, J., Code, C.F., Sauer, W.G. and Bargen, A.J. (1949), "A study of the action of Prostigmine on the bowel of human beings", Gastroenterology, 12, 970.

Mattsson, O., and Perman, G. (1962), "Small intestine transit time studied in patients with the dumping syndrome", Acta chir. scand., 124, 326.

Mattsson, O., Perman, G. and Lagerlöf, H. (1960), "The small intestine transit time with a physiologic contrast medium", Acta Radiol., 54,334.

Milton, G.W. and Smith, A.W.M. (1956), "The pacemaking area of the duodenum", Physiol., 132, 100.

Morris, G.C. Greenfield, L.J., Jordan, G.L., Peddie, G.H., Gordon, J.R., DeBakey, M.E. (1959), "Physiologic considerations in the dumping syndrome", Ann. Surg., 150, 90.

Muren, A. (1956), "Gastric motility after vagotomy in dogs", Acta chir. scand., 112, 98.

Peddie, G.H., Jordan, G.L. and DeBakey, M.E. (1957), "Further studies on the pathogenesis of the postgastrectomy syndrome", Ann. Surg., 146, 892.

Peltola, P. and Leppänen, V. (1963), "The possible role of serotonin in neuro-circulatory asthenia and functional cardiac disorders", Ann. Med. Int. Fenn., 52, 21.

Perman, G. and Mattsson, O. (1962), "The small intestine transit time in steatorrhoea", Acta med. scand., 171, 273.

v. Pfungen, R. (1887), "Versuche über die bewegungen des antrum pyloricum beim menschen", Centralblatt für Physiologie, 1, 220.

Posey, E.L. and Bargen, J.A. (1951), "Observations of normal and abnormal human intestinal motor function", Amer. J. med. Sci., 221, 10.

Posey, E.L., Dearing, W.H., Sauer, W.G., Bargen, J.A. and Code, C.F. (1948), "The recording of intestinal motility", Proc. Mayo Clin., 23, 297.

Quigley, J.P. and Brody, D.A. (1950), "Digestive tract: intralumen pressures: gastrointestinal propulsion, gastric evacuation, pressure-wall tension relationships", Medical Physics, 2, 280.

Quigley, J.P. and Brody, D.A. (1952), "A physiologic and clinical consideration of the pressures developed in the digestive tract", Amer. J. Med., 13, 73.

Quigley, J.P., Brody, D.A., McKay, B., Landolina, W.C. and McAlister, J.H. (1958), "Accurate registration of intralumen pressures of the digestive tract by two new methods", Fed. Proc., 9, 102.

Reid, P.E., Ivy, A.C. and Quigley, J.P. (1934), "Spiral propulsion of bolus in the intestine", Amer. J. Physiol., 109, 483.

Ritchie, J.A., Ardran, G.M. and Truelove, S.C. (1962), "Motor activity of the sigmoid colon of humans. A combined study by intraluminal pressure recording and cineradiography", Gastroenterology, 43, 642.

Ross, B., Watson, B.W. and Kay, A.W. (1963), "Studies on the effect of vagotomy on small intestinal motility using the radio-telemetering capsule", Gut, 4, 77.

Roth, H.P. and Beams, A.J. (1959), "The effect of vagotomy on the motility of the small intestine", Gastroenterology, 36, 452.

Roth, H.P., Fein, S.B. and Sturman, M.F. (1957), "The mechanisms responsible for the urge to defecate", Gastroenterology, 37, 717.

Rothnie, N.G., Kemp-Harper, R.A. and Catchpole, B.N. (1963), "Early postoperative gastrointestinal activity", Lancet, 2, 64.

Rowlands, E.N., Chapman, W.P., Taylor, A. and Jones, C.M. (1950a), "Multiple balloon-kymograph recording of the action of syntropan and of trasentin on the motility of the upper small intestine in man", Surg. Gynec. Obstet., 91, 513.

Rowlands, E.N., Chapman, W.P., Taylor, A. and Jones, C.M. (1950b), "Multiple balloon-kymograph recording of the comparative action of morphine and placebos on the motility of the upper small intestine in man", Surg. Gynec. Obstet., 91, 129.

Rowlands, E.N., Honour, A.J., Edwards, D.A.W., and Corbett, B.D. (1953), "Metal-capsule optical manometer for measuring pressure in the human gut with an open ended tube", Clin. Sci., 2, 299.

Rowlands, E.N. and Wolff, H.S. (1960), "The radio pill. Telemetering from the digestive tract", Brit. Comm. and Electr., 7, 598.

Schreiber, J. (1883), "Zur physikalischen untersuchung des oesophagus und des magens (mit besonderer berücksichtigung des intrathoracalen und intra-abdominalen drucks), Dtsch. Arch. klin. Med., 33, 425.

Schmid, E., Meythaler, K., Schön, H. and Henning, N. (1962), "Untersuchungen über die Ausscheidung von 5-hydroxyindoleessigsäute im Harm beim experimentell ansgelösten Dumping-Syndrom", Klin. Wschr., 40, 908.

Smith, A.N. (1962), Symposium: The Study of Normal and Disordered Function of the Small Intestine. Royal College of Physicians of Edinburgh Publication No. 17, pp 51 - 60. "Pressure Recording using the Radiotelemetering Capsule".

Smith, A.N. and Ridgway, M. (1962), "The use of telemetering capsules in disorders of the alimentary tract", Gut, 3, 366.

Smith, H.W., Texter, E.C., Stickley, J.H. and Barborka, C.J. (1957), "Intraluminal pressures from the upper gastrointestinal tract. II. Correlations with gastroduodenal motor activity in normal subjects and patients with ulcer distress", Gastroenterology, 32, 1025.

Spriggs, E.A., Code, C.F., Bargen, J.A., Curtiss, R.K. and Hightower, N.C. (1951), "Motility of the pelvic colon and rectum of normal persons and patients with ulcerative colitis", Gastroenterology, 19, 480.

Sprung, H.B. and Roisch, R. (1960), "Über die registrierung der dünndarm motilität mit dem intestinalsender", Gastroenterologia, 93, 145.

Streeten, D.H.P., Hirschowitz, B.I., Henley, K.S. and Pollard, H.M. (1957), "Effects of adrenocortical steroids on the propulsive motility of the small intestine", Amer. J. Physiol., 189, 108.

Templeton, R.D. (1928), "A new method of graphic representation of the motor activity of the empty stomach in intact animals", Amer. J. Physiol., 85, 512.

Templeton, R.D. and Lawson, H. (1931), "Studies in the motor activity of the large intestine. I. Normal motility in the dog, recorded by the tandem balloon method", Amer. J. Physiol., 96, 667.

Texter, E.C. (1961), "Fluorocinematography", Amer. J. dig. Dis., 6,983.

Texter, E.C. (1963), "Motility in the gastrointestinal tract", J. Amer. med. Ass., 184, 640.

Truelove, S.C. and Reynell, P.C. (1963), "Diseases of the Digestive System". Blackwell Scientific Publications, Oxford, 1963.

Uffelmann, J. (1877), "Beobachthungen und untersuchungen an einem gastrotomierten fiebernden knaben. Ein beitrag zur physiologie und pathologie der verdauung", Dtsch. Arch. klin. Med., 20, 535.

Vantrappen, G., Liemer, M.D. Ikeya, J., Texter, E.C. and Barborka, C.J. (1958), "Simultaneous fluorocinematography and intraluminal pressure measurements in the study of esophageal motility", Gastroenterology, 35, 592.

Vantrappen, G., Texter, E.C., Barborka, C.J. and Van Den Broucke, J. (1960), "The closing mechanism at the gastroesophageal junction", Amer. J. Med., 28, 564.

Wallensten, S., Garsten, P., Jonson, M. and Saltzman, G.F. (1959), "The dumping syndrome. I. Roentgencinematographic study of the motility of the small intestine in the dumping syndrome following partial gastrectomy", Acta chir. scand., 118, 117.

Watson, B.W., Ross, B. and Kay, A.W. (1962), "Telemetering from within the body using a pressure-sensitive radio pill", Gut, 3, 181.

Webber, B.M., Bender, M.A. and Moore, G.E. (1957), "Dumping syndrome. An evaluation of some current etiologic concepts", New Engl. J. Med., 256, 285.

Weeks, D.M. (1946), "Observations of small and large bowel motility in man", Gastroenterology, 6, 185.

Welsh, J.D. and Wolf, S. (1960), "Vascular responses in the exposed colon", Amer. J. dig. Dis., 5, 579.

Wener, J., Morton, H.S. and Polonsky, A. (1952), "The effects of vagotomy on colonic function: observations through a transverse colostomy in a patient with ulcerative colitis", Gastroenterology, 22, 250.

Wener, J. and Polonsky, A. (1959), "The reaction of the human colon to naturally occurring and experimentally induced emotional states: observations through a transverse colostomy in a patient with ulcerative colitis", Gastroenterology, 15, 84.

Wenger, M.A., Engel, B.T., Clemens, T.L. and Cullen, T.D. (1961), "Stomach motility in man as recorded by the magnetometer method", Gastroenterology, 41, 479.

Wood, I.J., Doig, R.K., Motteram, R. and Hughes, A. (1949), "Gastric biopsy. Report in fifty-five biopsies using a new flexible gastric tube", Lancet, 1, 18.