A RADIOTELEMETRY STUDY OF COLONIC MOTILITY IN PATIENTS WITH DIVERTICULAR DISEASE

A thesis submitted to the
University of Glasgow
for the degree of

Master of Science
in the
Faculty of Medicine

by

HEATHER ANNE THORBURN B.N., R.G.N.

Based on research conducted in the
University Department of Surgery
Glasgow Royal Infirmary

December, 1989.

CONTENTS **PAGE**

INDEX TO TABLES

TABLE **PAGE**

INDEX TO ILLUSTRATIONS

ACKNOWLEDGEMENTS

ACKNOWLEDGEMENTS

I would like to thank a number of people who have given me help and support during the course of this thesis. I am particularly grateful to Mr Ian G. Finlay, Consultant Surgeon, Glasgow Royal Infirmary, for giving me the opportunity to carry out this work and for his advice and encouragement. I wish also to thank Professor T.G. Cooke, St. Mungo Professor of Surgery, Glasgow Royal Infirmary, for his guidance and valuable assistance.

I am also grateful to Mr Kenneth Carter, Principal Physicist, Greater Glasgow Health Board, for his development of the new aerial and invaluable assistance with its laboratory and clinical evaluation. I wish also to acknowledge his continued support over the past two years.

My thanks also to Miss Jacqueline Goldberg, Registrar in Surgery, Glasgow Royal Infirmary, for her encouragement, support and, in particular, her friendship.

Mr Frank Toal and Mr Robert Rennie, University Department of Anaesthesia, Glasgow Royal Infirmary, have been extremely helpful in programming the Atari microcomputer.

I am grateful to Dr Gordon Murray, Senior Lecturer in Statistics, University Department of Surgery, Glasgow Royal Infirmary, for his advice and Dr Russell Pickard, Department of Radiology ,Glasgow Royal Infirmary, for his assistance in the classification of patients.

I wish also to thank Dr Robert Colson, Director, Remote Control Systems' Limited for his advice and permission to reprint the diagram of the radiopill.

Finally, thanks must be given to Mrs Winnie Hughes for her typing skills and advice and the Department of Medical Illustration, Glasgow Royal Infirmary, for diagrams.

This work was supported by a grant from Reckitt and Colman, Hull.

PRESENTATIONS AND PUBLICATIONS

PRESENTATIONS

Parts of this work have been presented at research meetings during the period of study.

A RADIOTELEMETRY PRESSURE STUDY OF THE EFFECT OF FIBRE THERAPY ON COLONIC MOTILITY IN PATIENTS WITH DIVERTICULAR DISEASE. - Presented at the Tripartite Meeting, Birmingham, June 1989.

IS THE GASTROCOLIC REFLEX ABSENT IN DIVERTICULAR DISEASE? - Presented to the Surgical Research Society of Great Britain and Ireland, Newcastle, July 1989.

RADIOTELEMETRY STUDIES OF COLONIC PRESSURE AND MOTILITY IN DIVERTICULAR DISEASE.- Presented at a symposium on "Functional and Related Disorders of the Large Bowel", Royal College of Physicians & Surgeons of Glasgow, November 1989.

PUBLICATIONS

Some aspects of this work have been accepted for publication. These are detailed below:-

Thorburn,H.A., Carter, K.B., Goldberg, J.A. & Finlay,I.G. (1989) Remote Control Systems' Radiotelemetry Receiver 7060: its use in clinical colonic motility measurement. Journal of Medical Engineering & Technology, 13, 252-256.

Carter, K.B., Thorburn, H.A., Finlay, I.G. & Goldberg, J.A. (1989) Novel multidirectional aerial for "near-field telemetry". Medical & Biological Engineering and Computing,27,631-634.

Thorburn,H.A., Goldberg,J.A., Carter,K.B. and Finlay,I.G. Is the gastrocolic reflex absent in diverticular disease? British Journal of Surgery. (Abstract- in press).

DECLARATION

DECLARATION

These studies were performed between September 1987 and September 1989 when I was a research nurse in the University Department of Surgery, Glasgow Royal Infirmary.

I declare that I am the sole author of this thesis. The patient investigations and data collection were carried out and processed by myself. Where assistance has been obtained from others such help has been freely acknowledged.

1: SUMMARY

1: SUMMARY

Diverticular disease of the colon has become increasingly prevalent in recent years. Reduced intake of dietary fibre resulting in a corresponding increase in intracolonic pressure is one hypothesis which has been suggested to be of importance in the pathophysiology of the disease. Fibre supplements have been prescribed empirically for this condition and promote symptomatic relief in the majority of patients. However, the relationship between fibre and colonic motility remains uncertain.

Studies performed using open-ended or balloon-tipped catheters have shown that diverticulosis is associated with raised parameters of colonic motility, although more recent work in asymptomatic patients with diverticular disease has failed to confirm this. The discrepancy may be due to the difference in technique used to measure colonic motility.

A non-invasive system for measuring colonic motility, based on a traditional pressure sensitive radiotelemetry capsule has been developed and validated. Patterns of intracolonic pressure associated with the pathophysiology of diverticular disease and fibre therapy have been re-examined.

Data from the studies described in this thesis has shown a link between certain parameters of colonic motility in the left hemicolon and severity of diverticular disease.

One parameter, the motility index increased with the severity of diverticular disease at rest, following food, and during sleep. The motility index of the right hemicolon has also been found to rise as the number of diverticula increase in the left hemicolon.

In another study reported here, four weeks of ispaghula therapy in patients with diverticular disease was shown to reduce whole gut transit time and increase motility, primarily by its effect in the right hemicolon.

The studies described in this thesis demonstrate changes in colonic motility associated with diverticular disease. Whether these changes are causal or result from the disease process cannot be established from the data. However, the technique for assessing colonic motility characterised here can be applied to future studies of diverticular disease and other colonic disorders.

2: HISTORICAL REVIEW

2: HISTORICAL REVIEW

2.1 General introduction

Diverticular disease of the colon and its clinical consequences have become increasingly prevalent among the population of Western countries (Almy & Howell,1980). This disease, almost unknown in 1900, has become one of the commonest afflictions of the colon (Painter & Burkitt, 1971). Indeed during an individual lifetime, the risk of developing colonic diverticula approaches 50% (Connell, 1977). Although most people with diverticulosis coli remain asymptomatic, the number of patients with symptomatic disease seeking medical help is increasing.

It has been demonstrated that patients with symptomatic diverticular disease have a raised colonic motility index (Arfwidsson and Kock,1964). In contrast, later studies in patients with asymptomatic diverticular disease have failed to confirm this (Eastwood, Smith et al, 1978; Howell et al,1978). It has also been shown that the diverticular colon develops an exaggerated response to the pharmacological stimulus of morphine (Painter & Truelove,1964b) and the physiological stimulus of eating (Arfwidsson & Kock,1964; Parks & Connell,1969). Results of colonic motility studies, however, may be influenced by the method of measurement (Parks and Connell,1969).

Historical and epidemiological studies suggest that a depletion in dietary fibre is involved in the pathogenesis of diverticular disease (Painter and Burkitt,1971; Burkitt et al,1972). Painter (1975) has argued that the propulsion of a small stool is associated with hypersegmentation of the colon and raised intraluminal pressures which results in mucosal herniation through the overlying muscle layers.

This hypothesis has resulted in the empirical treatment of diverticular disease with high fibre diets and fibre supplements. Although fibre therapy has been shown to promote symptomatic relief in most patients (Painter et al, 1972; Burkitt, 1975; Brodribb and Humphreys,1976), the effect of fibre on bowel motility is less clear (Eastwood, Brydon et al,1978).

Clearly, if the management of diverticular disease is to have a more rational basis, the pathophysiology of the disease requires further classification and this is the purpose of the studies described in this thesis.

2.2 Colonic motility measurements

Introduction.

Colonic motility is a term which encompasses two independent variables. It can refer to either the movements of the colonic wall or of faecal matter through the colonic lumen. The gross structure of colonic segments suggests that different patterns of flow and contraction may be associated with structurally different segments (Wingate,1983).

Methods of measuring gastrointestinal transit.

A variety of methods have been used to study the transit of materials through the gastrointestinal tract. These techniques can be classified as radiological, colorimetric, particulate and isotopic.

Radiological techniques.

Barium sulphate and bismuth subnitrate have previously been used as radiological markers (Holzknecht,1909;Ritchie et al,1971;Hertz and Newton,1913). This technique, however,is limited in that it can only determine the speed of transit of the head and tail of the marker column, leaving the transit pattern of the bulk of the radio-opaque solution undetermined . Furthermore, the administration of barium sulphate is thought to precipitate gastrointestinal

hurry, thus distorting the physiological normality of the measurements (Alvarez and Freedlander,1924).

Colorimetric techniques.

Coloured powders and glass beads have also been used to measure gastrointestinal transit (Alvarez & Freedlander,1924; Hoelzel,1930). This technique is thought to be of limited use as coloured powders are restricted to timing the first and last marker passed and the transit times of coloured glass beads is influenced by their specific gravity.

Particulate techniques.

A third method of studying gastrointestinal transit involves the administration of a given number of particles, for example radio-opaque pellets, which can be observed by taking serial radiographs of the abdomen or stool. This technique was developed by Hinton et al (1969), the total transit time corresponding to the time necessary for the excretion of 80% of the total number of ingested markers. In contrast to the findings of Hoelzel (1930), this study demonstrated a good correlation of transit times obtained from radio-opaque pellets, specific gravity 1.05 and 1.19 .

A later study by Metcalf et al (1987) comparing pellets of different shapes and sizes, confirmed these results. Other workers have administered radio-opaque markers over three consecutive days and calculated transit times by stool analysis on the fourth day but again this technique is restricted to measuring mouth to anus transit times and cannot determine the rate of progression of colonic contents through the various segments (Cummings and Wiggins,1976).

Since certain motility disorders may actually only involve localised colonic segments, several studies have been performed in an attempt to establish the rate of transportation of colonic contents through individual segments. These include a study performed to establish the mean segmental transit time of radio-opaque markers through the right colon, left colon and rectosigmoid areas of healthy adults and children. This involved the swallowing of twenty markers simultaneously and subsequent abdominal radiographs at twenty-four hour intervals until the markers were no longer apparent.Segmental transit times were calculated by applying a working formula which was independent both of the number of markers swallowed and the time interval between X-rays. Using this technique, the mean total colonic transit time did not differ significantly between adults and children. In the adult group, however, longer transit times were recorded through the right and left colon (Ahran et al,1981).

An alternative technique was established by Metcalf et al (1987) which measured segmental colonic transit times without exposing the patient to repeated X-radiation. Three sets of distinctive radio-opaque markers were ingested by twenty-four healthy persons on three consecutive days. Initially daily abdominal X-rays were performed until all the markers were passed. The results of this technique were then compared with calculations of transit times obtained from a single abdominal X-ray taken on the fourth day. There was close correlation between the techniques.

Isotopic techniques.

51-Cr labelled sodium chromate has also been used in transit studies but the recovery rate has been shown to be less than 85% (Hinton et al,1969). Other studies have enclosed radio-isotopic substances within a perspex capsule. Encapsulated 51-Cr (Holdstock et al,1970), 131-I (Rosswick et al,1967) and 57-Co (Ramsey,1965) have all been used in studies of gastrointestinal transit, thus enabling their movements within the gastrointestinal tract to be monitored. A similar experimental design has been developed by Misiewicz et al (1968), incorporating chromium within a radiotelemetry capsule, the pressure record indicating the location of the capsule and the propulsive activity being monitored by a collimated scintillation counter.

Methods of measuring colonic wall activity.

Colonic wall activity can be studied directly, by strain gauges attached to the muscle wall or indirectly, by sensors positioned within the colonic lumen (Wingate,1983). A variety of techniques have been used to investigate indirectly, the motor activity of the gastrointestinal tract; mainly balloon-tipped catheters, open-ended catheters, radiotelemetry capsules (Wingate,1983) and Gaeltec probes (Finlay et al,1986).

Initially, large air or water-filled balloons were used to study colonic wall activity. Their use was limited in that they responded not only to wall movements overlying the balloon, but to contractions occurring at a variable distance from the balloon (Connell,1968). Furthermore, the attempts of the colon to propel the tethered balloon created mechanical artefacts (Wingate,1983). Miniature balloons are able to record unstimulated colonic activity, but they too are affected by movements of the colonic wall (Wingate,1983).

Open-ended polyethylene catheters , continuously perfused with water, record intraluminal pressure changes resulting from colonic wall movements. They can, however, become blocked with bowel contents and are unable to distinguish between pressures generated near to or distant from their recording tips (Connell,1961;Wingate,1983).

The technique of bowel manometry employing open-ended or balloon-tipped catheters has several limitations. It involves the introduction of tubes or wires through the rectum, a procedure often requiring bowel preparation and causing some degree of bowel trauma. Moreover, orally and rectally administered laxatives used in bowel clearance before investigative procedures may increase the speed of transit of intestinal contents by primary effects on intestinal motility (B.N.F.,1988a). These investigations are often unpleasant and objectionable to the patient and may interfere with his/her emotional state, resulting in a possible "cephalic" reaction which might alter physiological conditions. In addition, bowel instrumentation may precipitate gastrointestinal pain, thus distorting the diagnostic picture (Connell et al,1963). Furthermore, the use of wires and tubes severely limits the length of the lower gastrointestinal tract which can be examined and enforced recumbancy is required for the duration of study (Painter and Truelove,1964a & b;Weinreich and Andersen,1976a & b).

The technique of radiotelemetry.

Following the availability of pressure endoradiosondes, "radiopills", in 1957, it was envisaged that they might play an important role in manometric investigation of the gastrointestinal tract (MacKay and

Jacobson,1957; Farrar et al,1957; Wolff,1961). The ingested radiopill is a theoretically more physiological means of studying colonic motility, eliminating bowel preparation and invasive instrumentation thus minimising patient discomfort and "cephalic" artefact.

In spite of these advantages, most investigators continued to rely on open-ended or balloon-tipped polyethylene catheters introduced per rectum (Painter and Truelove, 1964 a & b; Weinreich and Andersen,1976 a & b; Eastwood,Brydon et al,1978; Narducci et al,1987; Trotman and Misiewicz,1988) perhaps discouraged from using telemetry by technical problems such as signal loss and the degree of expertise which early telemetry systems required (Connell et al,1963).

Only a handful of workers have chosen the technique of radiotelemetry focussing largely on small intestinal motility. Horowitz and Farrar (1962) used the pressure-sensitive radiopill to investigate small intestinal pressures in both normal subjects and in those with functional gastrointestinal disorders. Radiotelemetry was also employed to study the effects of vagotomy on small intestinal motility (Ross et al,1963). A tethered ingested radiopill has also been used to record jejunal motility in healthy volunteers (Thompson et al,1980) and patients with irritable colon (Thompson et al,1979) and those with diarrhoea and constipation (Anders et al,1965).

Other workers have used radiotelemetry capsules to study colonic motility. Misiewicz et al (1968), investigated the effects of elevated body temperature and stress on colonic motility. Other studies of intraluminal pressures in the small intestine and proximal colon have employed radiotelemetry systems, but have continued to use air filled balloon-tipped catheters to record pressures within the rectosigmoid area (Holdstock et al,1969;Misiewicz et al,1969). Nevertheless the technique of radiotelemetry appears to be suitable for studying, in a more physiological manner, intraluminal pressures throughout the colon in diverticular disease.

Classification of colonic movements.

Movement within the human colon was first documented in the early 20th Century. Holzknecht (1909), during fluoroscopy , observed a form of colonic propulsion which he referred to as " mass peristalsis ". This described the distal progression of a contraction wave along a narrowed colonic section, devoid of haustration.

It was not until 1971 that Ritchie et al identified another form of peristaltic activity, "peristaltic ripples", which involved a number of progressive colonic contractions travelling more slowly than waves of mass peristalsis (<1cm/min), capable of transporting colonic contents in either direction. This peristaltic activity

predominated in the distal colon and effectively propelled viscid faecal matter (Ritchie,1968).

Hertz and Newton (1913) described a form of colonic activity which differed from that observed by Holzknecht. A uniform contraction of circular muscle around a distended colonic section produced an almost immediate propulsion of contents from this section. This was later termed "systolic propulsion" and was most commonly observed in the proximal colon where more liquid contents prevailed (Ritchie et al,1971).

In addition to the identification of "systolic" and peristaltic contractions, a form of segmental activity has been observed in which localised colonic wall contractions homogenise haustral contents but do not produce propulsion. This activity was commonly observed in the proximal colon (Ritchie,1968). Ritchie (1968) noted that this was the only activity seen in 38% of subjects at rest, suggesting a potential role of somatic activity in the transportation of colonic contents.

The influence of somatic activity on colonic propulsion was further examined in 1970 by Holdstock et al using a pressure-sensitive radiotelemetry capsule and radio-opaque pellets. They demonstrated that raised intracolonic pressure after food was rarely associated with propulsive activity in the resting patient but increased significantly with somatic activity. Indeed, colonic

motility studies in normal subjects and in patients with irritable bowel syndrome have illustrated the predominance of motor quiescence during sleep (Rosenblum & Cummins, 1954; Narducci et al,1987).

These different modes of transportation of colonic contents and other variables such as sleep and somatic activity suggest that there may be large individual variations in the rate of gastrointestinal transit.

Stimulated colonic activity in normal subjects.

Pharmacological stimuli.

Various studies have been performed to establish the effect of pharmacological stimuli on sigmoid motility in normal subjects. Painter and Truelove (1964b), using open-ended catheters found that the administration of therapeutic doses of morphine caused the normal colon to generate an increased number of pressure waves of amplitude usually less than 20mmHg but occasionally reaching 40mmHg. Pressures were found to occur independently at different recording sites, illustrating the ability of the sigmoid colon to segment in order to localise pressures in the vicinity of one recording tip (Painter,1964). A similar response was elicited following the administration of neostigmine methylsulphate (prostigmine) (Painter,1964; Arfwidsson and Kock,1964).

In contrast to these findings, the administration of pethidine 100mg intramuscularly reduced intrasigmoid pressures and decreased the tendency for segmentation (Painter,1964). Intrasigmoid pressures were further reduced by the administration of intravenous propantheline bromide which paralysed the bowel muscle (Painter,1964).

Physiological stimuli.

Other studies have investigated the colonic response to physiological stimuli. For example, the effect of eating on colonic activity has been documented since the turn of this century. Hertz (1909) referred to this as the "gastrocolic reflex" and, using radiological techniques, demonstrated large displacements of colonic contents post-prandially. Later studies, using balloon-tipped and open-ended catheters, have supported this phenomenon, observing an increase in both the wave frequency and total intrasigmoid pressure post-prandially (Arfwidsson and Kock,1964;Parks and Connell,1969). In a study by Misiewicz et al (1966) using a pressure-sensitive radiotelemetry capsule, intracolonic pressures increased with eating in both the proximal and distal colon although it was more apparent in the latter.

A more recent study by Narducci et al (1987) has shown that colonic motility was low before meals but significantly increased post-prandially. Most of this

activity was represented by low amplitude contractions but occasional high-amplitude propagating contractions (up to 200mmHg) occurred in the late post-prandial period or on early morning awakening. These contractions, termed giant migrating contractions by other workers (Karaus and Sarna,1987), are thought to be the manometric equivalent of mass movements and are often felt as an urge to defaecate.

The influence of stress on colonic motility has been investigated by several workers. Ritchie et al (1962) demonstrated sigmoid overactivity and inhibition which was attributable to some emotional response. Other workers have reported intracolonic pressure changes during stressful interviews (Almy and Tulin,1947;Almy et al,1949;Chaudary and Truelove,1961b). In contrast , Misiewicz et al (1968) using a radiotelemetry capsule were unable to detect any alterations in colonic motility attributable to stress induced by hand immersion in an ice/water mixture. The exact effect of stress on colonic motility has not been defined.

Analysis of intracolonic pressures.

Intraluminal pressure recordings can be either qualitatively or quantitatively analysed. Qualitative analysis was performed in early investigations of human colonic motility in an effort to classify waves of

different types. These studies described Type 1 waves, simple, monophasic waves of low amplitude (5-15 cmH_2O) with a duration of 5-20s; Type II, simple waves of greater amplitude (10-50 cmH_2O) and duration,12-60s, than Type 1, and Type III waves, complex waves involving a change in basal pressure on which waves of Type 1 and II are superimposed. All three types have been observed in normal subjects (Code et al,1952; Posey et al,1948;Posey and Bargen,1951). Type IV waves, large, simple waves;duration 1-2 minutes; amplitude 14-15 cmH_2O are described in patients with ulcerative colitis (Kern et al,1951;Spriggs et al,1951;Code et al,1952). However, other groups have found this classification unsatisfactory because it relies entirely on the subjective judgement of the observer (Davidson et al,1956;Chaudary and Truelove,1961a).

Later studies have selected a method of quantitative analysis which is independent of observer judgement. Total colonic motor activity has been mathematically calculated from recorded pressure traces and expressed in different ways. Chaudary and Truelove (1961a), calculated the product of the average height of pressure peaks (mmHg) multiplied by the percentage activity time over one hour and called this the "Colonic Motility Index". The result they obtained gave a number which was equivalent to twice the area under the pressure-time curve assuming a triangular waveform.

Connell, Avery-Jones and Rowlands (1965) in an analysis of post-prandial colonic activity, calculated an "index of total activity" by multiplying the mean wave amplitude by the percentage recording time during which pressure waves occurred. This index was later known by other workers as the colonic motility index (Attisha and Smith,1969;Weinreich and Anderson,1976a) although its method of calculation differed from that of Chaudary and Truelove (1961a).

2.3 Colonic structure in diverticular disease

Pulsion diverticula consist of a pouch of mucous membrane with a thin covering of longitudinal muscle which penetrates the colonic circular muscle to become situated in the pericolic fat and appendices epiploicae. Diverticular formation tends to occur at weak points in the muscle wall through which blood vessels, supplying the mucosa, penetrate. They commonly form two rows which run between the mesenteric and antimesenteric taeniae although, on occasions, a third row of small diverticula form between the two antimesenteric taeniae (Connell,1977). The sigmoid colon is affected in more than 90% of patients with diverticular disease (Hughes,1969a). More proximal colonic segments may be involved in the disease process but the rectum is never affected.

In addition to diverticular formation, there are other radiological and pathological features in diverticular disease which demonstrate a muscle abnormality within the sigmoid colon. The taeniae coli become thickened and cartilagenous and the circular muscle develops a thickened, corrugated appearance which narrows the colonic lumen. These muscular changes may affect the mucosal surface, producing folds of mucous membrane which can further occlude the colonic lumen. On occasions, this muscular abnormality has been noted in the absence of diverticula (Williams,1965: Hughes,1969b).

2.4 Aetiology and pathogenesis of diverticular disease

The fibre hypothesis.

Burkitt et al (1972) have been promoting the hypothesis that diverticular disease results from dietary changes which have occurred in western nations during the past century . The British diet changed markedly around the year 1880. The introduction of improved milling techniques reduced the consumption of bread, increased the use of refined sugar and reduced the fibre content of the diet . Painter and Burkitt (1971), claimed that diverticular disease took an estimated forty years to develop following alterations in the colonic environment. They believed that if this dietary change was responsible for the development of diverticular disease, then one would expect the incidence of the disease to increase in 1920 and, indeed, the condition was increasingly recognized in Britain at this time.

Gear et al (1979), however, pointed out that the association between increased prevalence of diverticular disease and decreased consumption of dietary fibre did not necessarily reflect a cause and effect relationship because dietary fibre intake may not be the only variable which exists between the two comparison groups. To investigate this they performed a study in Oxford which compared the incidence of symptomless diverticular disease in vegetarians and non-vegetarians. Vegetarians were found to

have a significantly lower incidence of diverticular disease (12%) than non-vegetarians (33%) carefully matched for age and sex , who were consuming significantly less vegetable, cereal and fruit fibre. They claimed that cereal fibre was the major component which protected the colon against diverticulosis. This reiterated the findings of a previous study by Burkitt,(1975).

Connell (1977) challenged the validity of the bran hypothesis as a complete explanation of the aetiology of diverticular disease. He argued that although the quantity of wheat bran consumed this century had probably diminished, it was difficult to substantiate the claim that the total dietary fibre content had been reduced.

Experimental work performed by Carlson and Hoelzel (1949) focused on the role of fibre on the aetiology of diverticular disease. They found that rats fed on a low residue diet developed diverticulosis whereas the disease did not develop in those rats given a bulk forming diet. They demonstrated that the colonic lumen narrowed in rats fed on a low residue diet and suggested that, in this situation, obstruction at the colonic flexures was more likely to occur, creating raised intracolonic pressures and consequent diverticula formation.

There are, however, important anatomical differences between human and rat colon. In man, nearly the whole of the colon is sacculated whereas no sacculated segments are

present in the rat colon (Christensen,1983). Such anatomical variables make it difficult to extrapolate directly from the animal work. Similar findings were demonstrated in a more recent study performed in New Zealand where white rabbits fed a low residue diet developed caecal diverticula (Hodgson,1975).

Primates are, perhaps, a more suitable animal model than rabbits and rodents as their colon is comparable anatomically to human colons and they consume a similar diet in terms of nutrient composition. In contrast to the rat and rabbit findings, a study of stump-tailed monkeys fed on a low fibre diet demonstrated the presence of raised intracolonic pressures but diverticula formation was not observed (Brodribb et al,1979).

Mechanical integrity of colonic wall.

The mechanical integrity of the colonic wall is another factor which is thought to have a bearing on the aetiology and pathogenesis of diverticular disease. For many years it has been accepted that a muscular disorder occurs in association with diverticular disease, but whether this abnormality is a primary or secondary factor in the causation of disease remains uncertain (Keith, 1910; Edward, 1939; Morson, 1963; Williams, 1963; Williams, 1965; Hughes, 1969b; Whiteway & Morson,1985).

It has been suggested that the physical properties of the bowel wall in diverticular disease have changed. Parks (1970) performed a study to assess colonic function after resection of the diverticular segment of colon. The response to stretch of the apparently normal remaining colonic muscle was similar to the unresected diverticular segments, though to a lesser extent. This, perhaps, implicates a functional disorder of the colonic wall which may have an important role in the causation of diverticular disease.

A more recent study investigating the effect of balloon distension of the distal colon in diverticular disease patients and normal subjects revealed a premature relaxation of the colonic wall in diseased colons suggesting that the inherent strength of the colon had diminished (Smith et al,1981). Collagen loses its flexability with increasing age and its tensile strength decreases, rendering the colon more susceptible to mucosal herniation (Johnson & Block,1985). In addition, there is a thickening of the circular and longitudinal muscle coats with age, accompanied by an increase in the amount of collagen, elastin and reticular fibres (Eastwood,1987). This could perhaps, partly explain the increasing prevalence of the disease with age.

The presence of diverticula in children (Rees & Griffen,1977) and young persons with the collagen disorders, Marfan's or Ehlers-Danlos syndromes, suggests that defective collagen may be an important factor in the disease aetiology (Cook, 1968; Beighton et al,1969).

This suspected abnormality of the colonic musculature was further investigated by Watters et al (1985). The different incidence of disease in Europeans and Africans led them to compare various mechanical properties of the colon in vitro and to determine whether such properties were demonstrated throughout the entire colon, whether they altered with advancing age and whether the changes detected influenced the formation of diverticula. They discovered that the tensile strength of the colon fell distally as the colonic wall thickness increased. This could, perhaps, explain why the sigmoid colon is affected in over 90% of patients with diverticular disease (Hughes,1969a).

The tensile strength of the colon in a Kampala group was greater than in an Edinburgh group. With advancing age, however, the tensile strength decreased significantly in both groups. The colon width at "burst" was greater in the Kampala group but this property also declined with age.

These findings suggest that the colonic mechanical properties may be influenced by environmental factors such as diet. Indeed, Burkitt et al (1972) have suggested that Africans demonstrate different colonic mechanical

properties from Europeans as they consume a higher fibre diet which produces larger stools and decreases the time of gastrointestinal transit.

Watters et al (1985), however, comparing the colons in Europeans subjects over fifty years of age with and without diverticular disease, detected no significant differences in the mechanical properties. They hypothesised that mechanical changes may have a primary role in the development of diverticular disease, rendering the colon more susceptible to diverticula formation rather than resulting from the disease. This reiterated the finding of Parks (1970).

It would seem, therefore, that certain segments of the colon are predisposed to developing the disease and that their mechanical properties change. It is more likely that this change is only one of several factors involved in the aetiology and pathogenesis of the disease.

Stimulated colonic activity in diverticular disease.

The role of raised intracolonic pressures in the aetiology of diverticular disease has been investigated by numerous workers. Arfwidsson and Kock (1964) showed that sigmoid activity in diverticular disease, measured by open-ended perfusion catheters, was greater than normal both under basal conditions and after stimulation with food

or prostigmine and postulated that muscular overactivity was a feature of diverticular disease. Other workers, however, refuted this finding (Painter and Truelove, 1964a &b; Painter et al,1965; Parks and Connell, 1969; Weinreich and Andersen,1976a & b; Leandro et al,1984).

Painter and Truelove (1964a & b) studied intracolonic pressure patterns at rest and following the infusion of morphine in healthy subjects and in patients with diverticular disease. Using open-ended perfusion catheters, they detected no significant differences between healthy and diseased subjects at rest but found that colonic segments bearing diverticula reacted excessively to this pharmacological stimulus producing pressures higher than those recorded in control subjects and, indeed, higher than those recorded from segments devoid of diverticula in the same subject. Future studies of colonic activity should perhaps focus on the relationship between intracolonic pressures and the severity of disease on x-ray.

Painter (1964) claimed that the absence of elevated intraluminal pressures at rest did not necessarily imply that abnormal intraluminal pressures were not involved in the development of the disease. He postulated that segments bearing diverticula may react excessively to certain physiological stimuli and produce pressure patterns similar to those observed following morphine and prostigmine infusion.

The effect of eating on the diverticular colon was examined by Parks and Connell in 1969. Different recording techniques were found to produce different results. Using a miniature balloon technique, overall colonic motility was similar in diverticular disease and health under basal conditions and post-prandially, whereas open-ended catheters detected an increase in basal and post-prandial activity in diverticular disease. However, it was not assumed that this necessarily reflected an increase in colonic wall activity because factors such as viscosity of bowel contents and colon diameter must be considered when interpreting pressure patterns.

A later study by Weinreich and Andersen (1976b) questioned whether raised intracolonic pressures and motility indices were consistent factors in the pathophysiology of diverticular disease. One hundred and thirty-nine patients with diverticular disease were subdivided into three groups; those with typical disease symptomatology, those with atypical symptoms and those who were asymptomatic. These groups were compared with normals and with patients presenting with irritable colon syndrome. A neostigmine stimulated motility test was performed and the motility index, expressed as the product of the mean wave amplitude and percentage recording time with wave activity, was calculated.

Symptoms of lower abdominal pain and intermittent abdominal pain were closely associated with a raised motility index irrespective of the presence or absence of diverticular disease. Asymptomatic diverticular disease patients displayed normal motility indices. More recent studies of asymptomatic diverticular disease patients using the catheter technique have failed to demonstrate raised intraluminal pressures (Eastwood, Brydon et al,1978;Howell et al,1978). These findings suggest that stage and severity grading may be important.

Failure of earlier studies to detect normal sigmoid pressures in diverticular disease may be attributed to bias towards symptomatic patients in the study population. Future work on colonic pressures should, therefore, record the symptomatic history of each patient in order to further examine the relationship between intracolonic pressure and disease symptomatology.

2.5 Colonic propulsion in diverticular disease

The rate of transit of gastrointestinal contents in normal human subjects has been widely investigated but few studies have been performed which examine gastrointestinal transit in patients with diverticular disease. Diverticular disease has been associated with features of prolonged intestinal transit and reduced stool weight, thought to be the result of a deficiency of dietary fibre (Painter, 1975). There is controversy regarding the significance of these "features".

Manousos et al (1967), in a study of 88 normal subjects and 43 patients with diverticular disease, administered 30mls barium sulphate with each of the four main meals in one day and performed subsequent abdominal x-rays at twenty-four hour intervals (to a maximum of six days) until the radio-opaque solution had almost completely disappeared. Using this technique, they found that transit times were significantly shorter in patients with diverticular disease than in normals and attributed this finding to a lack of coordination in the colonic musculature.

A later study by Leandro et al (1984) refuted these results.Using the technique of cineradiography following the ingestion of 250mls barium sulphate, they found that the transit time to the caecum and the mean total time of gastrointestinal emptying was essentially similar in both

healthy subjects and patients with diverticular disease. In diverticular disease patients, however, barium was propelled faster between the caecum and proximal sigmoid suggesting that the sigmoid exerts a breaking action in diverticular disease. Analysis of the pressure traces obtained from open-ended catheters demonstrated that this delay was not attributable to an increase in sigmoid motor activity as seen in constipated patients.Future transit studies should, perhaps, consider patients bowel habits when analysing the results.

It is important to acknowledge that these results must be interpreted with some reservation in view of the ability of barium to precipitate gastrointestinal hurry.

Eastwood, Brydon et al (1978), using the technique employed by Hinton et al (1969) , found that the transit times of patients with untreated diverticular disease was in the same range as normal (24-168 hours) and proposed that alterations in transit times may only become detectable at a certain stage in the disease. They believed that constipation may be a potential complication in diverticular disease but is not necessarily involved in the causation of the disease.

Although various workers have investigated gastrointestinal transit and intracolonic pressures in diverticular disease, the relationship between raised intraluminal pressures and propulsive activity has not been confirmed.

2.6 Treatment of diverticular disease

The medical profession has extrapolated the fibre hypothesis to treatment, prescribing high fibre diets and fibre supplements for patients with colonic diverticular disease. Various clinical studies demonstrating pain relief and improved bowel function with high fibre diets support this prescribing policy.

Painter et al (1972), in a study of seventy patients with diverticular disease, demonstrated that a change to a high residue, low sugar diet produced symptomatic relief in 88.6% of the study population. Moreover, bran was found to alter the bowel habit, reduce straining at stool and promote a feeling of complete bowel emptying.

Forty patients with diverticular disease were studied by Brodribb and Humphreys (1976) using open-ended fluid filled polyethylene catheters. They demonstrated that the administration of 24g wheat bran/day over a six month period provided good symptomatic relief and improved colonic function by increasing faecal weight, modifying colonic transit times towards a two day mean and reducing intracolonic pressures, especially during meals and post-prandially.

Unfortunately, neither of these studies included a control group. However, in the few controlled studies which have been performed, the results have been conflicting.

Ornstein et al (1981) concluded that the addition of dietary fibre only relieved the symptoms of constipation, whilst Hodgson (1977) found that fibre could elicit a placebo reaction in symptomatic patients. The results of Ornstein's study, however, provoked much criticism (Thornton,1981; Painter, 1981; Avery-Jones,1981). The patients studied had only mild symptoms and intestinal transit times and stool weights were similar to those in normal healthy subjects. Furthermore ,the daily intake of dietary fibre differed marginally between the placebo and bran periods. Moreover, the mean basal intake of dietary fibre of 15.2g/daily was below the standard amount of 20g/day (Heaton,1981).

In contrast to Ornstein's results Brodribb (1977), in a three month double-blind, controlled trial of eighteen patients with diverticular disease, found significant improvement on the high fibre regimen. This differed from Ornstein's study in that the patients had more severe symptoms at the time of study.

The high fibre regime, in addition to producing clinical improvement, is thought to reduce high intracolonic pressures. The ability of bran to diminish the colonic response to physiological and pharmacological stimuli was demonstrated in a study by Findlay et al (1974). The daily administration of 20g unprocessed bran significantly decreased intestinal transit time in

diverticular disease, increased stool weight and decreased the raised intracolonic pressure response to food and prostigmine.

Ispaghula husk is another treatment option for patients with diverticular disease. Its mode of action, however, is uncertain. Eastwood, Smith et al (1978) performed a study to investigate whether ispaghula husk and lactulose acted similarly to bran. They found that all the agents alleviated symptoms but functioned differently. The increase in stool weight was only significant with ispaghula. Bran significantly reduced intestinal transit times and decreased post-prandial high pressure waves. Lactulose had no effect on basal or post-prandial pressures. In contrast, ispaghula was found to elevate basal pressures and cause an increase in post-prandial pressure waves in the amplitude range 50-90cms water. The following year Archbold and Parks (1979) reported that ispaghula husk reduced the basal motility index, stool weight and transit time. However, both these studies involved the use of open-ended catheter systems which modify the physiological measurement of colonic motility.

These results highlight the need for further study into the effect of ispaghula husk on colonic motility in order to establish its therapeutic role in the management of diverticular disease.

2.7 Conclusion

The pathophysiology of diverticular disease, in spite of numerous investigations, remains unclear. Various hypotheses have been presented, proposing specific factors which may contribute to the disease aetiology. Inadequate dietary fibre, colonic muscular changes, raised intracolonic pressures and exaggerated stimulated motility responses have all been implicated but it seems unlikely that one specific factor is responsible.

Most investigations have centred on the role of raised intracolonic pressures in the pathophysiology of diverticular disease, the results of which although interesting are rather contradictory. Differing opinions and studies would seem to suggest that the disease has a multifactorial aetiology and that increased intracolonic pressures may be related to disease progression as a either a primary or secondary effect. More indepth study of the disease process is, therefore, advocated.

The role of dietary fibre in the treatment of diverticular disease and its therapeutic effects on disease symptomatology and bowel function are uncertain. Furthermore, the conflicting findings concerning the effect of ispaghula husk on colonic motility illustrate the need for further research in this field (Eastwood, Smith et al,1978; Archbold and Parks,1979).

3: AIMS OF STUDY

3: AIMS OF STUDY

This thesis was set up to examine:-

1) The relationship between colonic motility parameters and the radiological classification of disease severity.

2) The relationship between colonic motility parameters and the symptomatic classification of disease severity.

3) The relationship between radiological and symptomatic classification techniques.

4) The effect of food on colonic motility.

5) The effect of sleep on colonic motility.

6) The relationship between colonic motility parameters of the right and left colon.

7) The effect of Ispaghula husk on colonic motility in diverticular disease.

4: VALIDATION OF RADIOTELEMETRY SYSTEM

4: VALIDATION OF RADIOTELEMETRY SYSTEM

4.1 Radiotelemetry system

Introduction

Radiotelemetry is a technique which has been used to make pressure measurements accessible non-invasively from a variety of sites within the body (Connell et al,1963; Wolff,1961). The equipment, used in this study to measure intracolonic pressures,consisted of a pressure-sensitive radiopill,Type 7014, a receiver, Type 7060 and a "Type 5" belt aerial, all manufactured by Remote Control Systems Limited.

Radiopill 7014

The radiopill is shown diagrammatically in Figure 1. It consisted of a pressure-sensitive transducer, a low power transmitter and a replaceable mercury battery, sealed in a non-toxic perspex body measuring 26mmx9.4mm. According to the manufacturer's specifications, pressure pill 7014 had an operational life of 75 hours per battery.

The radiopill functioned as follows. A positive pressure on the metal diaphragm (a) caused the ferrite disc (b) to move closer to the oscillator coil (c).This produced an increase in the inductance and a resultant decrease in resonant frequency. A coil within the radiopill transmitted

this signal to a receiver outside the body via the belt aerial. Changes in frequency were, therefore, related to changes in pressure.Since the frequency-pressure characteristics of individual radiopills were different, a calibration value was obtained for each radiopill prior to its ingestion by a patient (see 4.4).

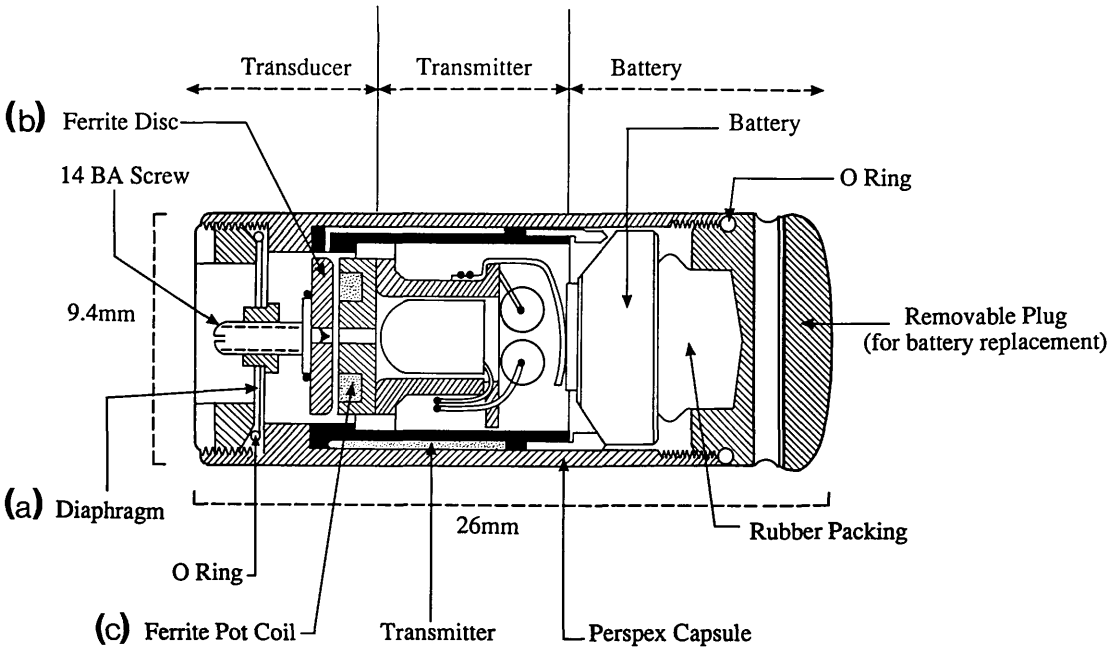


Figure 1.

Remote Control Systems' Pressure Sensitive Radiopill Type 7014.

Receiver 7060

Receiver 7060 is based on an Epson personal computer fitted with a telemetry interface cartridge (Figure 2). In the present study, it was used for monitoring pressure in conjunction with radiopill 7014, in the frequency range 390-460kHz. The user interacted with the receiver via five keys on a standard QWERTY keyboard, viz the "shift", "return", "stop" and "control" and its small liquid crystal display produced all the information required to set up and use the receiver. The unit was powered internally by rechargeable batteries which gave up to four hours running. In studies of longer duration an AC mains adaptor was used.

The receiver had a sub-miniature co-axial input socket for connecting an aerial. In addition, it had an analog output for the recording of pressure variations on a pen recorder and a digital (RS232) output for data transmission to a computer. An Atari 1040ST computer was purchased and linked to the receiver's digital output in order to facilitate data storage and analysis (Figure 3).

Figure 2.

Remote Control Systems' Radiotelemetry Receiver Type 7060.

DIAGRAM OF RADIOTELEMETRY SYSTEM

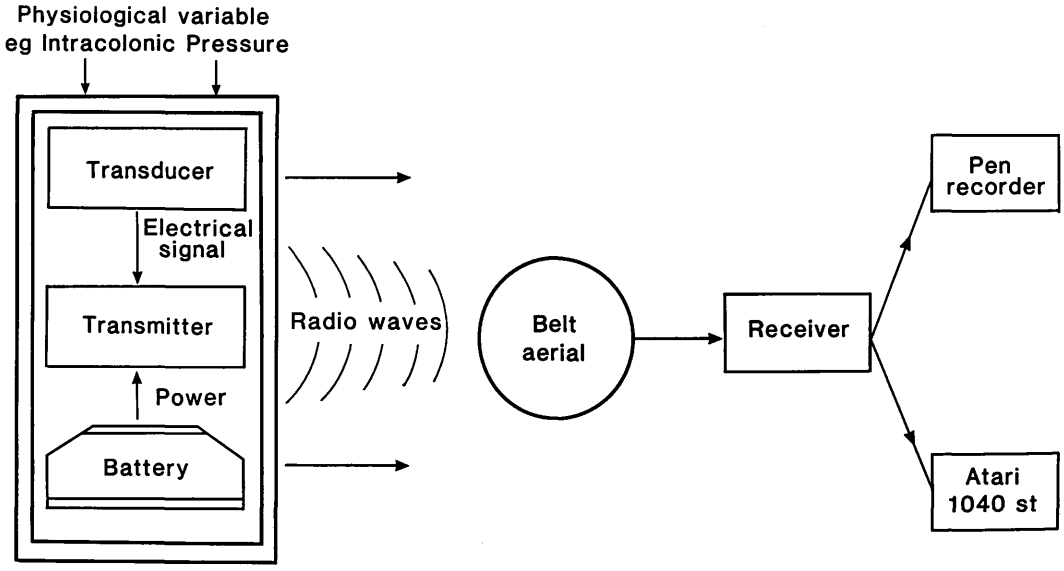


Figure 3.

Schematic Diagram of Radiotelemetry System.

Atari 1040ST microcomputer and visual display unit

The receiver transmitted data at the rate of 10 readings/second to the Atari. Software was developed to enable the computer to capture the readings and average them to obtain one reading/second. If more than five of the 10 readings were "poor quality" signals then the averaged reading was tagged a "poor quality" reading.

The visual display unit showed: (Figure 4)

(a) date and time of study
(b) patient details: surname,forename,hospital number
(c) system details i.e. memory (RAM) and disk capacity
(d) bowel pressure graph

The bowel pressure graphed and printed on the visual display unit was stored continuously in random access memory (RAM) until the memory allowance of 128000 bytes (=128000 seconds = 35.5 hrs storage) was filled or until the user clicked both of the Atari's mouse buttons simultaneously. When either of these occurred, the data buffer was stored to disk in a separate file. The maximum disk space was 720000 bytes (200 hrs approximately) which allowed more than one patient study to be stored on the same disk.

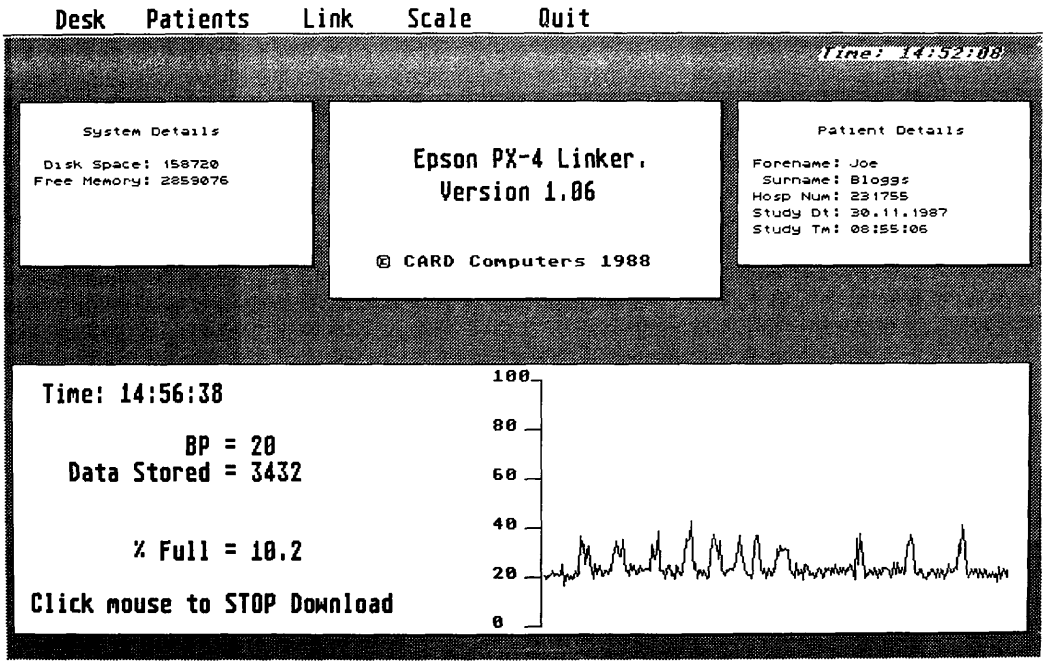


Figure 4.

Visual display unit showing pressure waveform.

Note: Vertical scale is in mmHg
Pressure waveform offset by 20 mmHg

4.2 Evaluation of radiotelemetry system

Introduction

Before the clinical work began, laboratory experiments and patient pilot studies were carried out to validate the technique of radiotelemetry. The following questions were addressed:

1) Does radiopill frequency remain stable for the duration of study?
2) Can the batteries be used in studies lasting longer than 75 hours?
3) Is calibration at room temperature a satisfactory procedure?
4) How does the radiopill response to intracolonic pressure changes compare with other recording techniques?
5) Is signal loss a problem with the unidirectional belt aerial?
6) How does radiopill orientation affect the accuracy of localisation?
7) How can we identify radiopill position within the colon?
8) Is the radiopill a suitable marker for measuring gastrointestinal transit times?

Study 1 Stability of radiopill frequency

This study was undertaken to determine the stability of the radiopill frequency over a five day period at a temperature of 35°C.

Method

Four batteries were taken from stock and the voltage of each was measured by a digital voltmeter (Fluke 75,RS Components Ltd.) prior to insertion into four radiopills. Following a four hour stabilization period at room temperature, each radiopill was calibrated (see 4.4). One radiopill was randomly selected and taped onto a rod aerial connected to the receiver. The rod with attached radiopill was placed in a laboratory incubator (LTE Ltd.,Oldham,U.K.) at 35°C controlled to ±1°C . A pen recorder attached to the receiver's analogue output charted the radiopill frequency over the five days. The remaining three radiopills were also placed in the oven distanced from the rod to prevent any R.F. interference. Atmospheric pressure was recorded daily on a mercury barometer. At the end of the fifth day the frequencies of all four radiopills were recorded after removal from the oven and the battery voltages were measured.

Results

Details of results are shown in Tables 1 , 2 and Figure 5.

Radiopill Number	F1-Day1 (kHz)	F6-Day6 (kHz)	Difference (%)
324	408.55	378.2	7.4
328	404.53	380.3	6.0
329	411.90	395.1	4.1
330	420.60	398.1	5.3

Table 1.

Frequency of radiopills at beginning and end of five day period at room temperature (corrected for changes in atmospheric pressure).

Radiopill Number	V1-Day1 (volts)	V6-Day6 (volts)	Difference (%)
324	1.353	1.334	1.4
328	1.352	1.333	1.4
329	1.354	1.332	1.6
330	1.350	1.332	1.3

Table 2.

Battery voltage at beginning and end of five day period of powering radiopill.

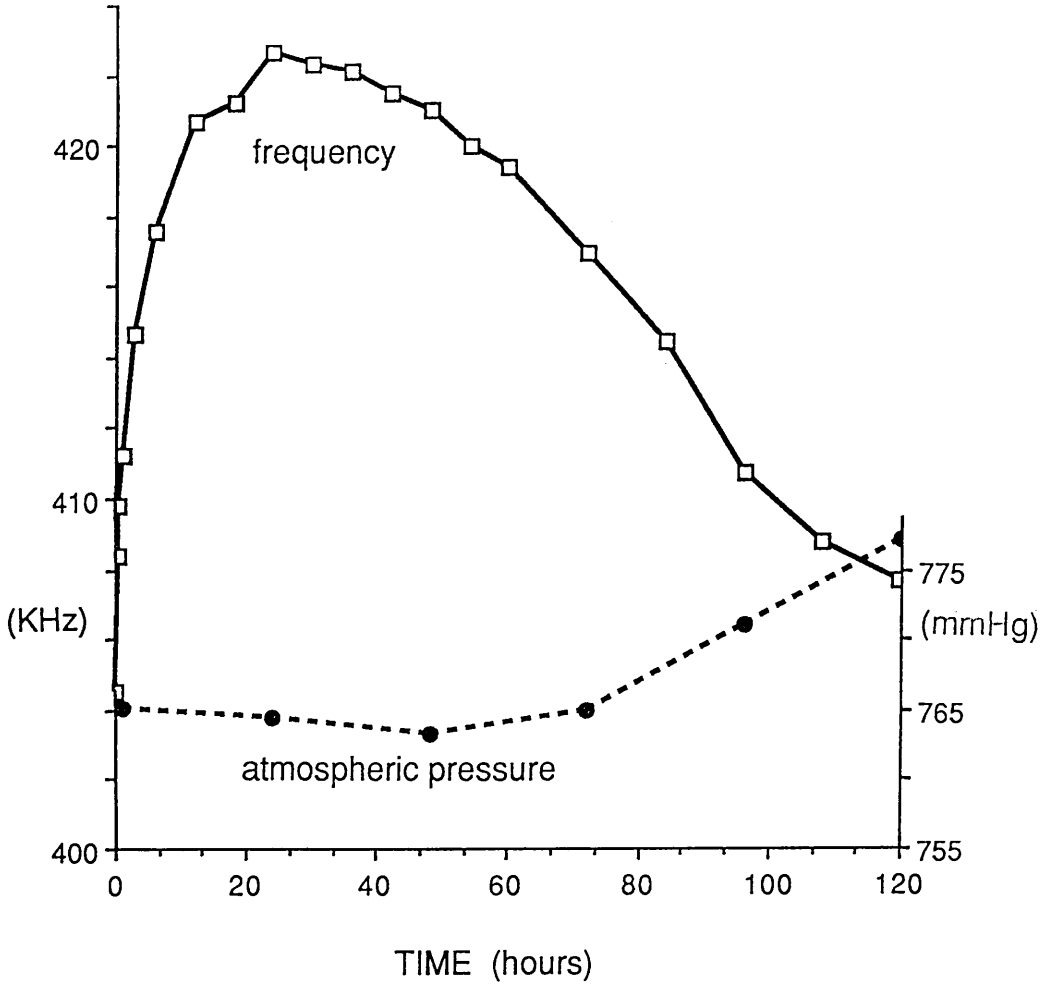


Figure 5.

Change in radiopill frequency over 120 hour period. Radiopill maintained at 35°C.

Figure 5 shows how radiopill frequency changed during five days in an incubator at 35±1°C. Atmospheric pressure is also illustrated and drawn to the same scale. When the radiopill was placed in the incubator, the frequency increased rapidly over the first 24 hours then began to gradually decrease and fall more rapidly after 72 hours. The change in atmospheric pressure from day 1 to day 5 was 11.9mmHg.

Discussion

Table 1 illustrates that in each case the frequency fell over the five day period. Using the calibration factors for each radiopill, the maximum frequency change was equivalent to a pressure increase between 73mmHg and 132mmHg. Atmospheric pressure changes could not account for this large drift.

From Table 2, battery voltage drift over the five days was <2%. Before this was eliminated as a significant source of frequency drift, a further experiment was performed to establish the relationship between battery voltage and radiopill frequency. It was found that when the battery voltage fell from 1.351 volts to 1.320 volts, the frequency only changed by 0.04kHz. Thus the drop in battery voltage would not affect pill frequency.

The initial increase in frequency could be partly due to an increase in the pressure of air under the diaphragm due to a rise in temperature and partly the result of design limitations of the radiopill which is of a relatively simple construction.

The initial reduction in frequency could be attributed to gradual leaks through the diaphragm at its most vulnerable area around the 14BA screw. Part of the reduction in frequency after 72 hours is due to an increase in atmospheric pressure.

Conclusion

The batteries performed satisfactorily over the five day period and could be eliminated as a significant source of frequency drift.

Radiopill frequency varied considerably over five days rendering the telemetry system unsuitable for measuring absolute intracolonic pressures. Following discussions with the manufacturer, (Remote Control Systems Ltd.), an automatic drift compensatory mechanism became available as a "plug in" chip which when selected was able to compensate for any long term drifts in the radiopill. Without this mechanism, any drifts would have caused the receiver to indicate a gradually changing pressure.

As a result of these initial experiments, the auto-compensatory module was used in this study to measure intracolonic pressure changes. This was regarded as a suitable design modification as the measurement of pressure changes necessary to propel faecal contents through the bowel was considered to be more important than the recording of absolute pressures present within the bowel.

Study 2 Stability of radiopill calibration factor

Radiopill calibration was performed at room temperature in accordance with the manufacturer's instructions. This was claimed to be an acceptable practice in applications of the radiotelemetry system which monitored relative pressure changes rather than absolute pressure values.

After initial clinical studies, however, pre and post study calibration factors were found to be different. This caused concern about the stability of the radiopill calibration factor at body temperature during the study period. A further test was, therefore, performed to determine whether temperature affected calibration factor.

Method

Following a four hour stabilization period after battery insertion, five radiopills were calibrated at room temperature (21.5±0.5°C) then placed in separate test tubes in a water bath (37±1°C) and allowed to equilibrate for 30 minutes.The radiopills were then calibrated at this temperature before removal from the water bath. After a further 30 minutes at room temperature, the radiopills were recalibrated. The above procedure was undertaken for each radiopill, fitted with three different diaphragms (D1,D2,D3). Prior to each experiment, the radiopill was tuned to approximately 430 KHz at room temperature and atmospheric pressure.

Results: see Table 3 and Figure 6.

Table 3.

Relationship between calibration factors at room temperature and calibration factors at 37°C.

(Atmospheric pressure=AP, calibration factor=CF,)

Radiopill 325

	22°C Frequency (kHz)	37°C Frequency (kHz)	22°C Frequency (kHz)	DIAPHRAGM NO.
AP	427.82	441.26	430.91	
80mmHg	405.93	423.4	409.94	D1
CF	0.27	0.22	0.26	
AP	427.25	450.57	430.33	
80mmHg	397.78	431.60	400.67	D2
CF	0.37	0.24	0.37	
AP	432.38	447.34	434.90	
80mmHg	406.97	432.43	405.75	D3
CF	0.32	0.19	0.36	

Radiopill 329

AP	427.28	434.13	434.78	
80mmHg	404.12	421.3	414.21	D1
CF	0.29	0.16	0.26	
AP	426.67	438.07	423.83	
80mmHg	406.33	422.38	404.13	D2
CF	0.25	0.20	0.25	
AP	427.76	437.90	427.59	
80mmHg	401.53	422.69	403.47	D3
CF	0.33	0.19	0.30	

Radiopill 335

AP	433.90	437.32	432.86	
80mmHg	406.10	421.43	409.79	D1
CF	0.35	0.20	0.29	
AP	430.62	440.26	425.20	
80mmHg	409.39	424.49	402.38	D2
CF	0.27	0.20	0.29	
AP	431.24	441.89	424.14	
80mmHg	407.26	426.04	400.75	D3
CF	0.30	0.20	0.28	

	22°C Frequency (kHz)	37°C Frequency (kHz)	22°C Frequency (kHz)	DIAPHRAGM NO.
Radiopill 330				
AP	431.27	445.29	430.94	
80mmHg	414.74	430.04	414.46	D1
CF	0.21	0.19	0.21	
AP	429.52	439.25	427.61	
80mmHg	398.46	423.28	400.49	D2
CF	0.39	0.20	0.34	
AP	432.43	447.49	431.49	
80mmHg	410.67	432.66	409.49	D3
CF	0.27	0.19	0.28	
Radiopill 334				
AP	429.06	439.11	426.40	
80mmHg	408.56	423.62	406.52	D1
CF	0.26	0.19	0.25	
AP	429.78	443.55	426.92	
80mmHg	410.71	428.51	407.40	D2
CF	0.24	0.19	0.24	
AP	430.23	442.16	422.25	
80mmHg	404.85	426.28	394.55	D3
CF	0.32	0.20	0.35	

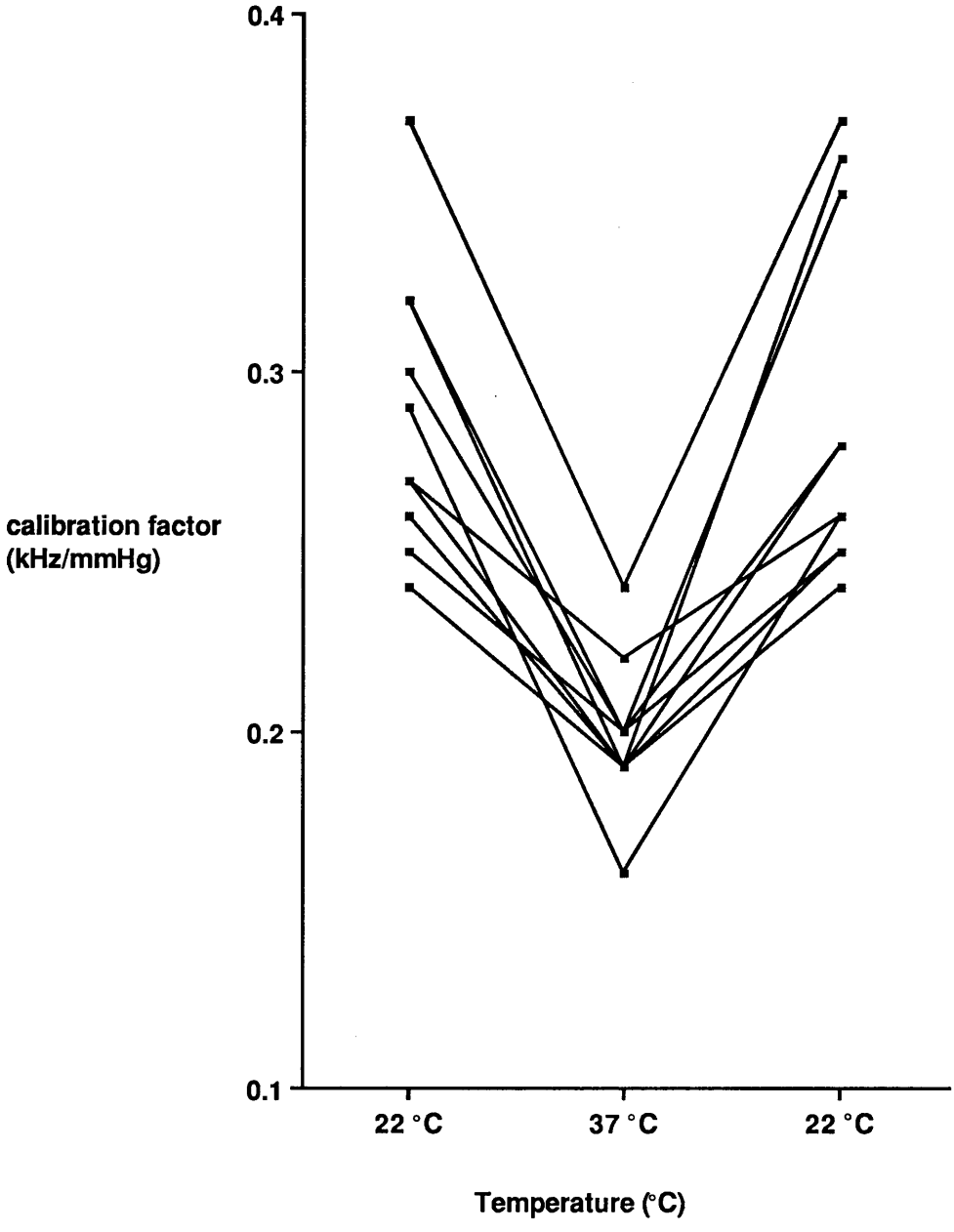


Figure 6
Variation of calibration factor between room and body temperatures.

Discussion

In each study, calibration factors at room temperature were greater than calibration factors at 37°C. Calibration factors at room temperature before and after insertion into the water bath varied in some cases but remained constant in others. Note that with the same radiopill, the calibration factor altered with different diaphragms. Analysis of the calibration factors at 37°C, however, revealed a surprising trend. Irrespective of the initial calibration values obtained at room temperature, the calibration factor for each radiopill with different diaphragms reduced to similar values at 37°C . On the basis of these results, early studies using calibration factors at 22°C were modified to their 37°C value.

Conclusion

Performing the radiopill calibration procedure at room temperature is unsatisfactory in colonic pressure studies as it gives erroneous values for calibration factor. It was decided, therefore, to calibrate each radiopill 30 minutes after immersion into a waterbath at 37°C. Recalibration after bowel manometry was also performed at 37°C. If the calibration factor had changed then a mean value was taken for analysis.

Study 3 Radiopill response to pressure changes within the colon

The frequency of response of the radiopill to intraluminal pressures within the gastrointestinal tract was assessed, using a Gaeltec catheter-tipped transducer (Type 16CT, Gaeltec Ltd.) as the reference measurement.

Method

The analogue output of the receiver was connected to one channel of an MX2 heated stylus recorder and the Gaeltec transducer linked to a second channel via a preamplifier. Each pressure transducer was calibrated against a mercury column and the stylus sensitivity was adjusted so that ten divisions represented 100mmHg.

A length of "viscing" tubing, diameter 1.27cm was tied at one end and one third filled with water. The radiopill and probe were immersed into the bottom of the tubing, encircled by a belt aerial . The walls of the tube were squeezed rapidly to create transient pressure changes of up to 100mmHg and the recorder running at 10mm/second was used to record the output voltage signals from the radiopill and the Gaeltec probe.

Results

Figure 7 illustrates part of a pressure/time recording made during the test. Note the "noise" on the radiopill trace at 100ms intervals, due to switching of the sampling circuit. There is a small delay of up to 200ms before the radiopill responds to a pressure transient.

Conclusion

Since colonic pressure changes are an order of magnitude less than those generated in this test, the radiopill will faithfully reproduce fluctuations in intracolonic pressure.

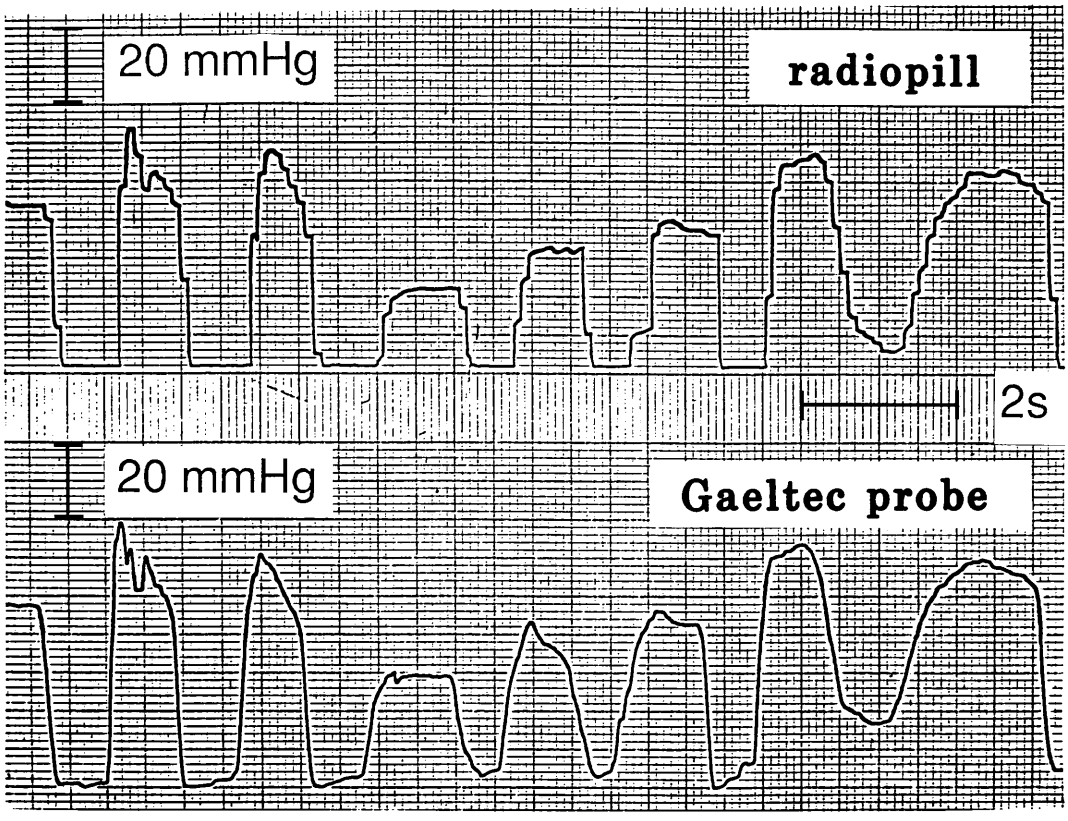


Figure 7.

Response of pressure radiopill and Gaeltec catheter-tipped transducer to pressure transients.

Study 4 Evaluation of unidirectional belt aerial

In preliminary patient studies, a concentric coil belt aerial was used to detect the signals emitted from the radiopill. Although previous workers highlighted the problem of recurrent signal loss with this type of directionally sensitive aerial (Connell and Rowlands,1960; Jacobson,1962; Evans et al,1980), it was anticipated that this could be minimised by utilising the "poor quality" signal generated by the receiver to trigger an audible alarm in the Atari 1040ST computer. This would inform the investigator and the patient that belt readjustment was required.

Early clinical experience using the belt aerial was variable. In some patients it worked well. In others, however, the "poor quality" indicator was frequently activated and it was difficult to position the belt aerial around the patient's abdomen to obtain a satisfactory signal. Furthermore, continual flexing of the co-axial lead whilst in use weakened its connection to the aerial and resulted in intermittent contact. This was traced to a fracture in the internal copper wire at the point where it joined the aerial's connection block.

Previous workers who encountered this problem of signal loss designed a system which multiplexed between two or three aerials arranged at right angles to one another (Jacob et al,1973; Evans et al,1980). The multiplexer then

selected the aerial with the strongest signal for connection to the receiver. Receiver 7060, however, did not have this multiplexing facility. Furthermore, it was undesirable to encumber the patient with more wires especially when these aerials required to be moved during the study when determining radiopill location.

It was, therefore, necessary to develop a new band aerial suitable for use with radiopills and to perform a series of laboratory tests to evaluate it and compare its range with that of the original belt aerial.

Method

The new aerial, measuring 500mmx50mm, was made by forming 22 interleaving loops of plastic-coated 16/0.2 stranded copper wire onto a flat sheet of adhesive plastic. Each loop was 35mm high and 30mm wide and overlapped its neighbouring coil by 10mm at its widest point (Figure 8). The aerial was terminated by a capacitor selected to tune the aerial to approximately 430KHz. An 8m length of miniature coaxial cable was soldered to the aerial's terminals and the assembly insulated by wrapping a thin plastic sheet around it. In order to ensure patient comfort, the aerial was then covered with Tubigrip bandage (size C), with an attached Velcro fastening , which could be worn as a belt.

Body aerial

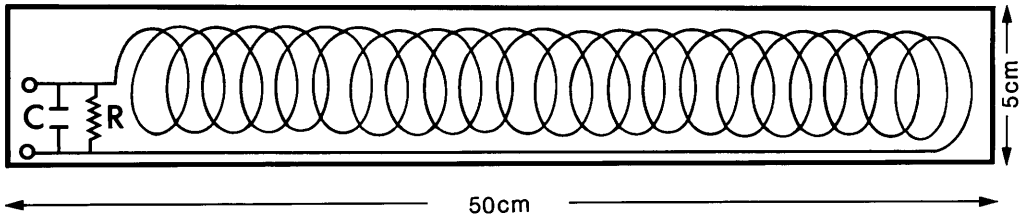


Figure 8.

THE NEW AERIAL

The winding arrangement of the distributed coil is shown.

Aerial performance was tested with reference to the receiver's liquid crystal display unit which indicated radiopill frequency and "signal quality" in 10% stages. As a rule the receiver required at least 30% signal quality to operate properly. An inadequate signal was shown by a "Poor signal" on the display.

The range of each aerial was measured in both horizontal and vertical planes with three different radiopill orientations. For these tests, the belt was formed into a circle of 250mm diameter (the fitting for normal sized subjects) and 400mm diameter (the fitting for obese patients).

The original aerial,connected to the receiver, was placed "edge on" to a flat sheet of paper and tested first at the smaller diameter. A radiopill randomly selected from stock, was fitted with a new battery and tuned to a frequency of 430kHz. It was placed on the paper with its transmitting coil parallel to the coil of the receiving aerial within the circular loop (position 1). The radiopill was then moved within the circle, maintaining its orientation, and the points where the received signal fell just below the "100%" level were marked. This was repeated with it at different heights above the aerial.

The radiopill was then placed with its coil perpendicular to the belt aerial's coil (position 2) and

locations of reduced signal level were plotted as before. Finally, the radiopill was rotated about its axis to be 90° from position 2 (position 3) before repeating the procedure. The above tests were then performed with the aerial widened to 400mm.

The new aerial underwent identical laboratory tests. For these it was formed into the arc of a circle 250mm and 400mm diameter and placed "edge-on" to the paper.

The clinical performance of each aerial has been evaluated retrospectively. Thirty-eight pressure recordings were examined and divided into two groups depending on the aerial used. Nine records were selected from each group in which the radiopill had progressed from the caecum to the transverse region of the colon during the period 10.00 to 18.00 hours of the first study day. A computer programme was then developed to calculate the number and duration of "poor signals" during the selected time interval.

Results

Laboratory

When the radiopill was positioned with its coil parallel to the coil of the belt aerial (position 1), an acceptable signal was obtained throughout the circular areas enclosed by the aerial for both diameters. In the two perpendicular radiopill orientations (positions 2 & 3), however, there were zones of signal loss within both circles (Figures 9 & 10). Areas where an acceptable signal

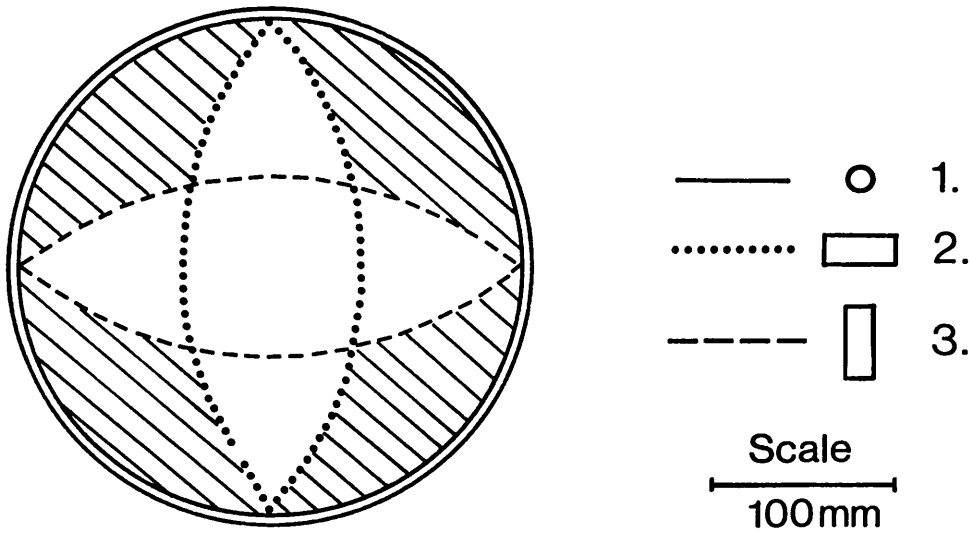


Figure 9.

BELT AERIAL PLAN VIEW : 250 mm diameter.

Lines show boundaries between signal "pick-up" and "loss" zones for radiopill orientations 2 & 3. Pick-up is obtained throughout the circle for orientation 1. Hatched areas are pick-up zones for the 3 orientations.

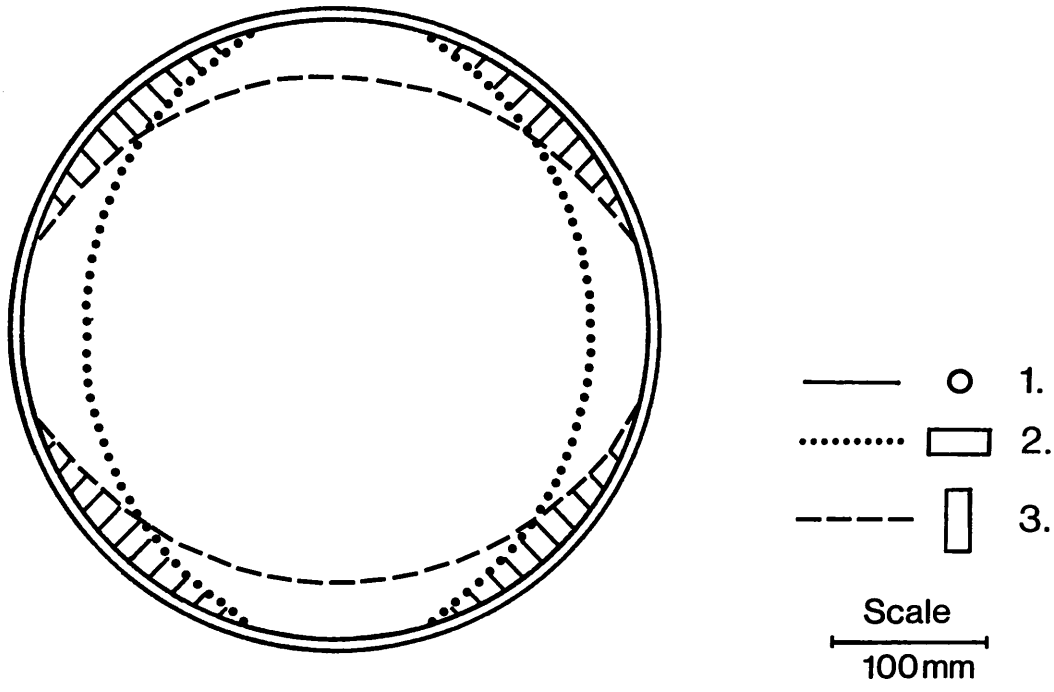


Figure 10.

BELT AERIAL PLAN VIEW : 400 mm diameter.

Lines show boundaries between signal "pick-up" and "loss" zones for radiopill orientations 2 & 3. Pick-up is obtained throughout the circle for orientation 1. Hatched areas are pick-up zones for the 3 orientations.

was obtained for all three orientations are shown hatched. These areas extended to 150mm above and below the aerial's mid-line.

In the two arrangements of the new aerial, zones of signal loss were found for all three orientations (Figures 11 & 12).The hatched areas of acceptable signal for the three orientations extended to 75mm above and below the aerial's mid-line.

Clinical

The clinical results are detailed in Table 4. With the new aerial, both the duration and number of poor signals were significantly reduced. Mann-Whitney test gives $p<0.01$ and $p<0.05$, respectively.

It was found that positioning of the new aerial on the patient was neither as critical or as difficult as with the belt aerial.

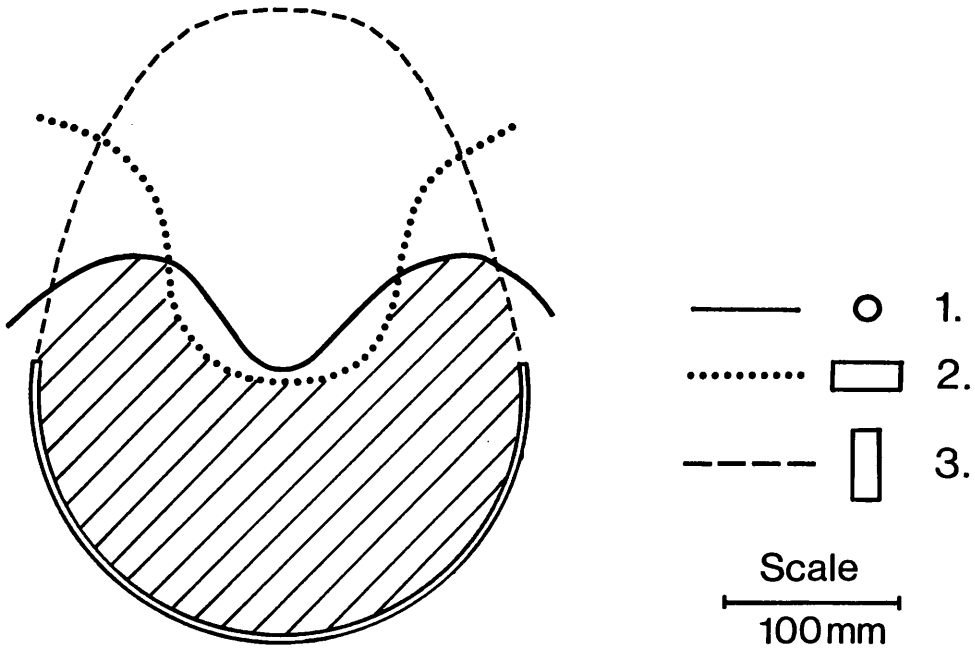


Figure 11.

NEW AERIAL PLAN VIEW : 250 mm diameter.

Lines show boundaries between signal "pick-up" and "loss" zones for radiopill orientations 1, 2 & 3. Hatched areas are pick-up zones for the 3 orientations.

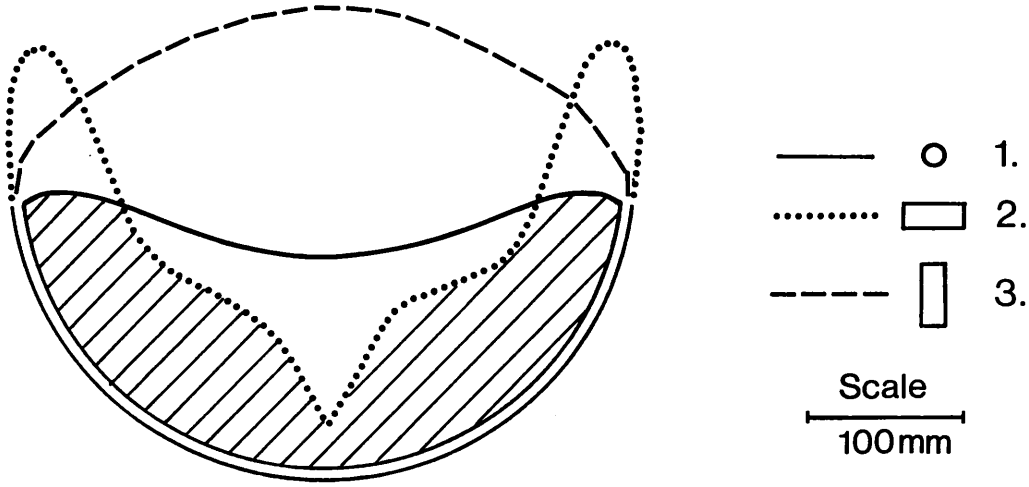


Figure 12.

NEW AERIAL PLAN VIEW : 400 mm diameter.

Lines show boundaries between signal "pick-up" and "loss" zones for radiopill orientations 1, 2 & 3. Hatched areas are pick-up zones for the 3 orientations.

Study No.	Aerial Used	% Time	Poor signals No./Hr
1	Belt	4.2	35
2	"	7.3	43
3	"	4.1	44
4	"	8.6	53
5	"	1.5	0.5
6	"	3.6	25
7	"	5.8	57
8	"	9.6	66
9	"	5.2	50
	Mean	5.5(SE±0.9)	41.5(SE±6.5)
10	Aerial	2.1	26
11	"	2.9	46
12	"	2.2	22
13	"	1.5	25
14	"	1.2	26
15	"	2.5	31
16	"	0.9	14
17	"	1.0	19
18	"	1.8	23
	Mean	1.8(SE±0.2)	25.8(SE±3.0)

Table 4.

Clinical studies with the 2 aerials between 10.00 and 18.00 hours.

Discussion

Clinical results demonstrated that the new aerial performed better than the belt aerial by reducing the time the pill was in the signal loss zone by one third and nearly halving the number of poor signals. Bench tests demonstrated that the original aerial performed well when its coil was parallel to that of the radiopill but was severely restricted in the other two orientations.

The pick-up areas were greater for the new aerial making it less sensitive to radiopill orientation. Although it had a diminished range in the vertical plane this did not give problems because large "mass movements" of colonic contents occur infrequently.

Conclusion

The new,less directionally-sensitive band aerial is a more suitable arrangement for monitoring the progression of an untethered radiopill through the gastrointestinal tract and its potential is being exploited commercially.

Study 5 Location of the radiopill within the human colon

The aim of the clinical study was not only to record pressure information transmitted by the radiopill but to also determine the location of it within the gastrointestinal tract. Several techniques are possible for tracking radiopill position. X-ray films could be used to determine the position of the radiopill within the colon, but this technique would have led to an undesirable exposure of patients to x-radiation.

Jacobson (1962) described a field strength meter which could be used to manually track the radiopill, the point of maximum needle deflection corresponding to the closest approach to the radiopill. Following this, he designed a servosystem which automatically tracked the movements of the radiopill and traced a map of them on paper. This technique was performed with the patient recumbant which restricted patient movements and influenced the physiological normality of the measurements.

Another method, incorporating radio-isotopes within a radiotelemetry capsule, has been used to assist localisation (Waller,1975). This technique is less convenient to implement and involves the introduction of a source of radiation within the patient.

Although a time consuming procedure, manual tracking with a field strength meter appeared to be a suitable technique being less restricting on patient mobility and, therefore, more physiological.

A detector box and rod aerial which picked up the radiofrequency signal emitted by the radiopill was available from the manufacturer, (Remote Control Systems Ltd.), as a means of detecting when the radiopill was excreted within a faecal mass. The detector emitted an audible "beep" when the rod aerial came within a metre of the radiopill. In addition, it had a small meter indicating the strength of the detected signal.

Following preliminary bench tests with this detector, the rod aerial was found to be sensitive over a large part of its length and, as a result, was unsuitable for pin-pointing the radiopill location. Moreover, the small indicating meter had insufficient travel to allow precise determination of maximum signal strength.

The system was, therefore, modified in two ways. Firstly, the small indicator was replaced by a larger 0-100uA edge meter (RS Components Ltd.) which allowed more accurate measurements of signal strength. Secondly, a new smaller rod aerial was made using ten turns of insulated copper wire wound round the end of a ferrite rod (10mm diameterx 65mmlong) which was secured by adhesive and placed inside a 5ml syringe to provide insulation and additional protection (figure 13).

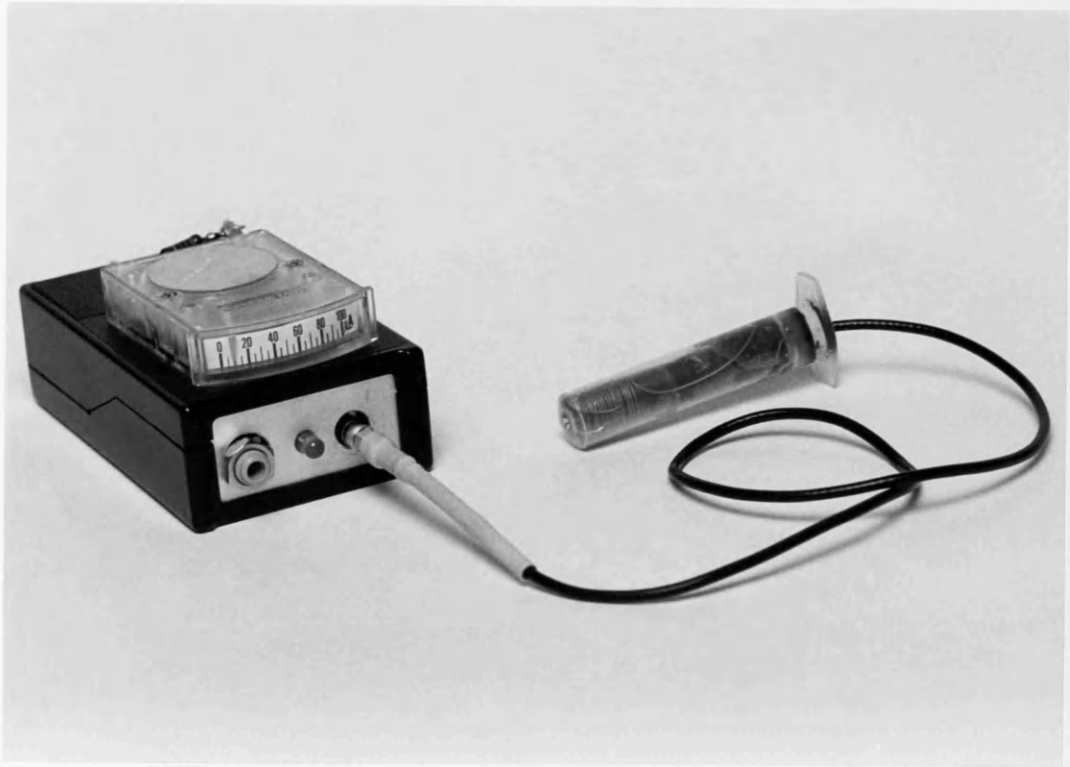


Figure 13.

Modified field strength meter with redesigned probe.

Following these modifications, an experiment was carried out to assess the ability of the field strength meter to accurately locate the radiopill and to establish the effect of radiopill orientation on localisation.

Method

Two persons were involved in the experiment. The first positioned the radiopill vertically, horizontally or diagonally on a sheet of graph paper(500mm x 350mm) taped onto a work bench. A cross was marked on the paper to indicate the central point of the radiopill's aerial. An identical sheet of graph paper was taped onto a cardboard box(545mm x 465mm x 50mm). At this height signal strengths in the range 45-60% of the value when the radiopill was beside the aerial, were obtained. As a result of preliminary patient studies which showed that signal strengths even in obese patients rarely fell below 60%, this distance was selected to simulate the clinical situation.

After positioning the radiopill on the graph paper, the cardboard box was placed over the radiopill and carefully positioned to ensure that both sheets of paper were in the correct alignment. The second person with the field strength meter attempted to locate the radiopill by moving the probe in all directions over the surface graph paper. A point was made at the estimated radiopill position and the strength of the signal was noted. The two sheets of

graph paper were compared and the distance between estimated and actual radiopill position was measured in millimetres. The radiopill was positioned thirty times.

Results

See Table 5.

RADIOPILL POSITION	SIGNAL STRENGTH	ERROR(mm)
V	60	15
H	55	13
D	55	14
V	55	00
H	55	14
H	50	17
V	50	06
D	50	11
D	50	18
H	50	09
H	50	16
H	45	11
V	55	05
D	50	10
D	45	05
V	45	07
H	45	14
H	45	20
D	50	06
D	50	05
D	50	10
H	50	15
H	55	07
D	55	10
D	55	05
H	55	09
H	55	10
D	55	00
D	55	25
V	60	06

Table 5.

Radiopill location -position,signal strength,error.

Where V=Vertical; H=Horizontal; D=Diagonal

Mean difference in vertical (V) position = 6.5mm

Mean difference in horizontal (H) position = 12.9mm

Mean difference in diagonal (D) position = 9.9mm

Total (V+H+D) mean difference = 10.4mm

Discussion

In an attempt to discover the source of the location error another bench experiment was performed to establish the effects on signal strength of various orientations of the radiopill in relation to the probe. An interesting finding was noted when the radiopill was perpendicular to the probe. Two places of maximum signal strength appeared, neither of which occurred directly above the radiopill. In fact, the radiopill was located at the point midway between the two peaks.

During the clinical studies, this "double peak" phenomenon was encountered when the position of the radiopill was being determined. Its effect was minimised by checking for the presence of a "double peak" first of all and when found taking the midpoint between the peaks as the location of the radiopill.

With the use of the modified field strength meter, manual tracking was performed at fifteen minute intervals during day-time or more frequently if the signal quality deteriorated during this time period. A pen was used to mark the patient's abdomen at the point of maximum needle deflection with a cross. Each cross was numbered and the time of each marking was noted. The distance between adjacent crosses was then measured.

Although this technique provided information concerning the position of the radiopill in relation to the abdominal wall, it could not be used alone to determine the location of the radiopill within the gastrointestinal tract. This is a recognized difficulty of techniques involving untethered radiopills.

Other workers have devised systems for surface monitoring of the radiopill, (Jacobson,1962) but at the time of this study, there were no published reports of a system suitable for determining radiopill position within the colon. An attempt was made to devise a method which would be relatively easy to implement and would not involve repeated interruption from the telemetry system.

This new technique involved retrospective analysis of the abdominal markings in conjunction with the patient's barium enema films. On completion of the telemetry study the patient's abdomen, with attached linear scale, was photographed. (Figures 14a & 15a). The photograph was then adjusted according to scale in order to superimpose it on the barium film. The resulting print illustrated the movements of the radiopill within the gastrointestinal tract (Figure 14b &15b). Thus pressures in different colonic segments could be evaluated.

Figure 14a.

Photograph of the abdomen (patient A) fixing the position of the radiopill throughout the study.

X SMALL BOWEL

◈ COLON

Figure 14b.

Barium enema erect film (patient A).

Overlay taken from the photograph (14a) to show the position of the radiopill within the colon.

▲ UMBILICUS

◆ COLON

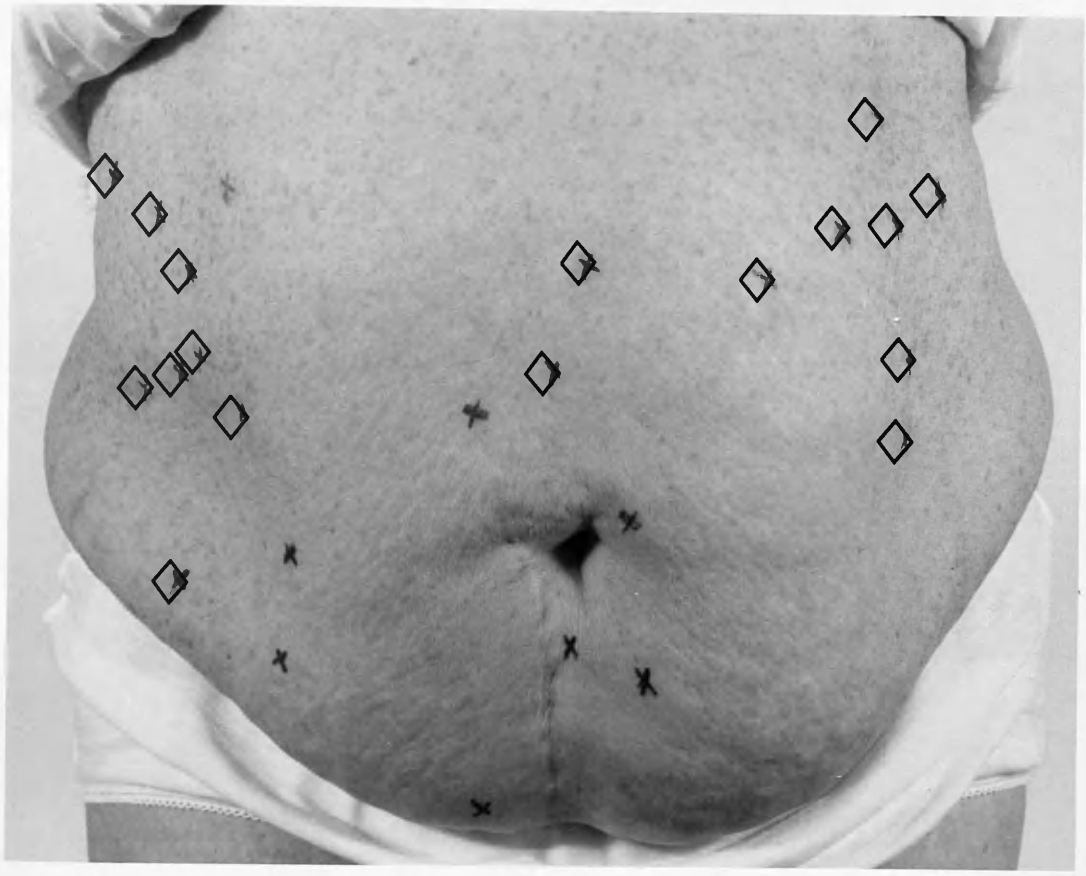


Figure 14 a.

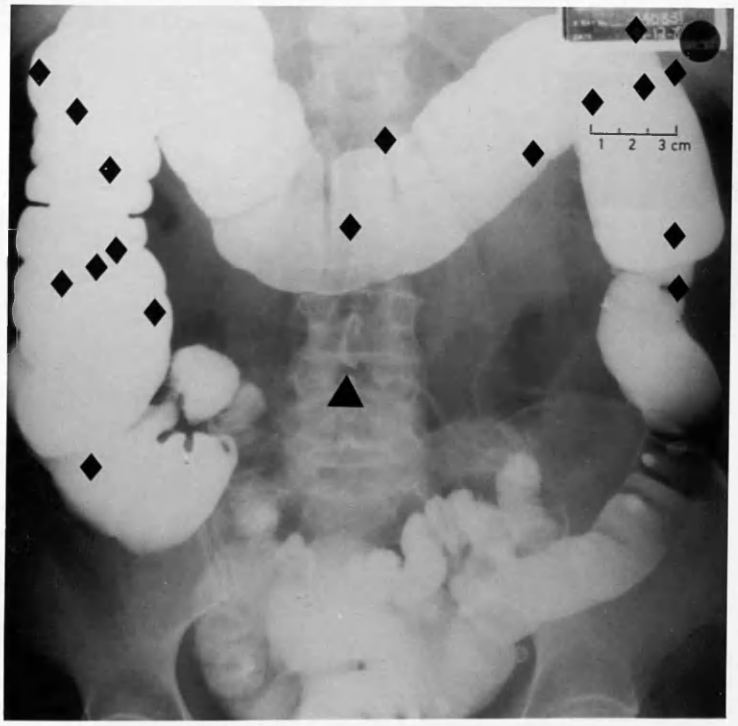


Figure 14 b.

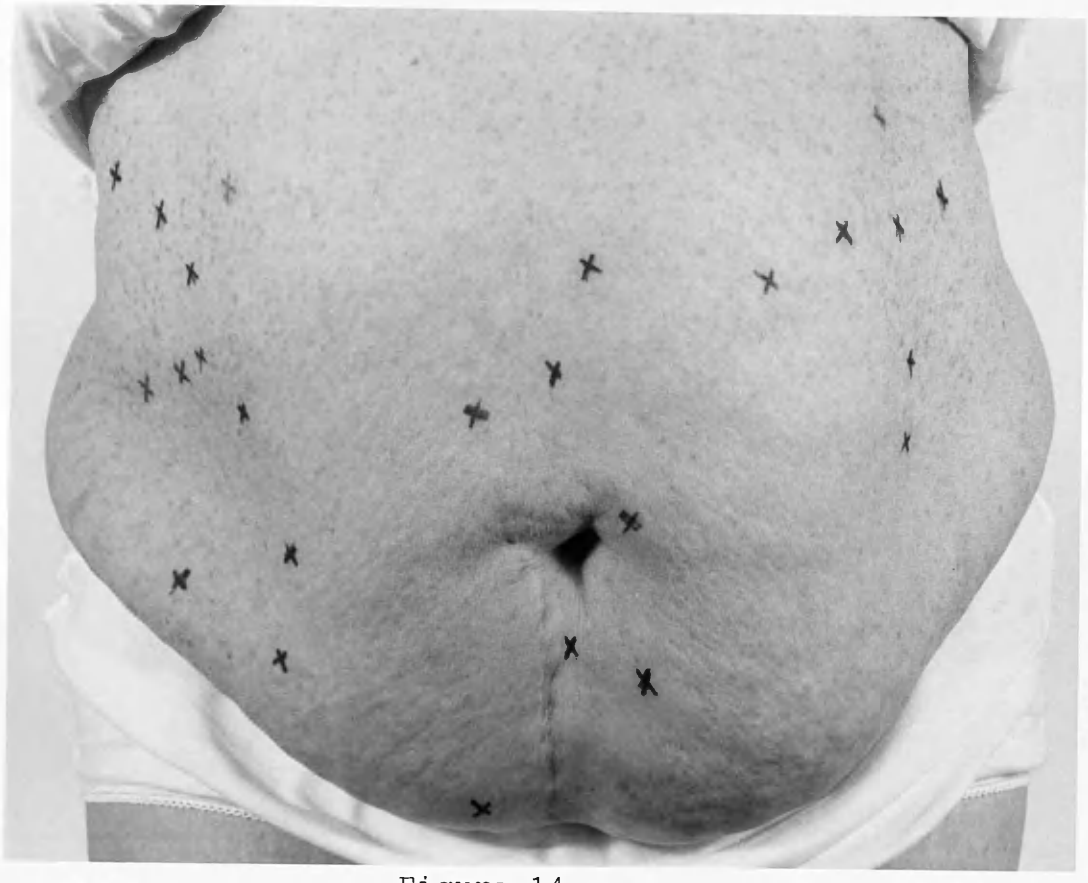


Figure 14 a.

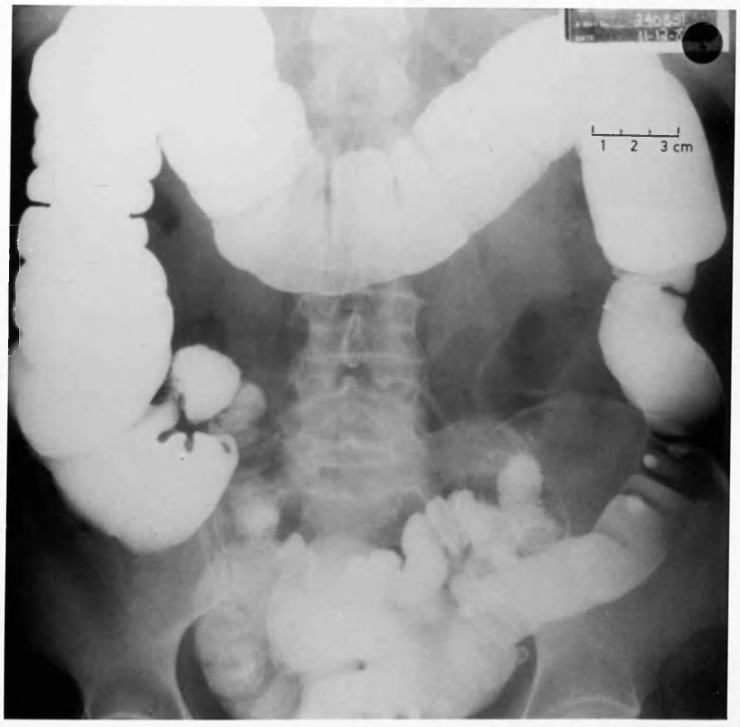


Figure 14 b.

Figure 15a.

Photograph of the abdomen (patient B) fixing the position of the radiopill throughout the study.

X SMALL BOWEL

⊗ COLON

Figure 15b.

Barium enema erect film (patient B).

Overlay taken from the photograph (15a) to show the position of the radiopill within the colon.

▲ UMBILICUS

◆ COLON

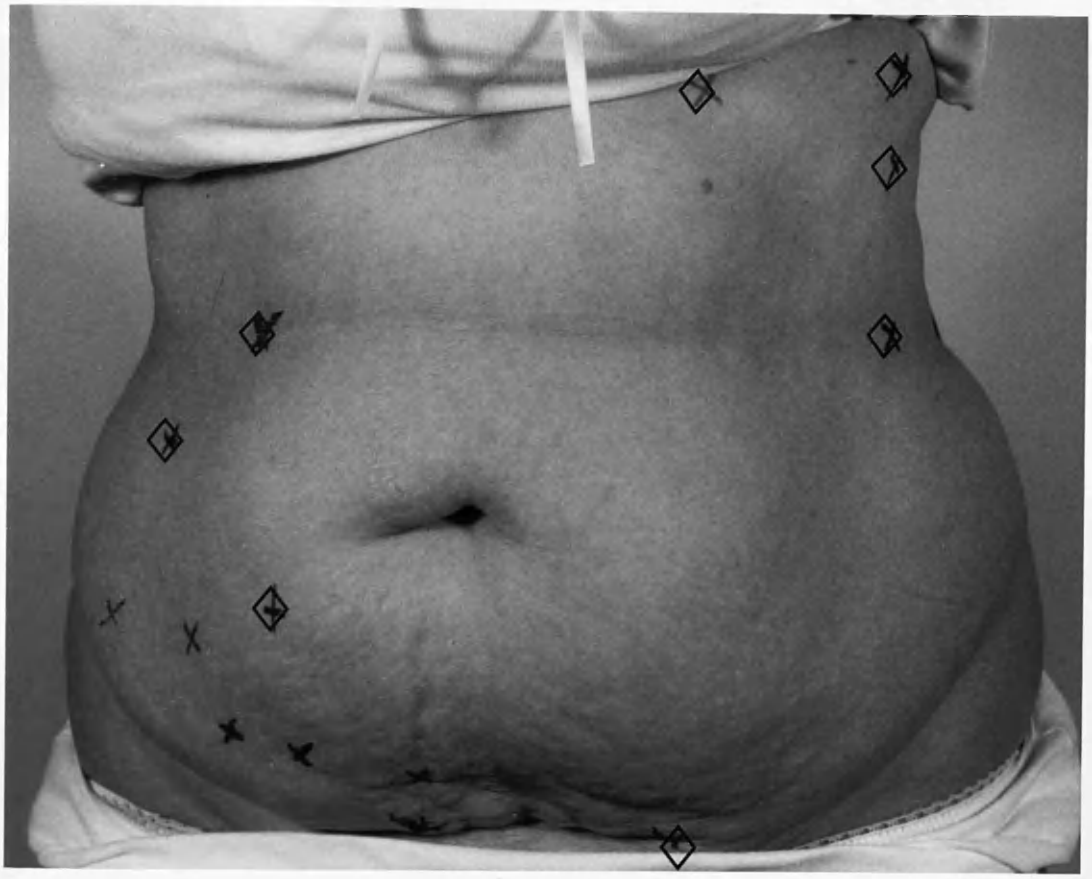


Figure 15 a.

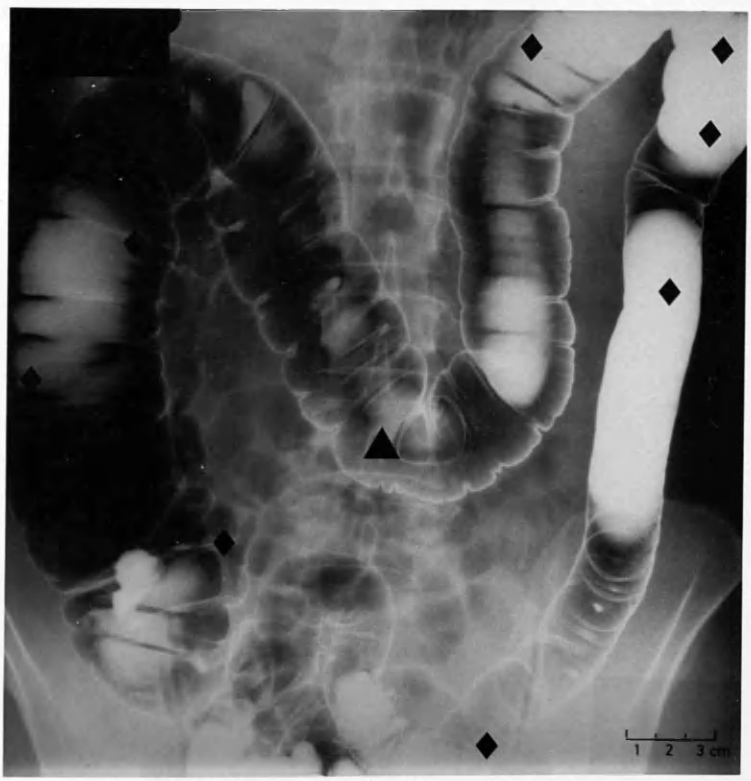


Figure 15 b.

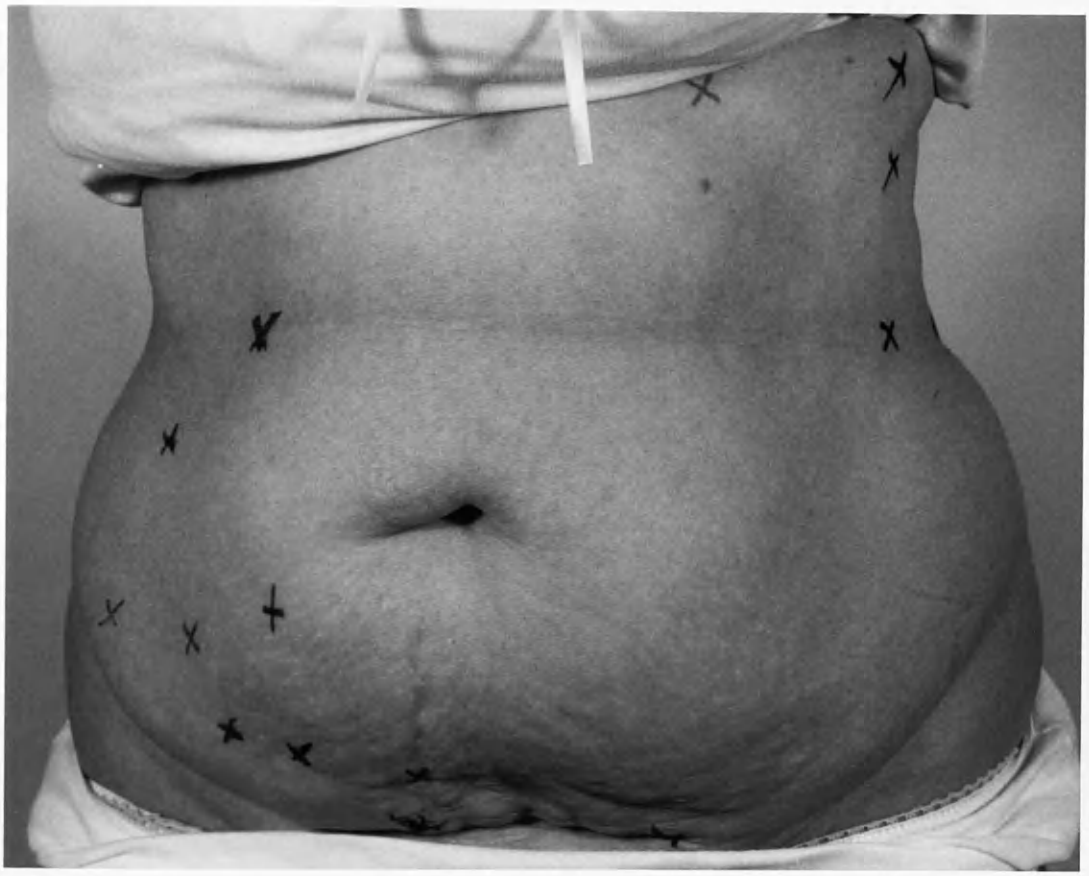


Figure 15 a.

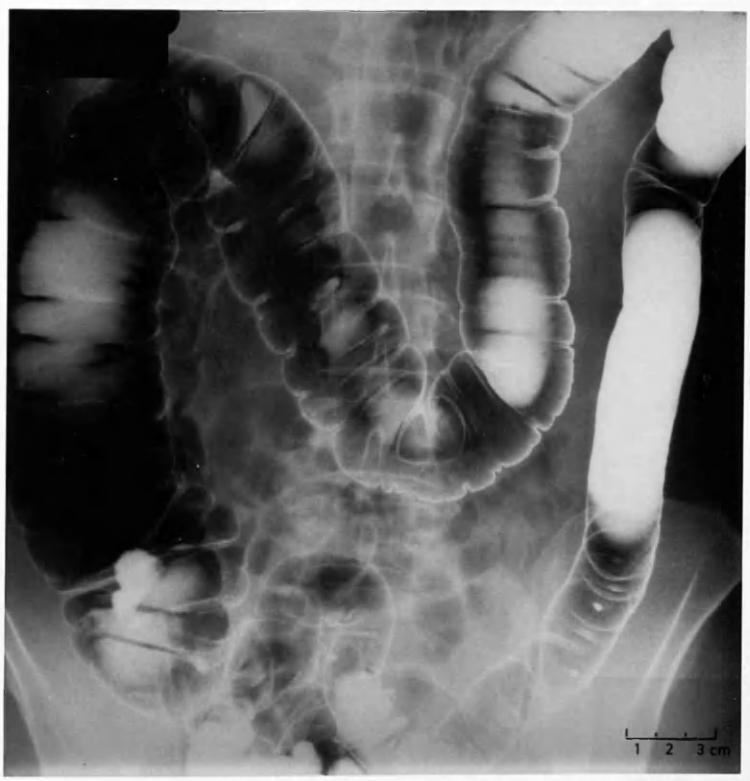


Figure 15 b.

It was hoped that entry into caecum could be determined by changes in pressure waveform as described by Misiewicz et al (1968). This, however, proved to be difficult. It was, therefore, decided to adopt the standard small bowel transit time of eight hours, previously used by Kirwan and Smith (1974).

As the passage of faecal material from sigmoid to rectum involves anterior to posterior movements, the time of entry into rectum was easily determined by noting the time when the maximum signal strength was detected over the sacrum.

Since validating this technique, Evans et al (1988) have shown that detecting the progress of the radiopill with a directional aerial probe correlates well with labelling the radiopill with a radioisotope and monitoring its position with a gamma camera.

Conclusion

The modified field strength meter is adequate for determining the segment of colon in which the radiopill is located and provides a reasonable estimate of large movements of colonic contents.

Study 6 Comparison of segmental transit as measured by radiopill tracking and ingestion of radio-opaque markers

Various studies have demonstrated the suitability of the radiopill for measuring gastrointestinal transit. Holdstock et al (1970) found that the transit time of a pressure-sensitive capsule and radio-opaque pellets ingested at the same time, was similar. These findings were complemented by a later study which found that mouth to caecum transit of a radio-isotopic capsule was closely comparable to mouth to stoma transit of radio-opaque pellets in healthy ileostomy patients. On the basis of these studies, it was assumed that the transport of radiotelemetry capsules and radio-opaque pellets through the colon was similar. (Waller,1975).

For the purposes of this study on diverticular disease, however, a further comparison of radiopill and marker transit was indicated. There were two reasons. First, it was desirable to compare the techniques in individual colonic segments. Second, it was necessary to determine if the radiopill, being of a larger shape and size than the markers, was delayed in the sigmoid colon, commonly narrowed in diverticular disease.

Metcalf et al (1987) developed a radio-opaque marker technique which enabled segmental transit times to be calculated. This involved the administration of three sets

of radio-opaque markers at twenty-four hour intervals and an abdominal x-ray on the fourth day. By counting the markers present on x-ray the colonic transit time could be calculated using the following formula:

$$MCT = \frac{1}{N} \sum_{i=1}^{j} ni \left(\frac{1}{2} [t\{i+1\} - t\{i-1\}] \right)$$

MCT = mean colonic transit; N = total number of markers given in each dose; ni = total number of markers present on a film taken at time ti; $\frac{1}{2}[t\{i+1\} - t\{i-1\}]$ = the time interval between successive films. j = number of abdominal films taken. Segmental times were calculated in a similar way using the above formula but referring to ni as the number of markers in each colonic segment.

Method

Segmental transit times as measured by radiopill tracking and ingestion of radio-opaque markers were compared using this multi-marker technique.

For the convenience of performing abdominal x-rays in the morning of day 4, markers were administered at 10am daily over three days. The radiopill was ingested at 10pm on the first day. Manual tracking (see study 5) commenced on the morning of day 2 and continued until the radiopill

entered the rectum. Segmental colonic transit times were calculated for both techniques.

Results; see Table 6

Patient 1	RIGHT	LEFT	RECTOSIGMOID	TOTAL
marker transit	13.2	4.8	21.6	39.6
pill transit	35.6	23.7	1.3	60.6
Patient 2				
marker transit	9.6	2.4	3.6	15.6
pill transit	7.5	7.3	12.5	27.3
Patient 3				
marker transit	22.8	1.2	1.2	25.2
pill transit	4.7	2.7	3.7	10.9
Patient 4				
marker transit	1.2	15.6	8.4	25.2
pill transit	2.8	18.3	13.0	34.1
Patient 5				
marker transit	7.2	0	0	7.2
pill transit	0.7	1.8	20.0	22.5
Patient 6				
marker transit	0	4.8	1.2	6.0
pill transit	4.0	0.8	8.0	12.8

Table 6.

Radiopill and marker transit times (hours).
Dosing at 24 hour intervals.

These results showed that in five of the six patients studied, the radiopill recorded longer colonic transit times than the markers.

With this dosing regime, each marker contributes 1.2 hours to the transit time through the segment in which it was located. To improve the resolution to 0.6 hours the frequency of dosing was doubled and the patient was x-rayed 24 hours earlier.

Method

The modified dosing was as follows:

Day 1	10pm; ingestion of first dose of markers
	10pm; ingestion of radiopill
Day 2	10am; ingestion of second dose of markers
	10pm; ingestion of third dose of markers
Day 3	10am; abdominal x-ray

For patients in whom the mouth to anus transit of the radiopill was greater than 48 hours, a further two doses of markers were administered at 10am and 10pm on day 3 and the abdominal x-ray was carried out at 10am on day 4. Four patients were given the modified dosing of markers.

Results ; see Table 7.

Patient 7	RIGHT	LEFT	RECTOSIGMOID	TOTAL
marker transit	11.4	2.4	0.0	13.8
pill transit	13.6	10.5	3.1	27.2
Patient 8				
marker transit	10.2	14.4	4.8	29.4
pill transit	15.8	9.8	5.8	31.4
Patient 9				
marker transit	7.2	6.0	4.8	18.0
pill transit	6.1	0.7	21.8	28.6
Patient 10				
marker transit	8.4	7.8	4.8	21.0
pill transit	1.5	5.2	16.8	23.5

Table 7.

Radiopill and marker transit times (hours).
Dosing at 12 hour intervals.

These results showed that colonic transit times were longer for the radiopill than the markers in all four studies.

Discussion

The radiopill recorded longer colonic transit times, irrespective of the marker dosing rate. (42% and 35% longer than the 24 and 12 hour marker techniques respectively). These are interesting findings which require a larger study population to investigate this further.

In the rectosigmoid area, the radiopill again recorded consistently longer transit times. It was felt that this delay may have been attributable to the radiopill being trapped in a narrowed segment of the sigmoid colon. The results were, therefore, analysed further by dividing the rectosigmoid into the sigmoid and rectum. The difference in techniques was again compared (Table 8).

	SIGMOID	RECTUM
Patient 1		
marker	12.0	9.6
radiopill	0.3	1.0
Patient 2		
marker	0.0	3.6
radiopill	2.3	10.2
Patient 3		
marker	0.0	1.2
radiopill	0.3	3.4
Patient 4		
marker	7.2	1.2
radiopill	12.2	0.8
Patient 5		
marker	0.0	0.0
radiopill	1.0	19.0
Patient 6		
marker	0.0	1.2
radiopill	0.3	7.7
Patient 7		
marker	0.0	0.0
radiopill	3.0	0.1
Patient 8		
marker	0.0	4.8
radiopill	0.5	5.3
Patient 9		
marker	1.8	3.0
radiopill	4.0	17.8
Patient 10		
marker	1.2	3.6
radiopill	4.1	12.8

Table 8.

Radiopill and marker transit times (hours).
Division of sigmoid and rectum.

The mean sigmoid transit time determined by the radiopill was 26% longer than the mean marker transit time (2.22hrs vs 2.80hrs) . In the rectum, however, the mean radiopill transit was 277% greater than the mean marker transit (2.82hrs vs 7.81hrs).

Conclusion

Assessment of large bowel transit by radiopill tracking and marker dosing gives different times. The pill measures the transit time of a bolus of material whereas the markers spread out and average over a larger mass of colonic contents. The pill measurement is continuous whereas the markers are essentially a series of "snapshots" taken at the dosing intervals. These differences are usually small except in the rectum where the pill can remain for a considerably longer time than the markers.

Since the rectum is not involved in diverticular disease, tracking the radiopill from caecum to distal sigmoid is a suitable method for measuring segmental colonic transit times.

4.3 Summary of system studies

Assessment of the radiotelemetry system under controlled laboratory conditions and evaluation of its performance in preliminary clinical work have demonstrated the following important points.

Radiopill performance

A battery can power the radiopill for up to 5 days and the dynamic response of the radiopill is adequate for following intracolonic pressure changes. However, for accuracy, the radiopill requires to be calibrated at 37°C before and after each study and a means of drift compensation is necessary to overcome the problem of frequency drift. Use of the drift compensation programme limits the system to the measurement of pressure changes.

Localisation of radiopill

With our modifications, the field strength meter was able to localise a radiopill in the colon to within 10mm. Superimposition of the abdominal markings onto the corresponding barium enema provided anatomical information on the progress of the radiopill. Tracking the radiopill in this way gave gastrointestinal transit times which correlated well with those obtained by a radio-opaque marker clearance technique.

Aerial performance

The belt aerial supplied by the manufacturer was unsatisfactory for this application because of frequent signal loss. Our newly developed band aerial has overcome this problem.

4.4 Preparation of the system for clinical use

The receiver software was organised as a menu which offered a choice of "configure", "calibrate" or "monitor" . In the "configure" mode, the programme requested selection of one of three parameters for study, the units of measurement required and the analog output update rates. The configure options selected in our study are illustrated in Figure 16.

Having selected the units of measurement, the analog output was calibrated. With a chart recorder or other analog device connected, the receiver output 0 volts and +2.4 volts corresponding to zero and full scale deflection of the units selected.

Radiopill calibration was then selected. The radiopill was calibrated on the receiver prior to each pressure study. In accordance with the manufacturer's recommendations, a new battery was inserted four hours prior to calibration in order to allow sufficient time for the radiopill frequency to stabilize.

Initially the radiopill frequency at atmospheric pressure and room temperature was adjusted to obtain a mid-band frequency value of approximately 430kHz. This was achieved by adjusting the position of the 14BA screw which altered the position of the ferrite disc relative to the ferrite pot core.

The Configure Menu

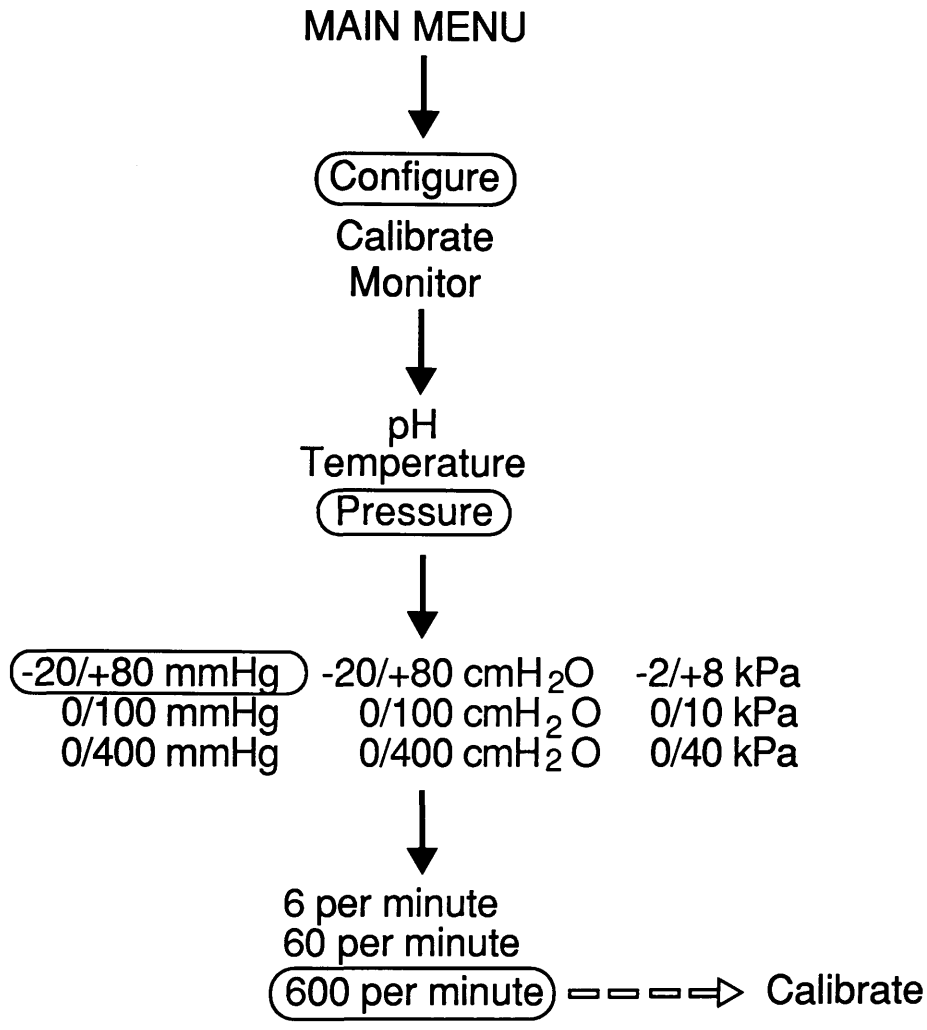


Figure 16.

Route through "Configure" Menu to set up the receiver for pressure.

The radiopill was then placed in a sealed plastic container, attached via a three-way tap to a medical mercury sphygmomanometer, and immersed in a water bath (37±1°C) for 30 minutes. The belt aerial was wrapped around the syringe to obtain a 100% signal which enabled the calibration procedure to be initiated.

In accordance with display instructions, the radiopill was initially pressurized to 80mmHg by injecting air from a syringe. The incoming telemetry signal, picked up by the belt aerial, was measured by the receiver and its frequency, drift rate (Hz/minute) and percentage signal strength were displayed. The calibration value was accepted once the drift rate was less than 100Hz/minute. The above procedure was then repeated at the lower pressure to complete the calibration programme. A calibration value expressed in kHz per mmHg was then displayed and stored in programme memory. On completion of each study, the radiopill was recalibrated to establish whether radiopill sensitivity had changed.

The "monitor" mode was selected when the study was due to begin. In this mode the receiver displayed the radiopill frequency and corresponding pressure data in both digital and bargraph format. The frequency and digital values were updated once per second and the bargraph updated 10 times per second (Figure 17).

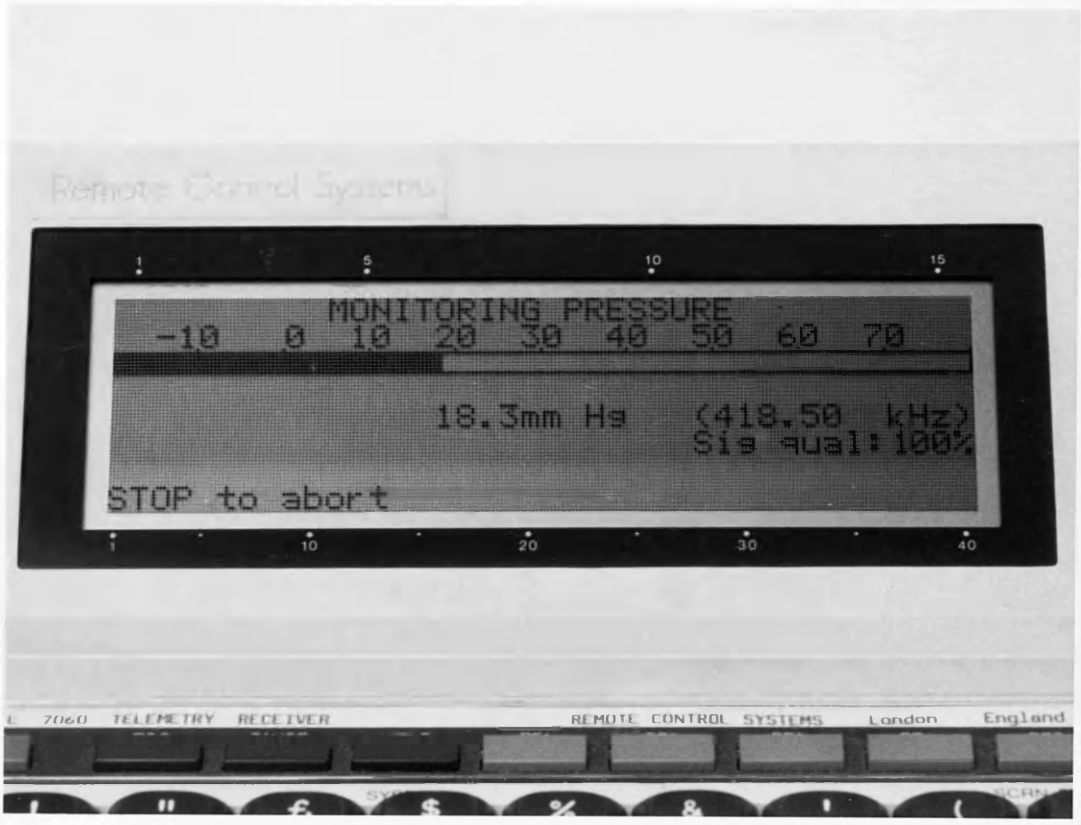


Figure 17.

Receiver's display when monitoring pressure.

4.5 Discussion of system

This study differs from the majority of reports in which colonic motility was measured in patients with diverticular disease because the ingested radiopill is more physiological, eliminating bowel preparation and invasive instrumentation. Although Receiver 7060 is not suited to ambulatory monitoring, by extending the belt aerial lead to 8 metres, the patient was given freedom of movement within the single room in which the studies were performed. Patients found this arrangement to be comfortable and certainly more desirable than other invasive tests involving per-rectally positioned catheters or probes.

The design and performance of Receiver 7060 is a considerable improvement on early telemetry systems. Preparation of the system for clinical use was made simple by the receiver software which prompted and guided the user carefully through the "configure", "calibrate" and "monitor" modes.

Since continuous supervision was not practical, the visual display of "poor quality" was of limited value. The development of an audible warning of poor quality was essential to prompt the patient to reposition the belt.

Even after this modification had been effected, the belt aerial was found to be unsatisfactory due to its sensitivity to radiopill orientation. The new band aerial

solved the problem of directional sensitivity and has proved to be ideal for monitoring an untethered radiopill as it progresses through the gastrointestinal tract.

Owing to the prolonged study time together with the frequent sampling rate, a large amount of data was generated. The Atari 1040ST microcomputer was particularly useful in providing a compact and automatic method for data storage and analysis.

5: DIVERTICULAR DISEASE:

- CLASSIFICATION OF SEVERITY AND CHANGES IN COLONIC MOTILITY.

5: DIVERTICULAR DISEASE: - CLASSIFICATION OF SEVERITY AND CHANGES IN COLONIC MOTILITY.

In this section a number of inter-related patient studies are described. They examine the effects of fibre therapy and physiological events on colonic motility and how these relate to severity of diverticular disease. They are as follows:

1) The effect of ispaghula husk on intestinal transit times.

2) The effect of ispaghula husk on right and left colonic motility.

3) Intestinal transit times and the radiological classification of disease severity.

4) Intestinal transit times and the symptomatic classification of disease severity.

5) Left colonic motility and the radiological classification of disease severity.

6) Left colonic motility and the symptomatic classification of disease severity.

7) The effect of food on left colonic motility.

8) The effect of sleep on left colonic motility.

9) Motility of the right and left colon.

5.1 Patients

Selection of patients.

Data was collected prospectively from 28 patients, 20 females (median age 65.5 yrs,range 33-77yrs) and 8 males (median age 68.5 yrs, range 39-79yrs) who were referred to the Royal Infirmary, Glasgow, between September 1987 and March 1989 with signs and symptoms suggestive of large bowel disease and whose barium enema demonstrated colonic diverticula but no other abnormality.

Patients who were being treated with drugs known to have an effect on colonic motility (e.g.opiate analgesics) and patients with a clinical diagnosis of irritable bowel syndrome and no diverticula on barium enema were excluded from the study. In 12 patients, 4 females (median age 70yrs, range 60-73yrs) and the 8 males it was possible to examine the effect of treatment by comparing the results of tests performed before and after ispaghula husk. These were then added to a group of 16 patients who were already taking various forms of fibre therapy. This resulted in a group of 28 patients, standardised on 7g (2sachets) ispaghula husk daily.

The control group.

A control group of healthy volunteers with no previous history of gastrointestinal disease and who were not receiving medication were studied. They comprised 3 females (median age 23 yrs, range 23-43yrs) and 5 males (median age 48 yrs, range 23-71yrs).

Classification of patients.

In order to obtain an assessment of the severity of diverticular disease, two methods of patient classification were used:

a) the severity of disease on x-ray.

b) the severity of disease on symptoms after standardisation on 7g ispaghula husk/day.

Severity of disease on x-ray.

For the purpose of this classification, the colon was divided into two segments; A (caecum to mid-transverse) and B (mid-transverse to distal sigmoid). A radiologist within the hospital independently examined the barium enema films of each patient and classified the findings according to the number of diverticula present within the left colon. The presence of less than five diverticula was defined as mild, between five and twenty diverticula as moderate and more than twenty as severe. Where diverticula extended into the right side of the colon, this was noted.

Severity of disease on symptoms after standardisation on ispaghula husk 7g/day.

Patients were classified into mild, moderate and severe disease groups according to the severity of abdominal pain after they had been receiving the standard medication for at least 4 weeks. Patients were given an ordered category assessment in which they were asked to define their abdominal pain as either mild, moderate or severe.

Results.

Table 9 shows patient details and classification of severity of disease on x-ray and symptoms and Table 10 gives details of the control group. The two selected methods of patient classification were then compared to determine whether the severity of abdominal pain reflected the severity of disease on x-ray. Table 11 demonstrates that there was no correlation between symptomatic and radiological severity of diverticular disease.

Sex	Age	X-ray	Symptoms
M	79	moderate	mild
M	64	moderate	mild
F	60	mild	moderate
M	52	mild	severe
M	73	moderate	mild
F	74	severe	mild
F	71	moderate	severe
F	64	mild	moderate
M	76	moderate	mild
F	55	severe	moderate
F	67	mild	mild
F	57	severe	mild
F	77	severe	mild
F	73	mild	moderate
F	63	mild	severe
F	72	severe	mild
M	78	moderate	mild
F	62	mild	mild
F	73	severe	mild
F	63	moderate	moderate
F	55	moderate	mild
F	51	moderate	mild
F	73	severe	mild
F	67	severe	severe
F	33	severe	severe
M	57	mild	moderate
M	39	moderate	moderate
F	70	severe	mild

Table 9.

Radiological and symptomatic classification of study population.

SEX	AGE
F	23
M	41
M	23
M	48
F	23
M	71
M	66
F	43

Table 10.

Age and sex distribution in control group.

		SEVERITY OF SYMPTOMS		
		MILD	MODERATE	SEVERE
SEVERITY OF DISEASE ON X-RAY	MILD	**2**	4	2
	MODERATE	7	**2**	1
	SEVERE	7	1	**2**

Table 11.

The relationship between radiological and symptomatic classification techniques.

Discussion

Radiology has for many years played an important part in the diagnosis of diverticular disease . It is, however, surprising that the only previous attempt to quantify this condition radiologically was undertaken by Hughes (1969a). He defined early disease as the presence of less than five diverticula in the sigmoid colon.

For the purposes of classification of patients it is useful to have three categories of disease, namely mild, moderate and severe. A numbering system has to be agreed upon to correspond with the severity of disease. Also the whole of the left colon needs to be considered because diverticula are often found proximal to the sigmoid colon.

An experienced radiologist established the presence of less than five diverticula within the left colon as mild disease, between five and twenty diverticula as moderate disease and more than twenty as severe diverticular disease. This may not be the optimal method of classification but so far it is the only way of defining severity of disease in an objective manner.

The classification of patients with bowel problems on symptoms is difficult. In the symptomatic classification of disease severity, a broad spectrum of symptoms was initially considered. This included abdominal pain, abdominal distension, straining, flatulence and the passage of mucus and blood per rectum. Analysis of case histories

showed that the presence of these symptoms was very variable. However, abdominal pain stood out as being the most frequently reported symptom. In addition, this has been shown to be associated with raised intracolonic pressure (Holdstock et al,1969; Weinreich & Andersen, 1976b). For these reasons it was decided to classify patients according to the severity of abdominal pain.

Since perception of pain is highly subjective, it is not surprising that pain does not correlate with the number of diverticula on x-ray. At one end of the clinical spectrum are patients with pancolonic diverticula who are asymptomatic; at the other end are patients with few diverticula and severe pain. This confirms the findings of previous studies (Parks, 1969; Almy & Howell,1980).

Despite the foregoing, pain is the best indication of severity of symptoms and when allied to the radiological classification should provide a good insight into the pathophysiology of diverticular disease. This will be explored in Section 5.3.

5.2 Methods

Intracolonic pressure measurements.

Written informed consent was obtained from each patient before tests began. Patients were admitted to the ward the day before the study. Patients continued taking their normal diet and no bowel preparation was given. Prior to ingestion at 10pm that evening , the calibrated radiopill was sealed in a plastic finger stall to prevent faecal clogging and etching of the diaphragm with gastrointestinal secretions.

Recording of pressure from the radiopill commenced at 8.30am the following morning when the system, consisting of the receiver with attached belt aerial, the Atari computer and visual display unit and the Servoscribe pen recorder assembled on a trolley, was taken to the patient (Figure 18). The computer programme was initialised and the receiver switched onto the "monitor" mode to start recording data. Optimisation of aerial position in relation to the radiopill was obtained by reference to the receiver's liquid crystal display unit which indicated the percentage signal quality in 10% stages in addition to the radiopill frequency and pressure, expressed in digital and bargraph format (Figure 17). The belt aerial was moved from waist to mid-thorax or hips in order to obtain a 100%

Figure 18.

Trolley-mounted receiver, computer, VDU and pen recorder set up for colonic pressure measurement.

signal. If the signal quality fell below 30%, frequency display and digital values were blanked out, a "poor signal" message was displayed and an audible alarm was triggered.

External location and plotting of radiopill position using a field strength meter also began at 8.30am. This continued until 10pm and resumed the following morning. The position of the radiopill at fifteen minute intervals was marked on the patient's abdomen and meal times were noted. Patients were able to move, sit or lie down limited only by the 8m length of co-axial cable connecting the belt aerial to the receiver.

Intracolonic pressure recording and surface tracking of the radiopill continued until the radiopill entered the rectum, taken to be the time when the maximum signal was detected in the sacral area. The patient's abdomen was then photographed for correlation with his/her barium enema. Patients remained in hospital from the time of administration of the radiopill until its recovery. The radiopill was then recalibrated.

In the 12 untreated patients, assessment of colonic motility was made before and after treatment with ispaghula husk.

Data analysis.

The development of an off-line system of computer analysis has enabled the following parameters to be investigated.

(1) Colonic motility index
(2) Percentage activity
(3) Number of pressure peaks above 5mmHg/hour and 50mmHg/hour
(4) Gastrointestinal transit times

Colonic motility index.

This index provides a means of objectively measuring colonic motor activity and enables comparisons to be drawn between different patients. In the present study the colonic motility index is computed as:

$$M.I. = \frac{2 \times \text{area under pressure curve}}{\text{measurement time}} \times 100$$

The motility index is a convenient way of expressing the energy expended by the colon. However, expressing colonic motility changes solely as a "motility index" may mask the nature of the motor activity within the colon. For example, a similar motility index could result from a large number of small waves or a less frequent number of large amplitude waves (Eastwood, Smith, et al,1978).

To obtain a complete analysis therefore, it was important to calculate another three parameters of colonic motility, namely the percentage activity, the number of pressure peaks greater than 5mmHg/hour and the number of pressure peaks greater than 50mmHg/hour.

Percentage activity.

This refers to the percentage of the total recording time during which pressure waves occurred. For the purpose of this analysis, waves of amplitude < 5mmHg have been excluded to take account of any "noise".

Number of pressure peaks >5mmHg/hour and >50mmHg/hour.

A computer programme has been developed to enable the operator to adjust a threshold line to a certain amplitude in order to calculate the number of peaks above that amplitude. For the purpose of the present study, waves above 5mmHg and 50mmHg were selected. Calculation of the number of peaks above 5mmHg/hour gives an indication of the frequency of contractions and calculation of the number of peaks above 50mmHg/hour gives an indication of the number of strong contractions. The system was unable to record pressure waves > 80mmHg. This is an acknowledged limitation.

Gastrointestinal transit times.

Various transits were considered for analysis.

(a) mouth to anus
(b) mouth to rectum
(c) caecum to mid-transverse (right colon)
(d) mid-transverse to distal sigmoid (left colon)

All transit data was obtained from the manual tracking of the radiopill through the colon (see Study 5, Section 4.2).

Statistical testing.

The Wilcoxon signed rank test was used to examine the effect of ispaghula husk on transit times and colonic motility. Results are expressed as median (range).

As an initial step in the data processing of the total study population, results from the four groups were analysed using the Kruskal-Wallis test for statistical significance. This was used to determine significant differences between the groups.

Note, however, that this test does not show if an order exists in the groups. Since the control group had a mean age considerably less than the other groups it may not

reflect the colonic motility pattern of normal older age-matched subjects. For this reason, it was decided to look for ordering only in the disease groups using the Spearman rank correlation test.

On examining the colonic response to food, the percentage change in each of the motility parameters pre and post-prandially was calculated. An exception was made with the number of peaks>50mmHg/hour because the absence of these peaks in the pre-prandial hour necessitated the determination of absolute change.

The Kruskal-Wallis test was not used in the analysis of sleep and colonic motility owing to the small number of control subjects.

5.3 Results

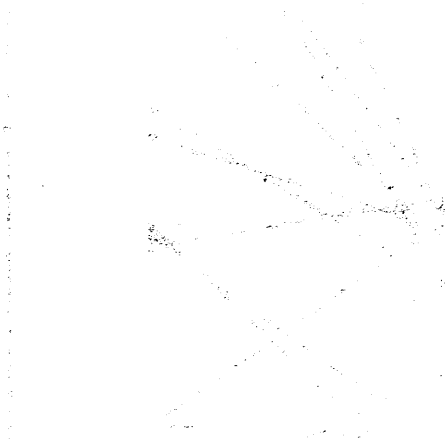
Patient Study 1: The effect of ispaghula husk on intestinal transit times.

The transit times of the 12 untreated patients, as measured by the radiopill, were examined before and after standardisation on ispaghula husk. Mouth to anus transit times decreased significantly following treatment from 36.9 (18.5-68.6) hours [median (range)] to 32.5 (18.8-35.9) hours, $p<0.05$, (Figure 19). Mouth to rectum transit times decreased similarly from 33.9 (9.3-67.2)hours to 23.7 (13.6-35.0) hours, $p<0.05$, (Figure 20).

In the colon, this reduction in transit was restricted to the right colon, decreasing from 17.2 (1.1-38.8) hours to 8.9 (0.5-15.3) hours ,$p<0.05$, (Figure 21). There was no significant reduction in transit apparent in the left colon, 9.6 (2.3-24.0) hours to 8.4 (2.5-16.3) hours, p=NS, (Figure 22). These results are set out in Table 12. Individual values are documented in Appendix 1.

Although small numbers preclude consideration of transit times by disease severity, it is of interest to note that on radiological classification the group contained 3 patients with mild disease, 6 with moderate disease and 3 with severely diseased colons. Seven of these

patients improved symptomatically, 3 were unchanged and 2 became worse when treatment with ispaghula husk was instituted. However, there was no apparent relationship between the modification of symptoms and the change in colonic motility parameters following treatment.



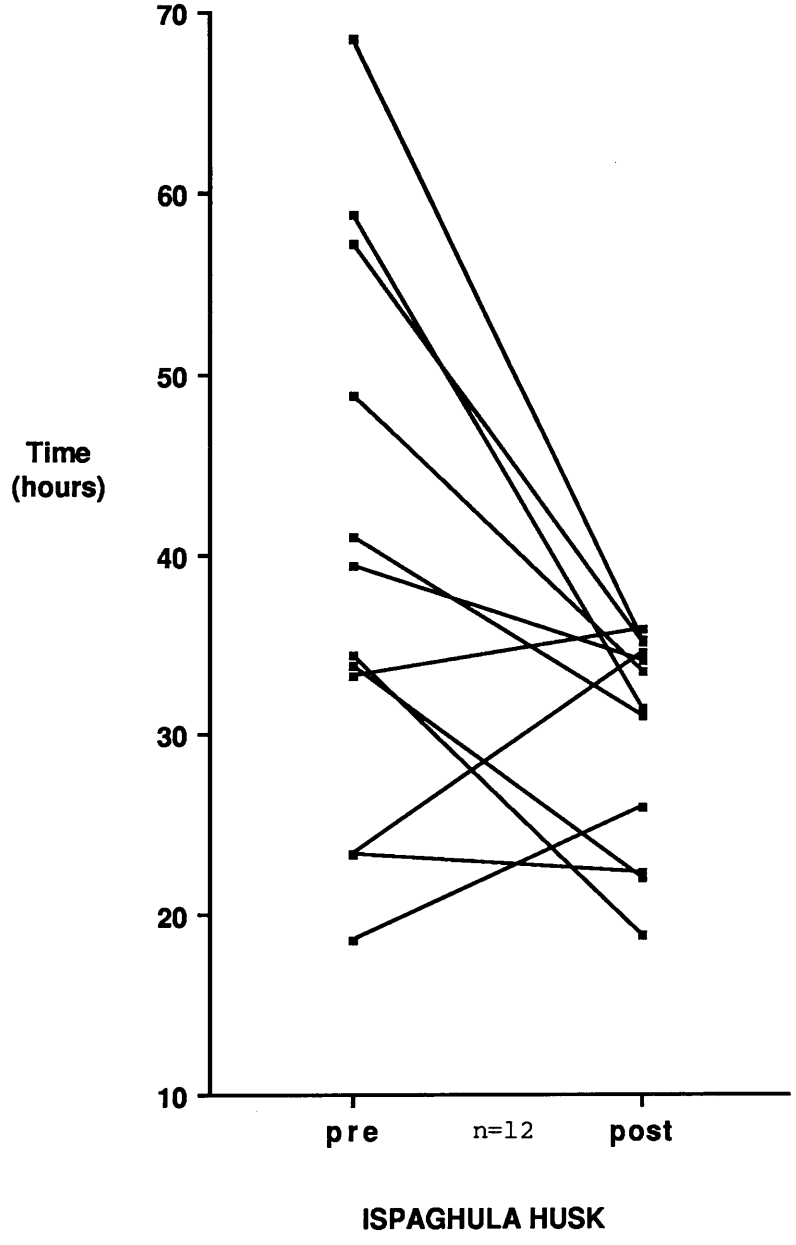


Figure 19.
The effect of ispaghula husk on mouth to anus transit times.

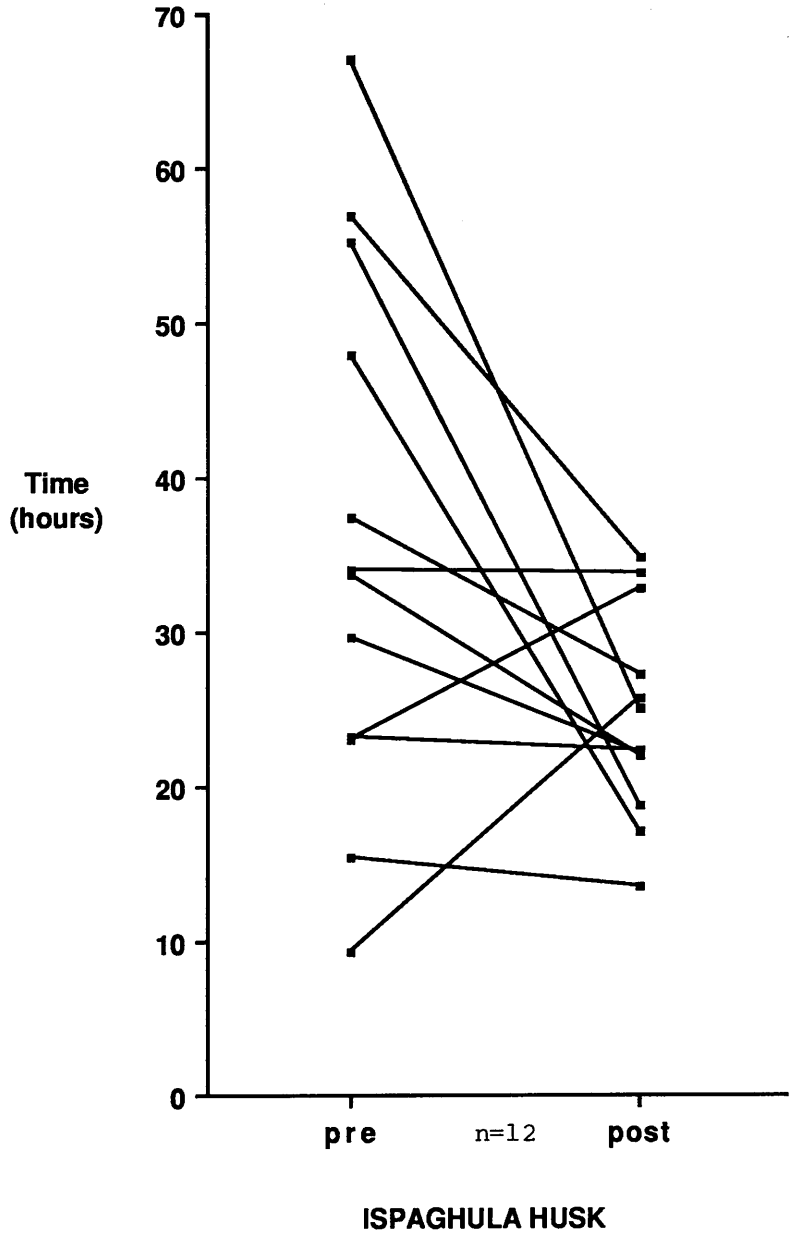


Figure 20.
The effect of ispaghula husk on mouth to rectum transit times.

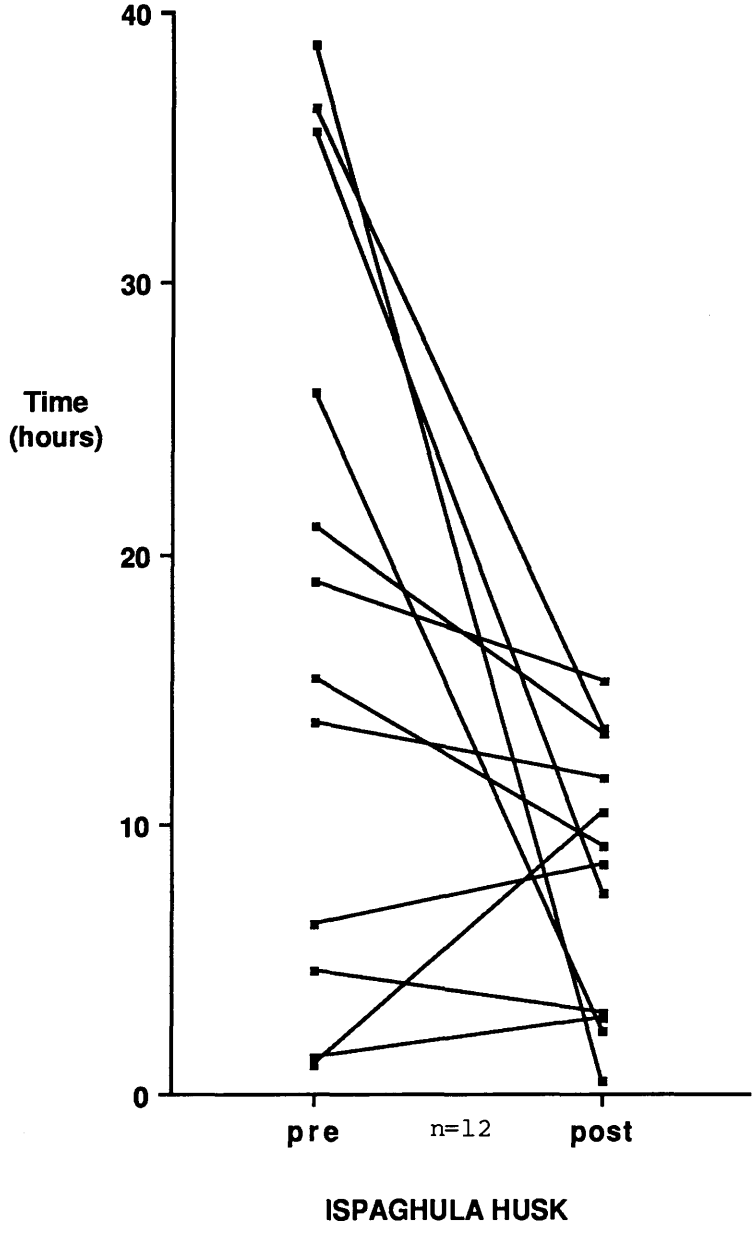


Figure 21.
The effect of ispaghula husk on right colonic transit times.

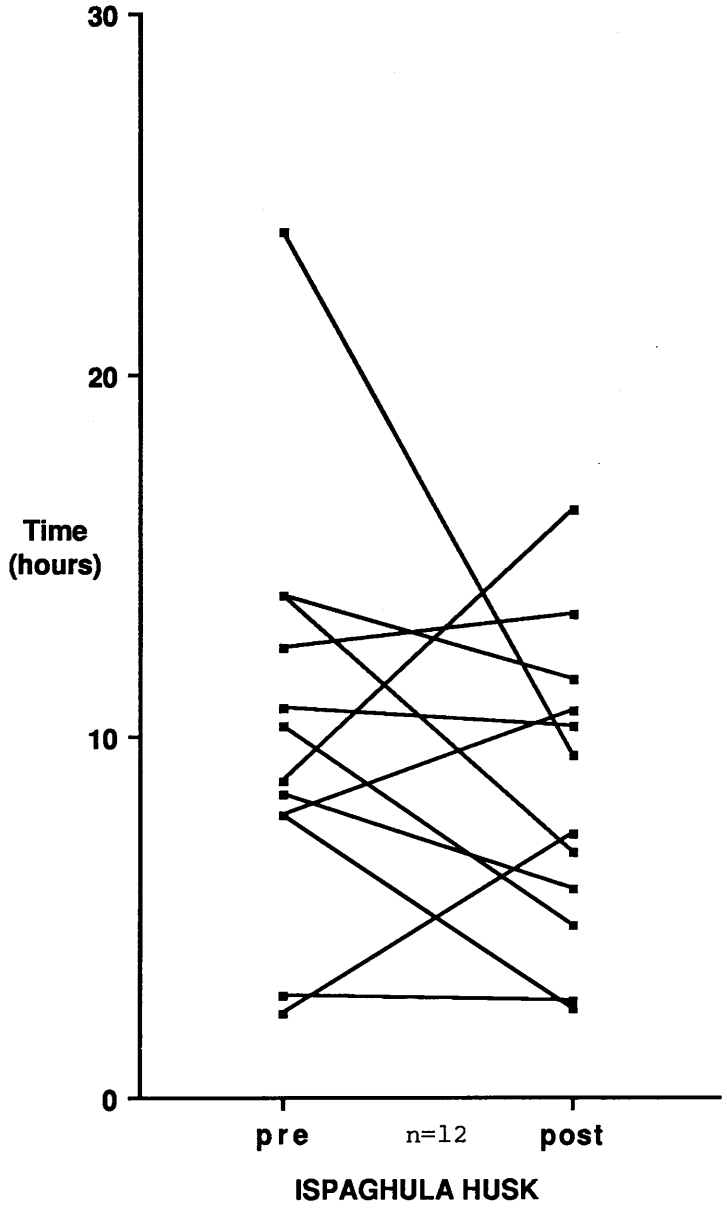


Figure 22.
The effect of ispaghula husk on left colonic transit times.

	Pre-treatment median (range) (hours)	Post-treatment median (range) (hours)
Mouth to anus	36.9 (18.5-68.6)	32.5 (18.8-35.9)
Mouth to rectum	33.9 (9.3-67.2)	23.7 (13.6-35.0)
Right colon	17.2 (1.1-38.8)	8.9 (0.5-15.3)
Left colon	9.6 (2.3-24.0)	8.4 (2.5-16.3)

Table 12.

The effect of ispaghula husk on intestinal transit times.

Patient Study 2: The effect of ispaghula husk on right and left colonic motility.

The motility parameters of the 12 untreated patients were also compared before and after administration of ispaghula husk. Following a minimum 4 week treatment period, the motility index increased significantly in the right colon from 224 (73-630) [median (range)] to 481 (126-1016), $p<0.05$, (Figure 23) whereas no significant increase was demonstrated in the left colon, 616 (136-1572) to 705 (267-1520), p=NS, (Figure 24).

Similarly, percentage activity increased significantly in the right colon from 10 (4-20) to 20 (8-37), p=0.005, (Figure 25) and although there was some rise in the left colon this was less marked, 17 (4-37) to 25 (4-38), p=NS, (Figure 26).

The number of peaks greater than 5mmHg/hour following treatment with ispaghula husk increased from 50.0 (18.2-119.3) to 106.0 (72.8-188.3) in the right colon, p=0.005, (Figure 27) whereas no significant increase was demonstrated in the left colon, 60.2 (21.3-152.6) to 95.7 (29.2-151.2), p=NS (Figure 28).

In contrast, ispaghula husk had no significant effect on the number of peaks greater than 50mmHg/hour in either the right or left colon (Figures 29 & 30). Tables 13 & 14 detail the medians and ranges and Appendix 2 documents individual values.

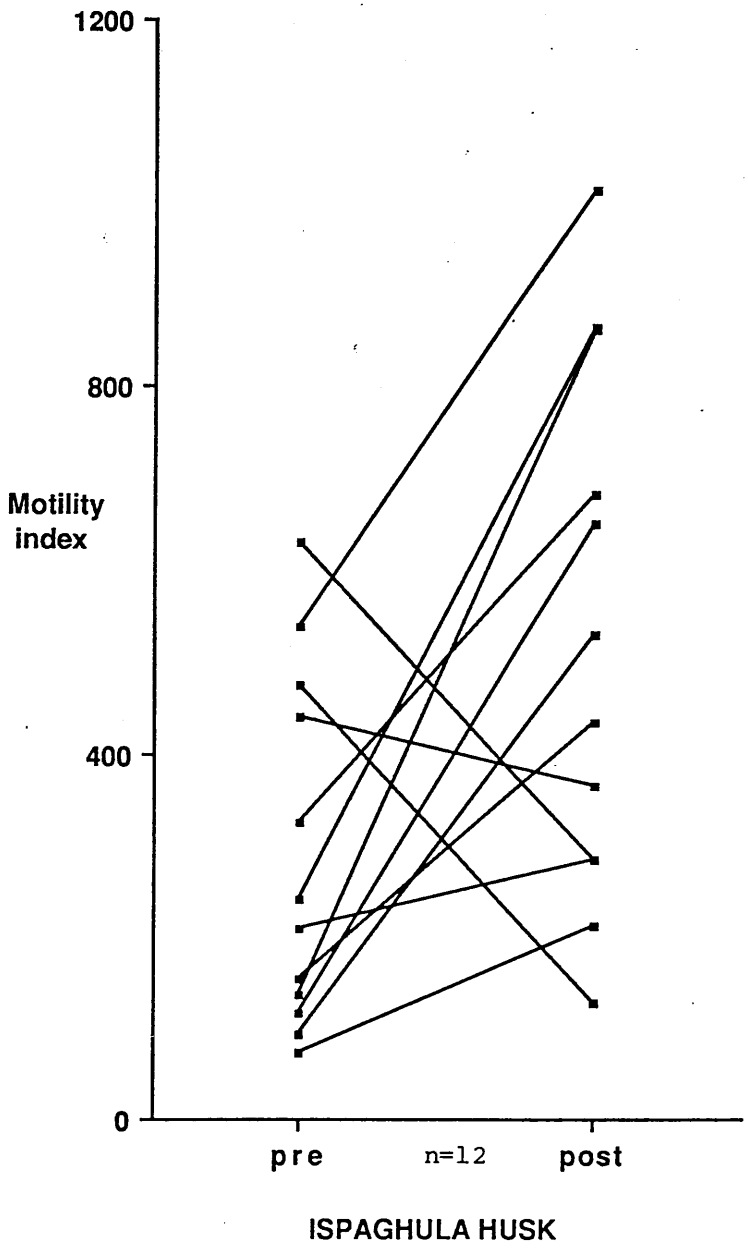


Figure 23
The effect of ispaghula husk on right colonic motility index.

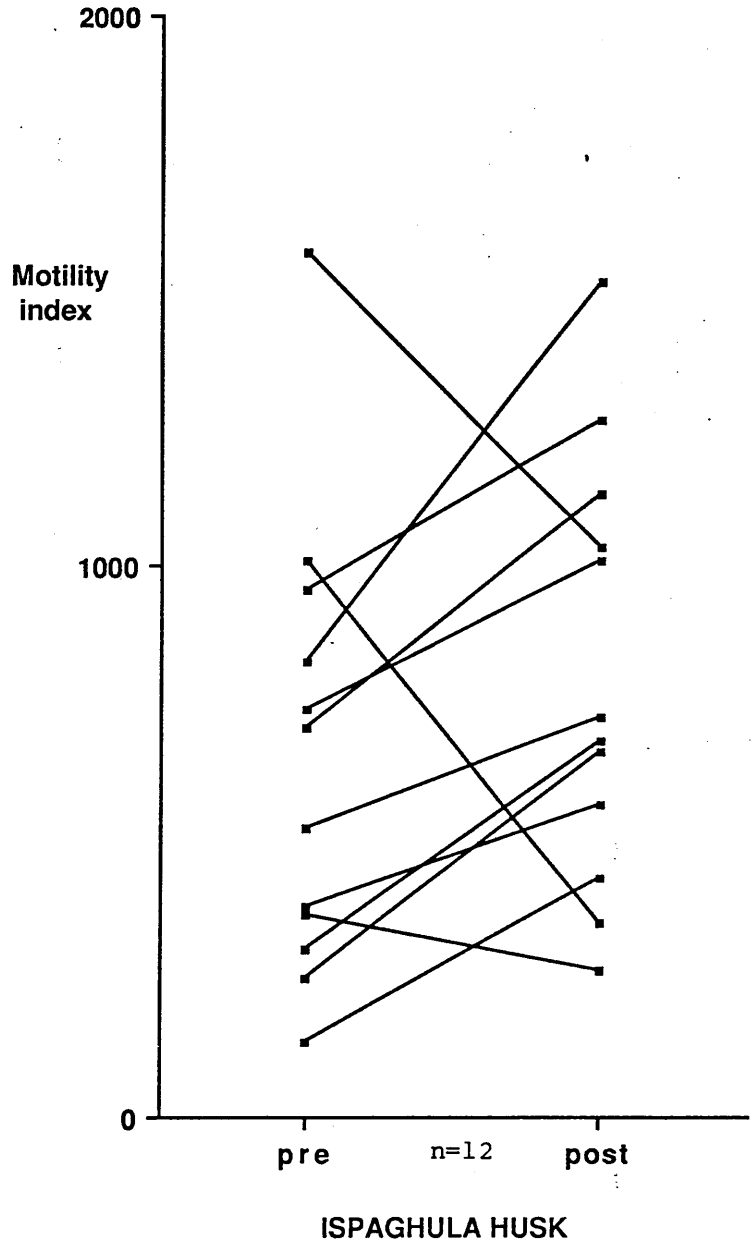


Figure 24
The effect of ispaghula husk on left colonic motility index.

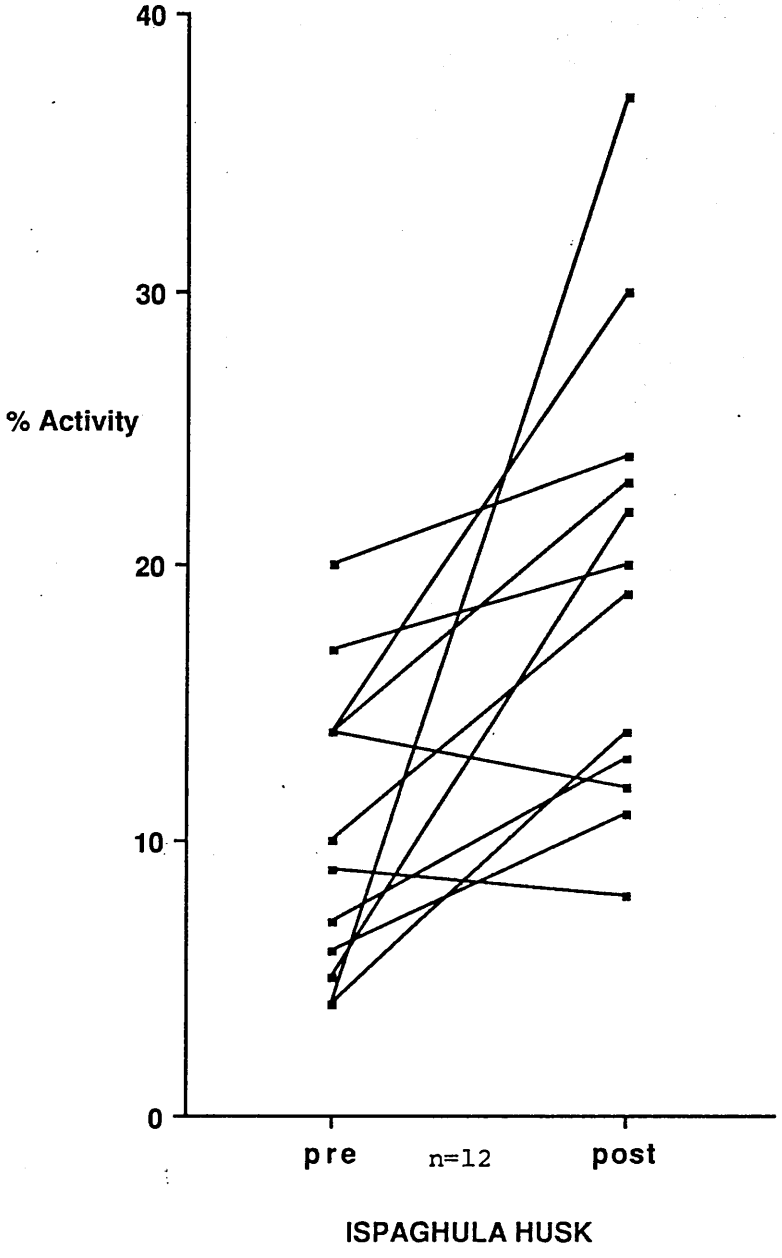


Figure 25
The effect of ispaghula husk on right colonic % activity.

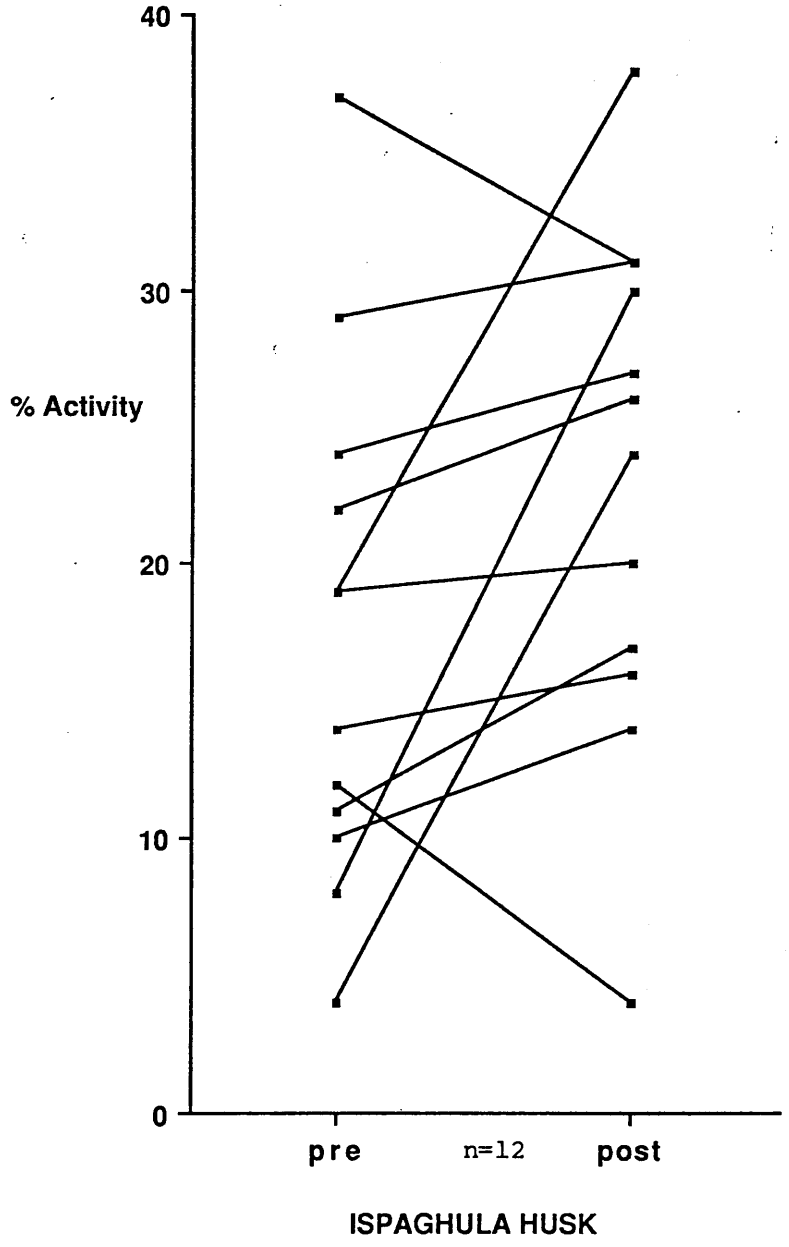


Figure 26
The effect of ispaghula husk on left colonic % activity.

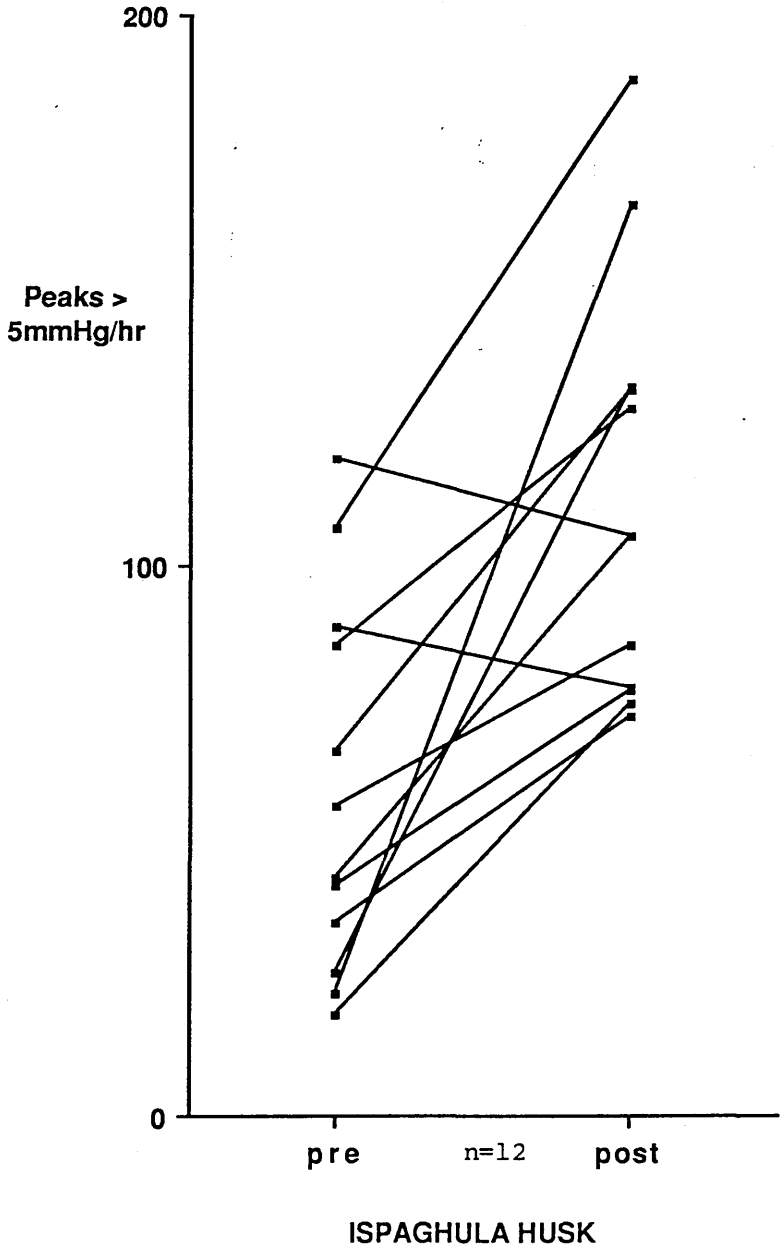


Figure 27

The effect of ispaghula husk on the right colonic number of peaks >5mmHg/hour.

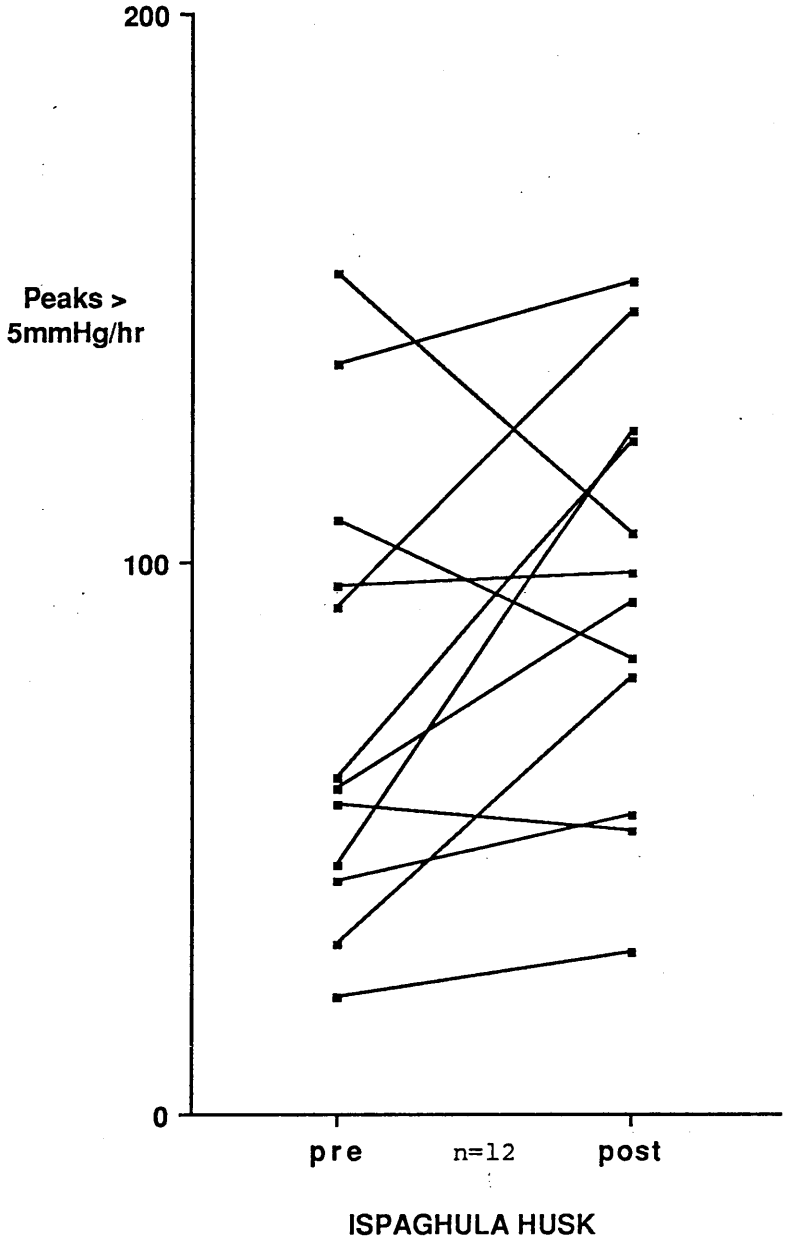


Figure 28
The effect of ispaghula husk on the left colonic number of peaks >5mmHg/hour.

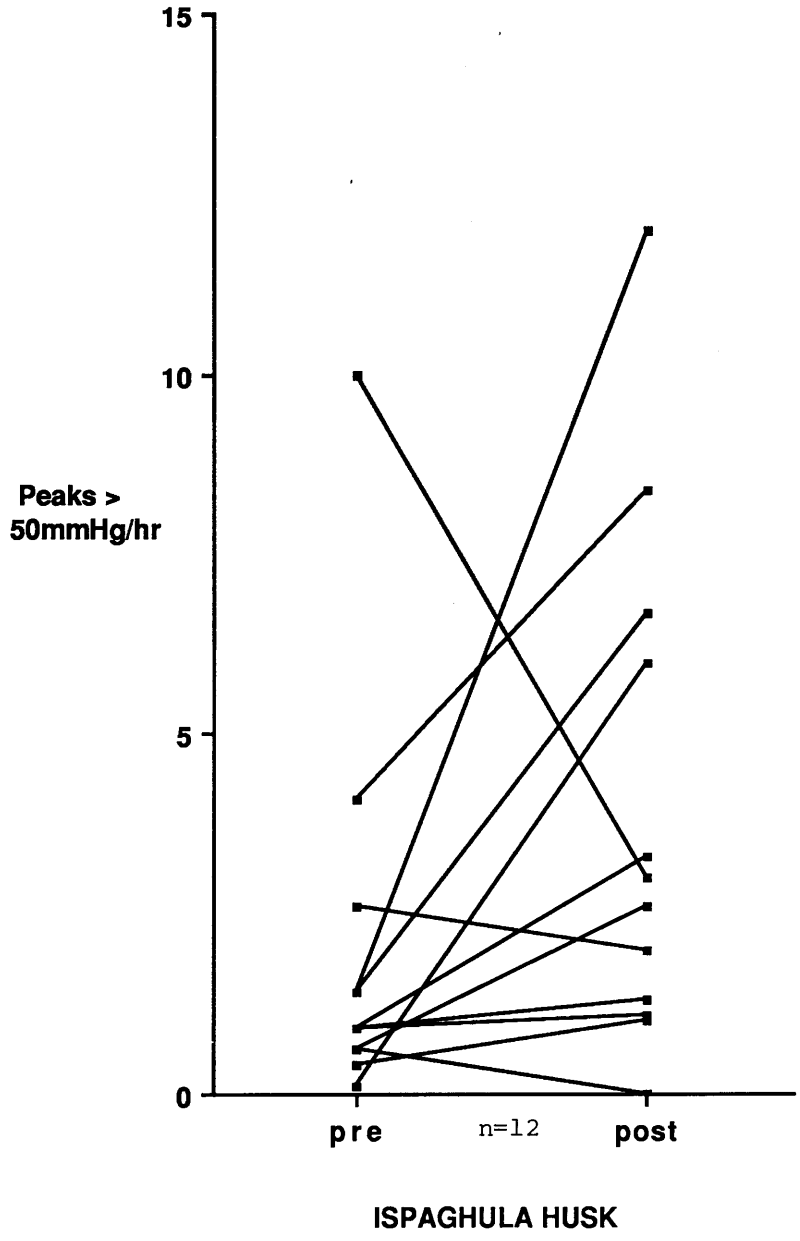


Figure 29.
The effect of ispaghula husk on the right colonic number of peaks >50mmHg/hour.

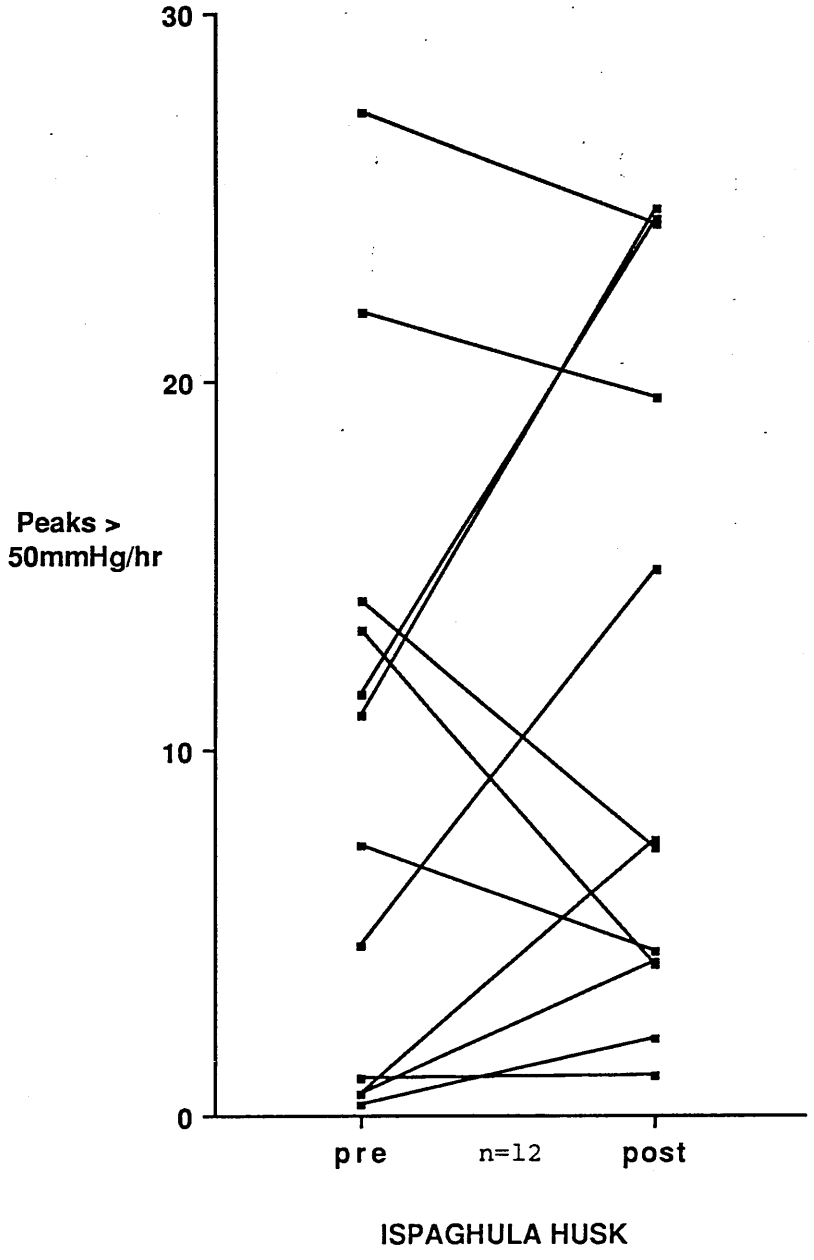


Figure 30
The effect of ispaghula husk on the left colonic number of peaks >50mmHg/hour.

	Pre-treatment median (range)	Post-treatment median (range)
Motility index	224 (73-630)	481 (126-1016)
% Activity	10 (4-20)	20 (8-37)
Peaks>5mmHg/hr	50 (18.2-119.3)	106 (72.8-188.3)
Peaks > 50mmHg/hr	0.9 (0.1-10.0)	2.8 (0-12.0)

Table 13.

The effect of ispaghula husk on right colonic motility.

	Pre-treatment median (range)	Post-treatment median (range)
Motility index	616 (136-1572)	705 (267-1520)
% Activity	17 (4-37)	25 (4-38)
Peaks > 5mmHg/hr	60.2 (21.3-152.6)	95.7(29.2-151.2)
Peaks >50mmHg/hr	9.2 (0.3-27.3)	7.4 (1.1-24.7)

Table 14.

The effect of ispaghula husk on left colonic motility.

Discussion

Ispaghula husk is a standard treatment option for patients with diverticular disease (B.N.F.,1988b). Its mode of action on colonic motility, however, is uncertain. In particular, there has been controversy surrounding its effect on transit times and motility in the large bowel (Eastwood, Smith et al, 1978; Archbold and Parks, 1979). Consider transit times first of all. Eastwood, Smith et al (1978) from Edinburgh found that ispaghula husk had no significant effect on transit time whereas Archbold and Parks (1979) from Belfast showed that transits were reduced following treatment. The results of this study agree with the Belfast group and point to the right colon as being the site where colonic contents were speeded up.

An interesting additional finding was that initially fast transit times became slower after treatment. The effect of fibre therapy on the group could be described as a "normalisation" of mouth to anus transit times towards a 32.5 hour median. A similar "normalisation" effect has been reported by Prior and Whorwell (1987) when ispaghula husk was given to patients with irritable bowel syndrome and when wheat bran was given to patients with diverticular disease (Brodribb & Humphreys, 1976).

Next, looking at motility of the left colon, there is again a conflict between the Edinburgh and Belfast groups (Eastwood, Smith et al, 1978; Archbold & Parks , 1979). The Edinburgh group found a raised motility index on ispaghula husk largely attributable to an increase in the number of pressure peaks in the range 50-90 cms water whereas the Belfast group reported a reduction in the mean motility index post treatment. The findings of this study were unable to demonstrate a significant change in any of the motility parameters.

Although ispaghula husk appeared to be having a minimal effect on the left colon, transit data suggested that this was not the case for the right colon. Examination of the right motility index, percentage activity and the number of pressure peaks greater than 5mmHg/hour showed that they all increased significantly following treatment. This is an interesting finding which has not so far been recognized in previous studies of colonic motility which have confined their measurements to the distal colon, easily accessible to tubes or wires per rectum.

The prescription of ispaghula husk in the management of diverticular disease has been questioned because it is thought to hyperstimulate the diseased bowel (Eastwood, Smith et al,1978). This study, however, showed that this stimulant effect primarily involved the unaffected right colon with minimal extra stimulation on the left side.

Patient Study 3: Intestinal transit times and the radiological classification of disease severity.

The transit times of all 28 patients and 8 controls were examined. Of the 28 patients (see Table 9), 8 were allocated to the mild group (median age 62.5yrs, range 52-73yrs), 10 to the moderate disease group (median age 67.5yrs, range 39-79yrs) and 10 were considered to have severe disease of the left colon (median age 71yrs, range 33-77yrs). The median age of the 8 control subjects was 42 years and ranged from 23-71 years (Table 10).

Figures 31-34 illustrate the total and segmental transit times for each group and Table 15 details the medians and ranges. Individual values are documented in Appendix 3.

Use of the Kruskal-Wallis test demonstrated that intestinal transit times did not differ significantly between the four groups. In the disease groups, there was no correlation between transit times and increasing severity of disease on x-ray.

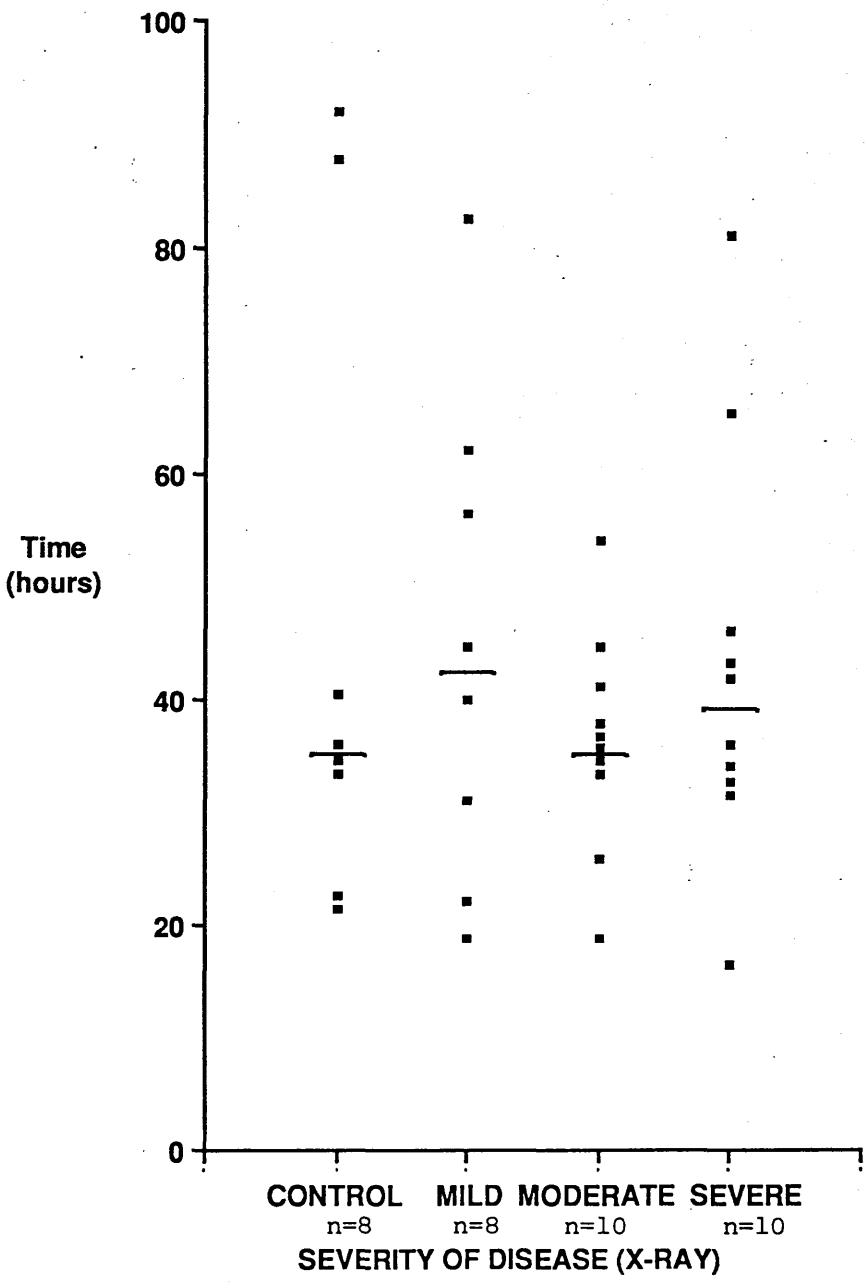


Figure 31

Mouth to anus transit times and the radiological classification of disease severity.

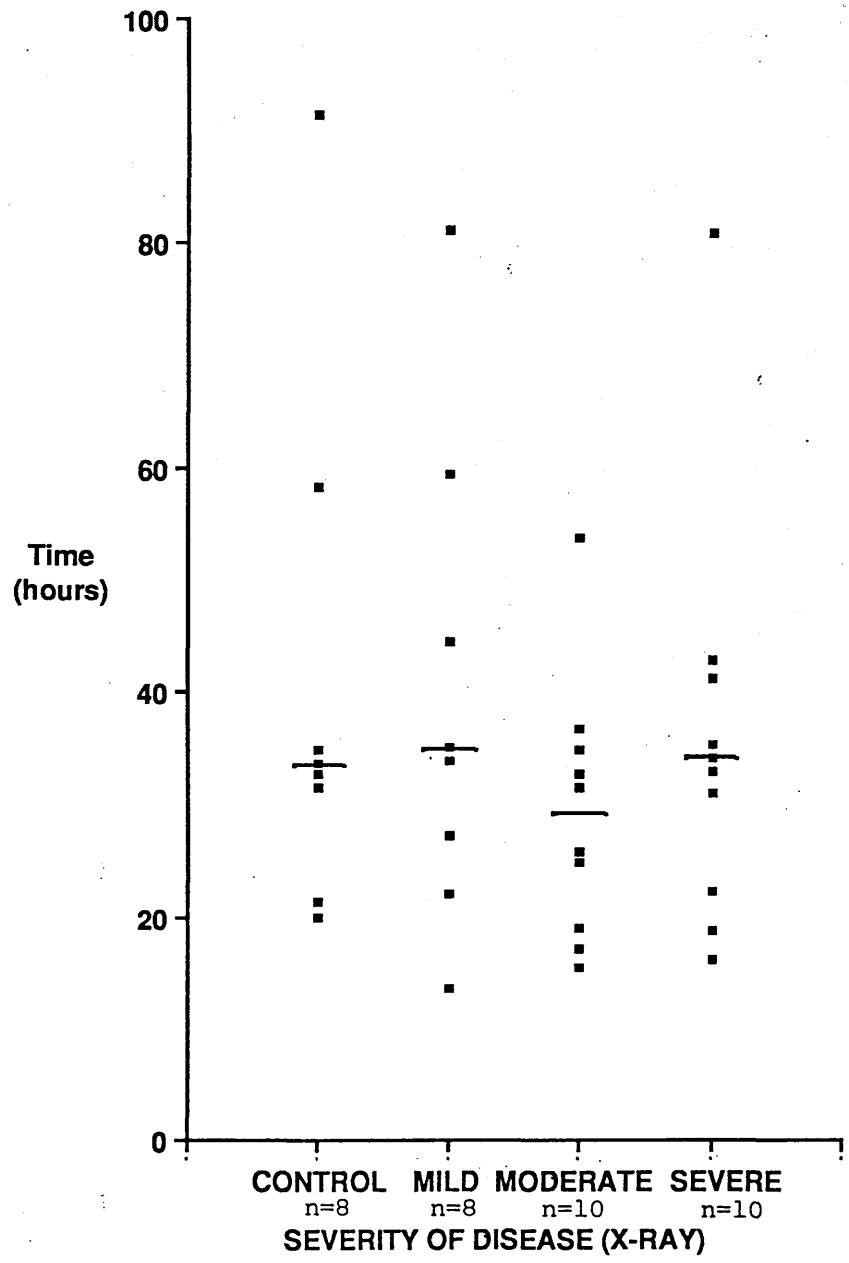


Figure 32

Mouth to rectum transit times and the radiological classification of disease severity.

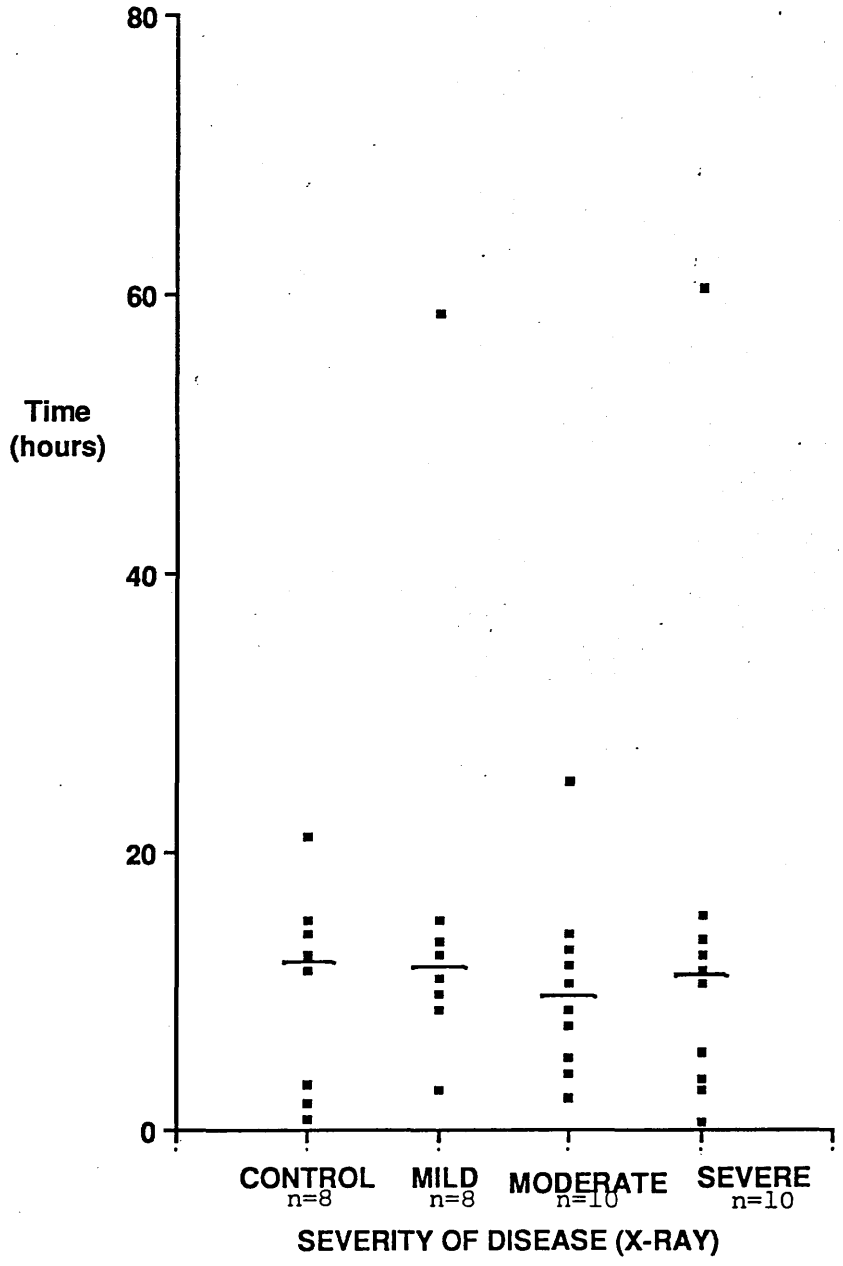


Figure 33

Right colonic transit times and the radiological classification of disease severity.

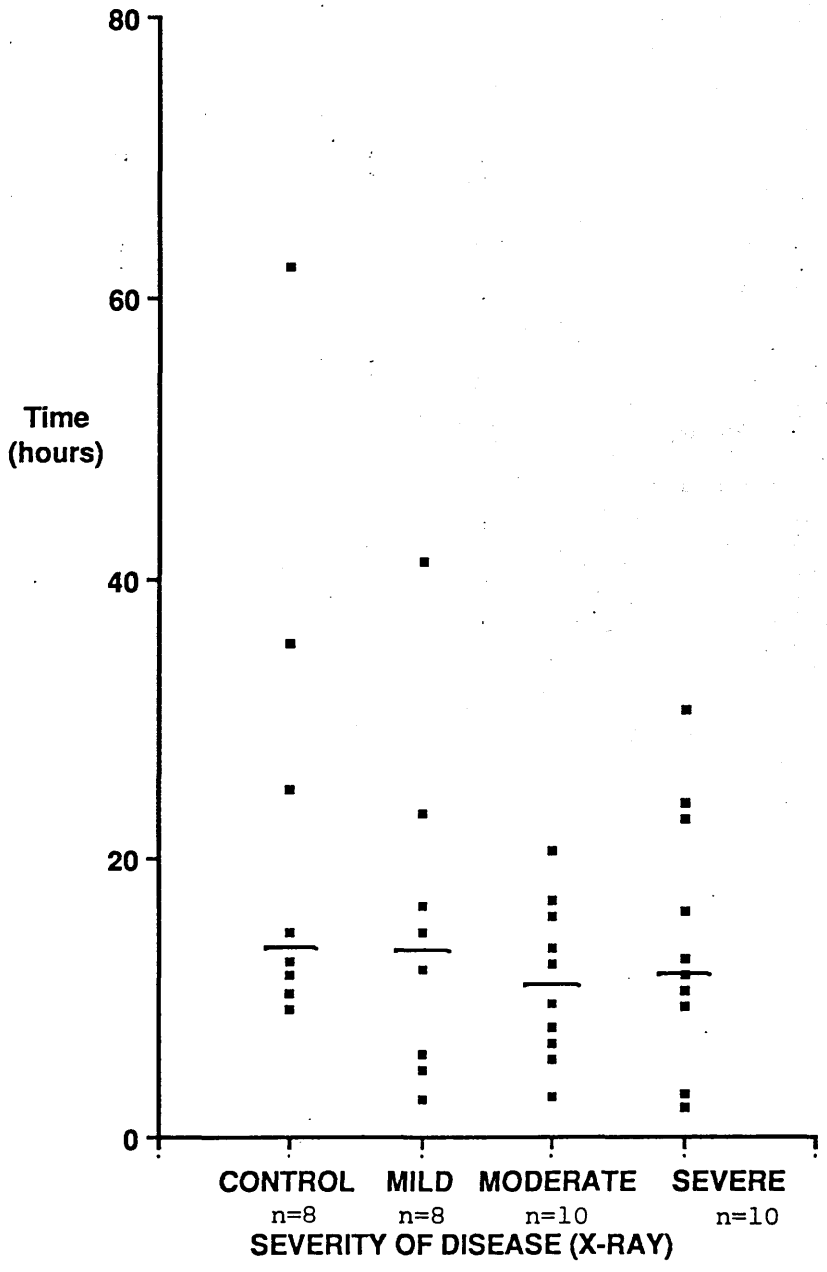


Figure 34

Left colonic transit times and the radiological classification of disease severity.

	CONTROL	MILD	MODERATE	SEVERE
Mouth-anus				
median	35.05	42.35	35.15	38.95
range	21.5-92.0	18.8-82.7	18.9-54.0	16.4-81.2
Mouth-rectum				
median	33.5	34.8	29.05	34.2
range	20.0-91.5	13.6-81.2	15.5-53.7	16.2-81.0
Right colon				
median	11.95	11.7	9.5	11.0
range	1.3-21.2	2.9-58.6	2.3-25.1	0.5-60.6
Left colon				
median	13.4	13.35	10.9	11.55
range	9.2-62.3	2.7-41.2	2.9-20.6	2.5-30.5

Table 15.

Intestinal transit times and the radiological classification of disease severity.

Patient Study 4: Intestinal transit times and the symptomatic classification of disease severity.

The 28 patients documented in Table 9 were divided according to severity of abdominal pain with the following results; 16 were allocated to the mild group (median age 72.5yrs, range 51-79yrs), 7 were allocated to the moderate group (median age 60yrs, range 39-73yrs) and 5 were considered to have severe symptoms (median age 63yrs, range 33-71yrs). The control group was as described in Patient Study 3.

The total and segmental transit times for each group are illustrated in Figures 35-38 and Table 16 details the medians and ranges. Individual values are documented in Appendix 4.

Intestinal transit times did not differ significantly between the four groups on Kruskal-Wallis testing. There was no correlation between transit times and increasing severity of symptoms in the disease groups.

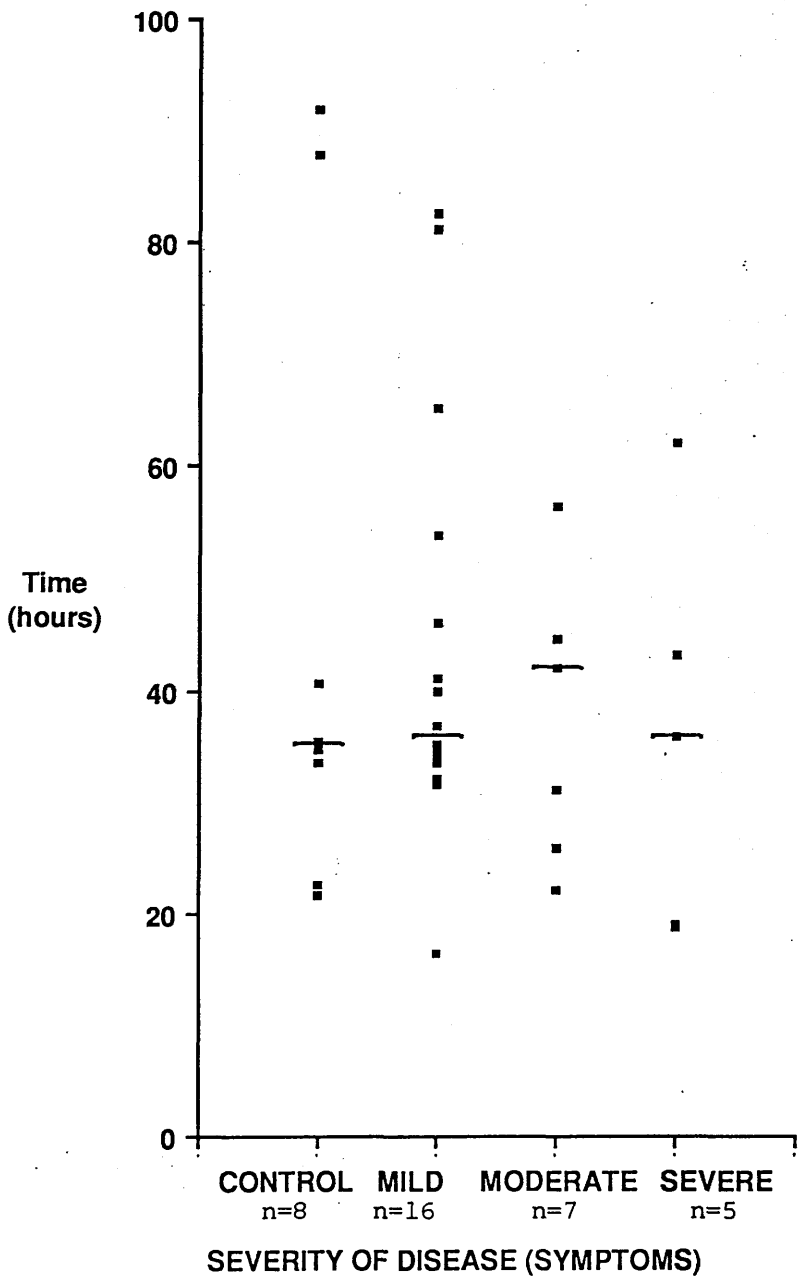


Figure 35
Mouth to anus transit times and the symptomatic classification of disease severity.

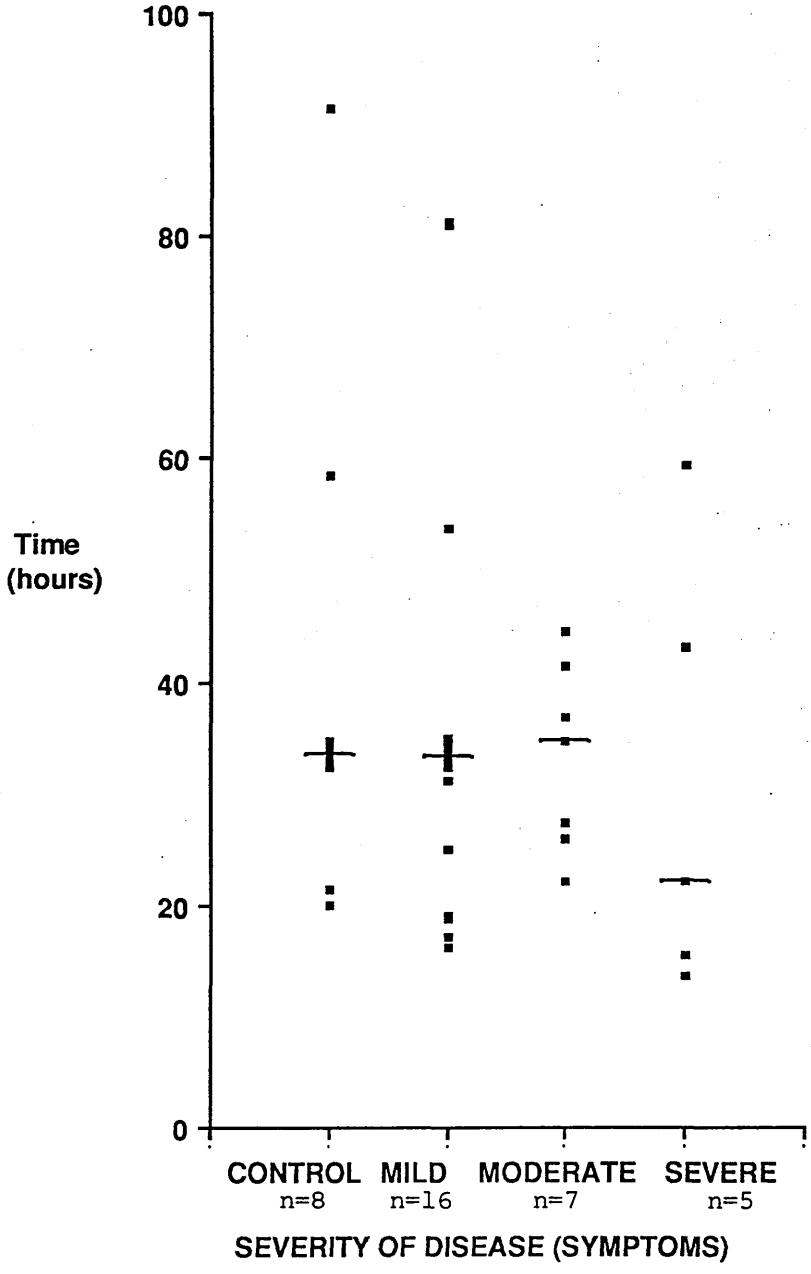


Figure 36

Mouth to rectum transit times and the symptomatic classification of disease severity.

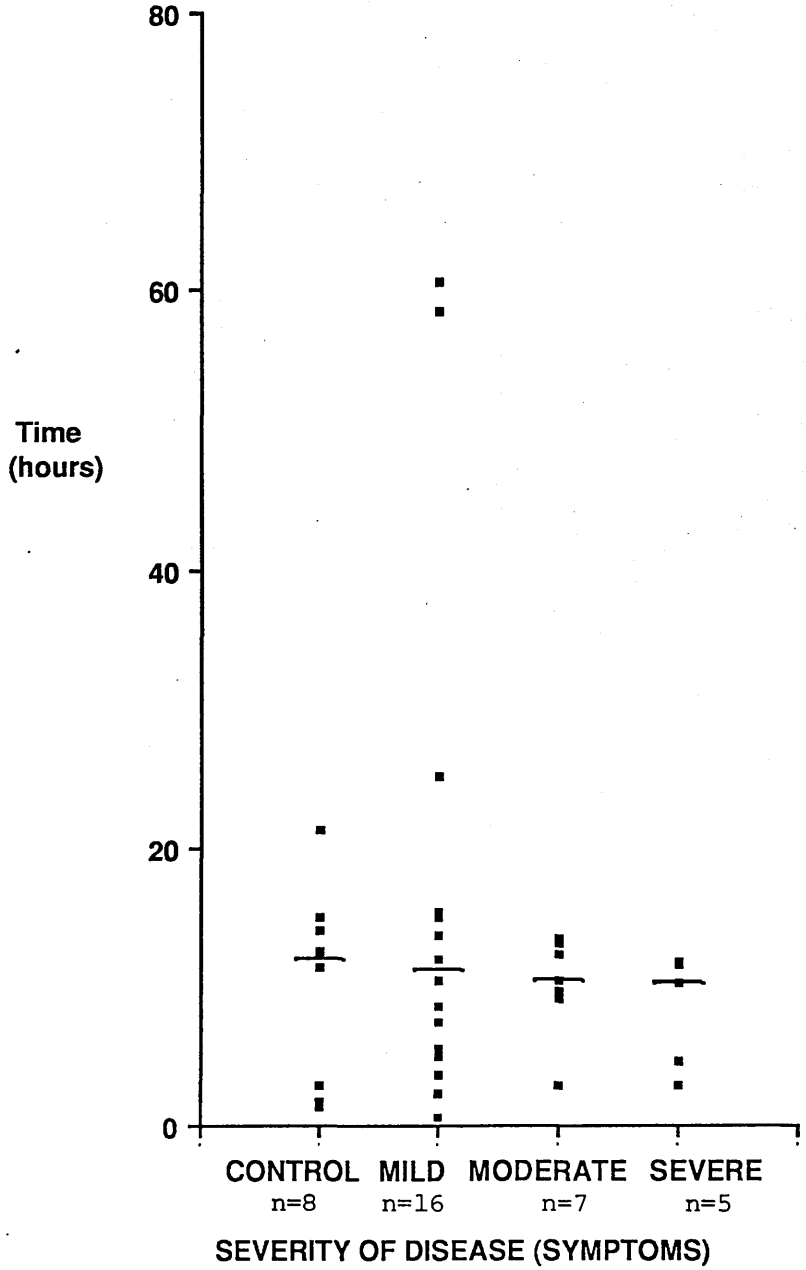


Figure 37
Right colonic transit times and the symptomatic classification of disease severity.

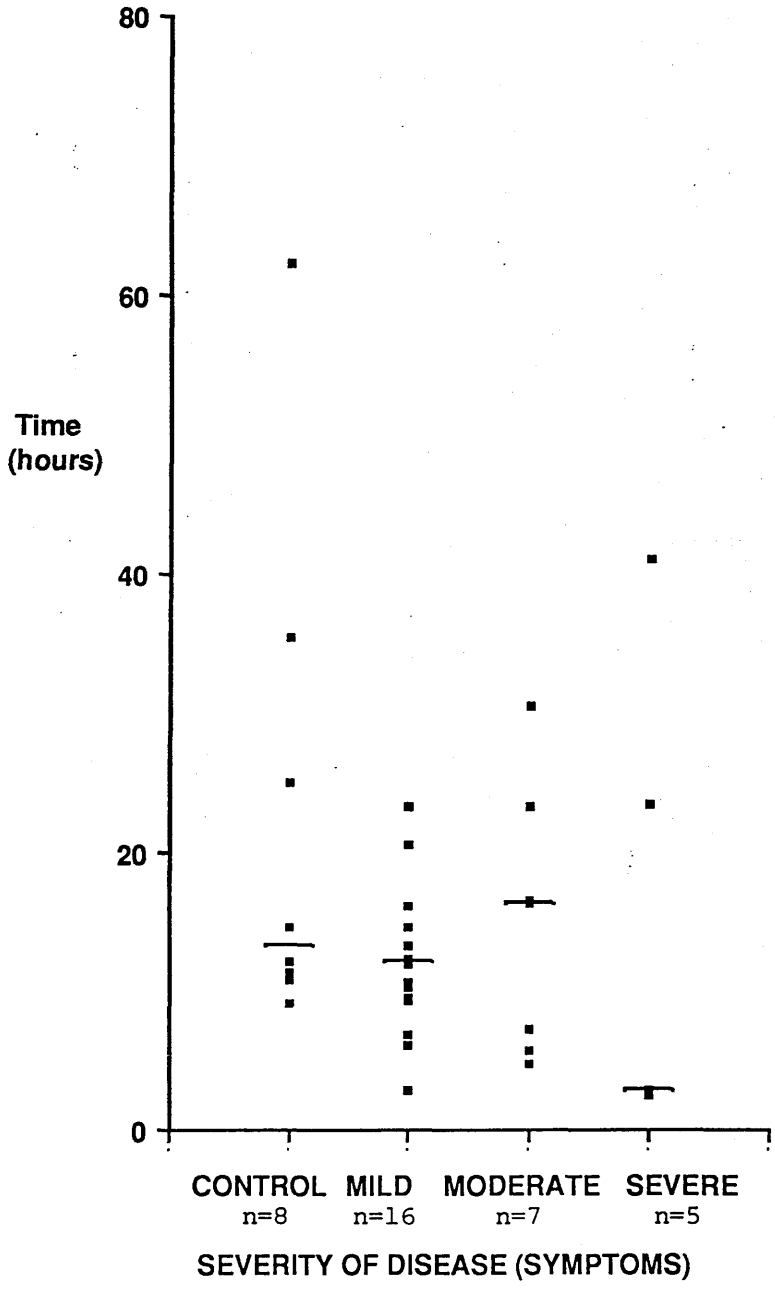


Figure 38
Left colonic transit times and the symptomatic classification of disease severity.

	CONTROL	MILD	MODERATE	SEVERE
Mouth-anus				
median	35.05	35.95	42.0	35.9
range	21.5-92.0	16.4-82.7	22.0-56.5	18.8-62.2
Mouth-rectum				
median	33.5	33.35	34.6	22.2
range	20.0-91.5	16.2-81.2	22.0-44.5	13.6-59.4
Right colon				
median	11.95	11.2	10.5	10.2
range	1.3-21.2	0.5-60.6	2.8-13.4	2.9-11.7
Left colon				
median	13.4	12.15	16.4	2.9
range	9.2-62.3	2.8-23.2	4.8-30.5	2.5-41.2

Table 16.

Intestinal transit times and the symptomatic classification of disease severity.

Discussion

Segmental transit times have been recorded in the control population. Ahran and his colleagues (1981), using a multi-marker technique, found a mean right and left colonic transit time of 13.8 hours and 14.1 hours respectively in a group of healthy adult volunteers and in a more recent study Metcalf et al (1987) reported a transit time through the right colon of 11.3 (1) hours [mean (SE)]. Transit through the left colon was 11.4 (1.4) hours but this measurement excluded transit time through the sigmoid colon (Metcalf et al,1987). In this study, the radiopill recorded median segmental transit times of 11.95 hours and 13.4 hours in the right and left colon respectively which appear to be comparable to these earlier reports.

When the 28 patients were divided into groups by symptoms and disease severity, it was not surprising to discover that transit times of the groups approached the median value of 35 hours recorded in the untreated control group. This finding is in agreement with the results of the previous study (Patient Study 1) on 12 patients representing a wide spectrum of the disease.

Patient Study 5: Left colonic motility and the radiological classification of disease severity.

The motility parameters of all 28 patients and 8 controls were examined. Patient classification and details of control subjects are documented in Patient Study 3. The transit time of the radiopill through the left colon determined the period for analysis of the other motility parameters.

Figures 39-42 illustrate the motility parameters for each group and Table 17 details the median values and ranges. Individual values are listed in Appendix 5.

The motility index increased from 283 (80-726) [median,(range)] in the mild group to 429 (119-1132) and 949 (227-1566) in the moderate and severe groups respectively. Median motility index in the control group was 344 (range, 32-1266). Use of the Kruskal-Wallis test demonstrated a significant difference between the four groups, KW=(7.935)3 d.f.,$p<0.05$. In the disease groups , there was also a significant correlation between the motility index of the left colon and increasing severity of diverticular disease on x-ray, $r=0.504$, $p<0.01$, (Figure 39).

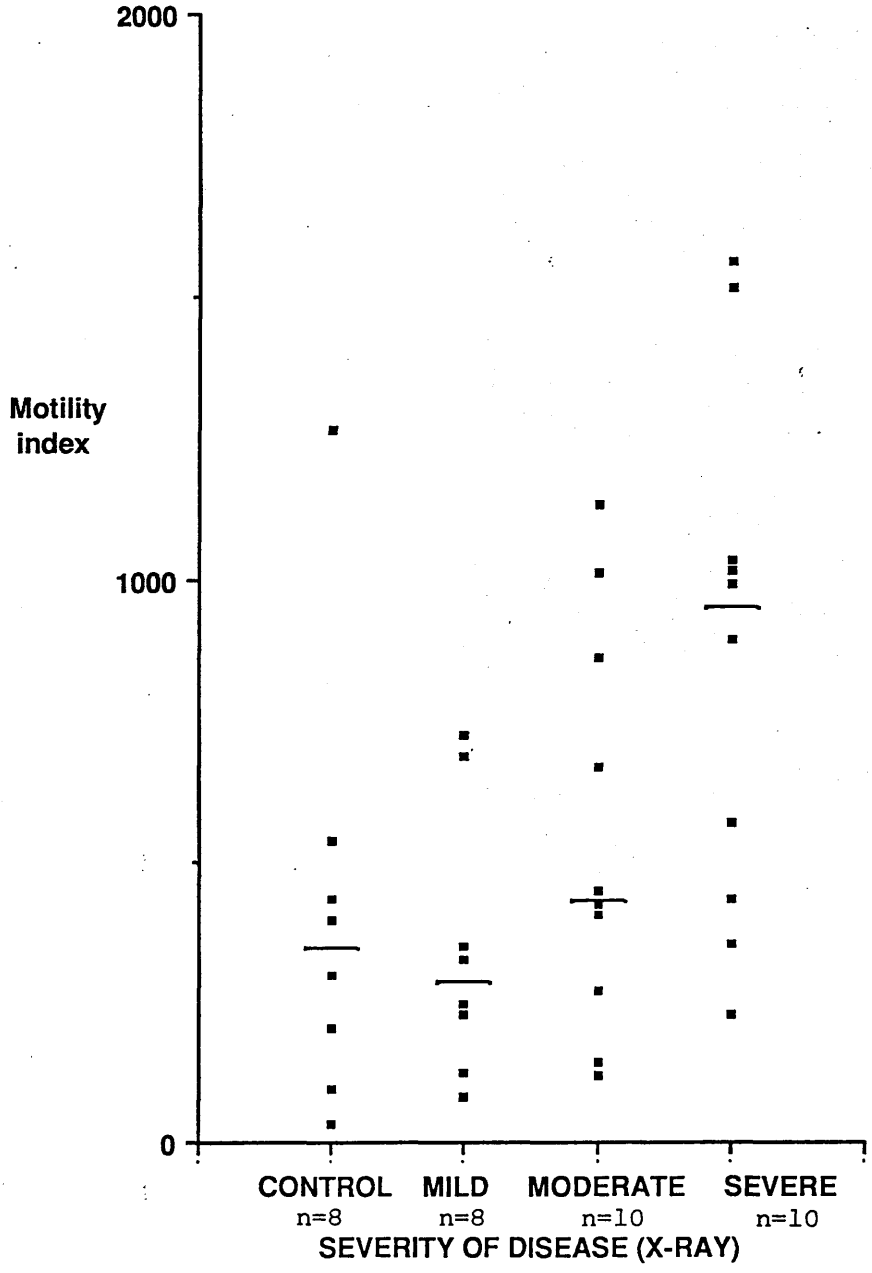


Figure 39
Left colonic motility index and the radiological classification of disease severity.

Percentage activity and peaks greater than 5mmHg/hour did not differ significantly between the four groups (Figures 40,41). Peaks greater than 50mmHg/hour also increased with severity although this trend did not reach statistical significance (Figure 42).

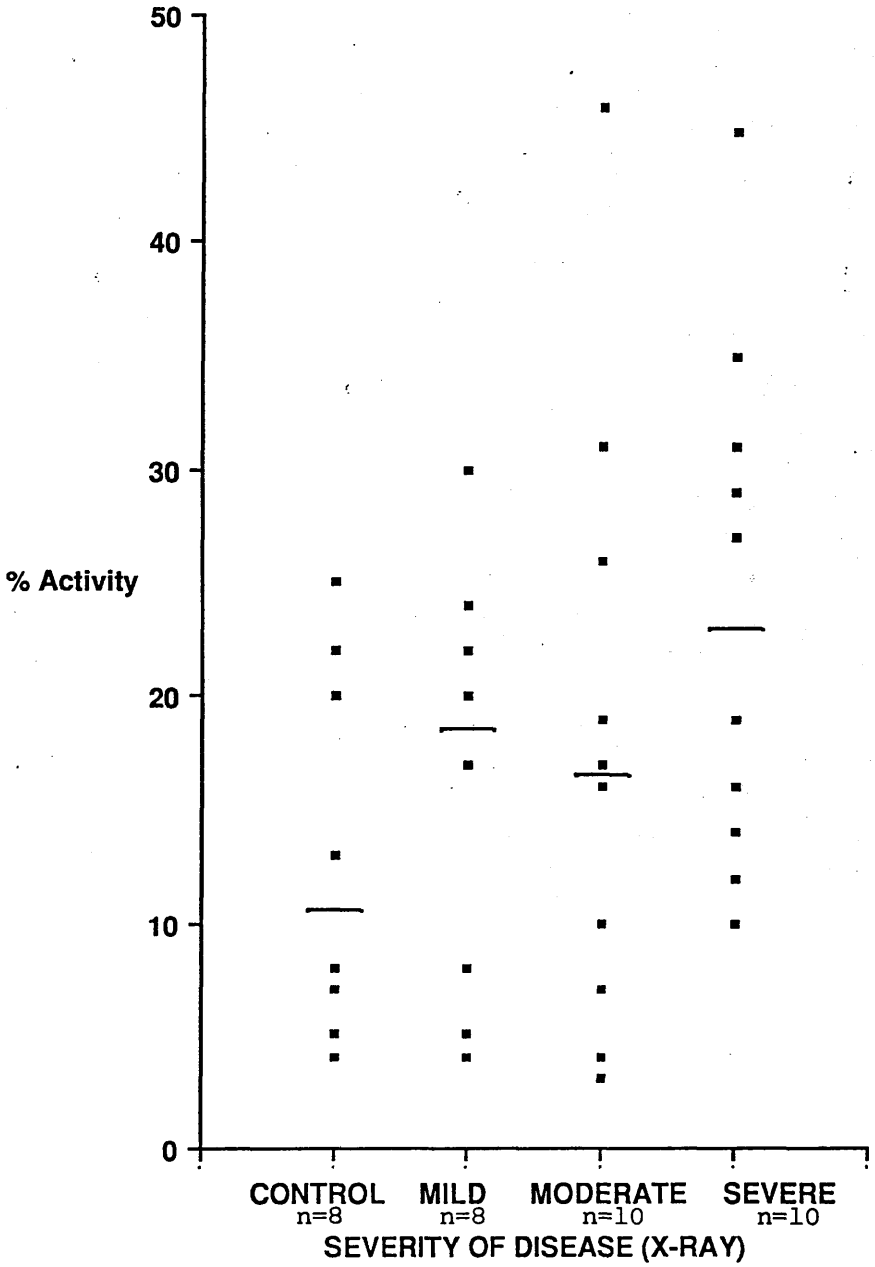


Figure 40

Left colonic % activity and the radiological classification of disease severity

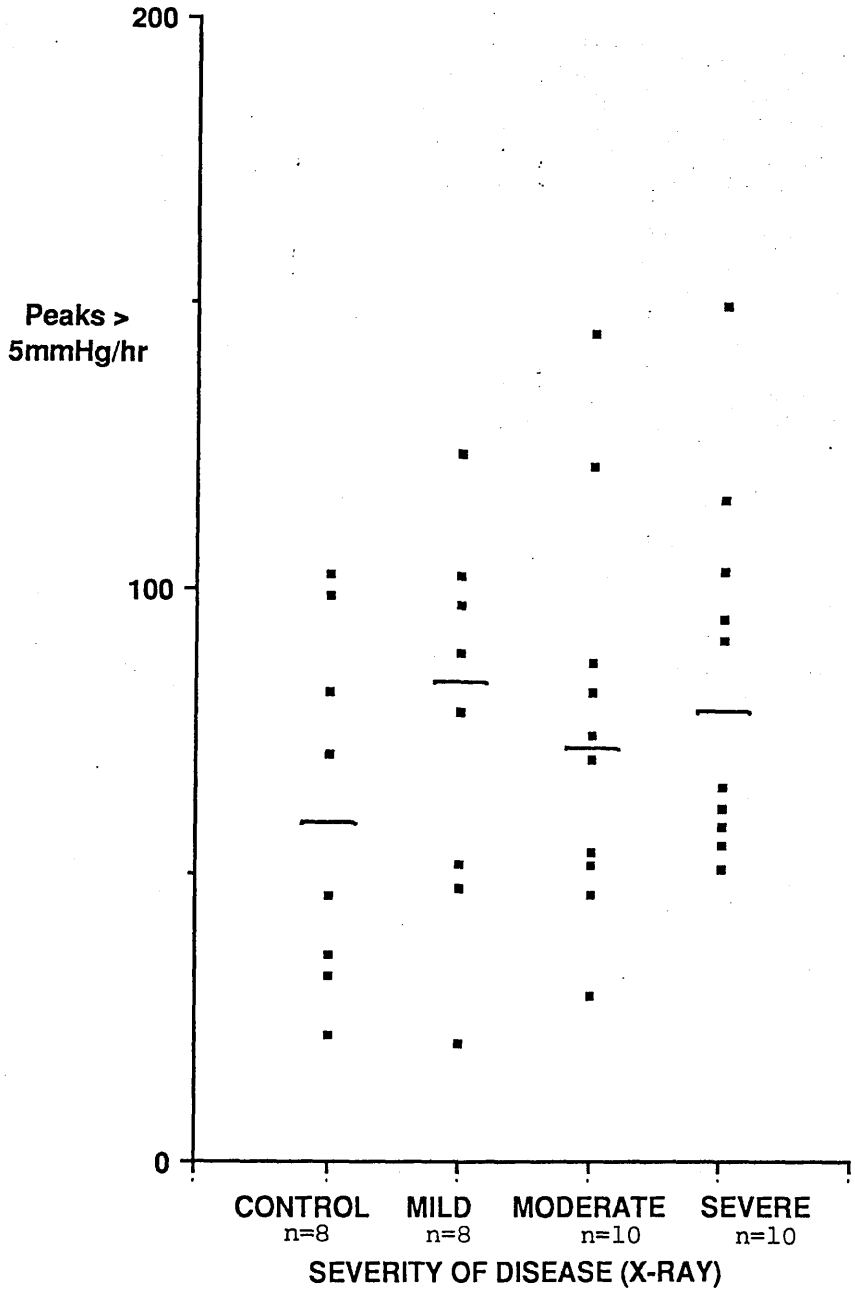


Figure 41

Left colonic number of peaks >5mmHg/hour and the radiological classification of disease severity.

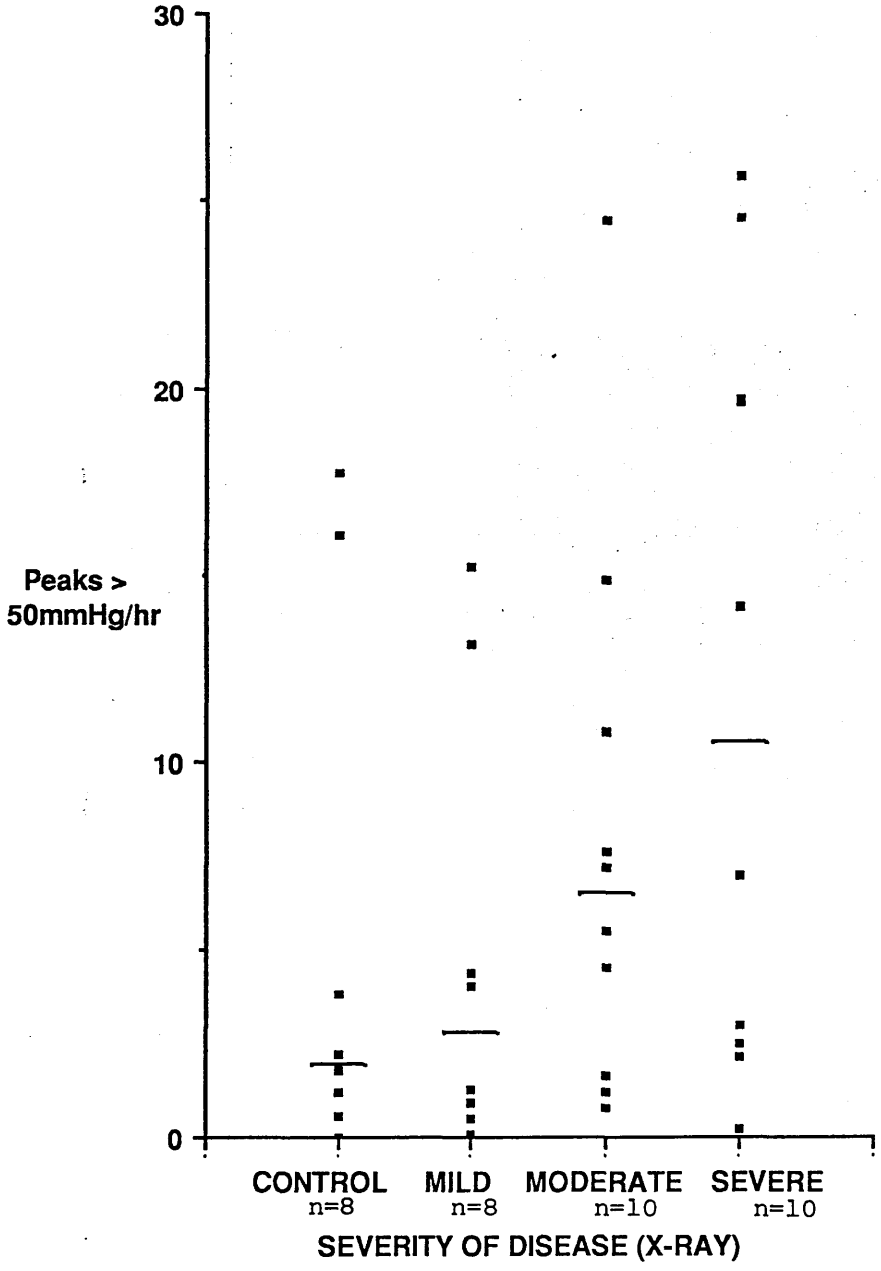


Figure 42

Left colonic number of peaks >50mmHg/hour and the radiological classification of disease severity

	CONTROL	MILD	MODERATE	SEVERE
Motility index				
median	344	283	429	949
range	32-1266	80-726	119-1132	227-1566
% Activity				
median	10.5	18.5	16.5	23.0
range	4.0-25.0	4.0-30.0	3.0-46.0	10.0-45.0
Peaks >5mmHg/hr				
median	59.1	84.0	72.9	79.2
range	22.0-100.3	20.5-124.5	29.2-146.2	51.7-151.2
Peaks >50mmHg/hr				
median	1.9	2.8	6.5	10.6
range	0-17.7	0.1-15.2	1.0-24.4	0.2-25.6

Table 17.

Left colonic motility and the radiological classification of disease severity.

Patient Study 6: Left colonic motility and the symptomatic classification of disease severity.

28 patients with symptomatic diverticular disease and 8 control subjects were studied. Patient details are documented in Patient Study 4 and data concerning the control group is documented in Patient Study 3. Results are illustrated in Figures 43-46 and the medians and ranges for each group are set out in Table 18 . Appendix 6 lists the individual values.

Use of the Kruskal-Wallis test demonstrated that the motility index, percentage activity, the number of peaks greater than 5mmHg/hour and the number of peaks greater than 50mmHg/hour did not differ significantly between the four groups.

In diverticular disease, percentage activity and the number of pressure peaks greater than 5mmHg/hour increased with increasing severity of symptoms although these trends did not reach statistical significance.

Increasing severity of diverticular disease did not correlate with an increase in either the motility index or the number of pressure peaks greater than 50mmHg/hour.

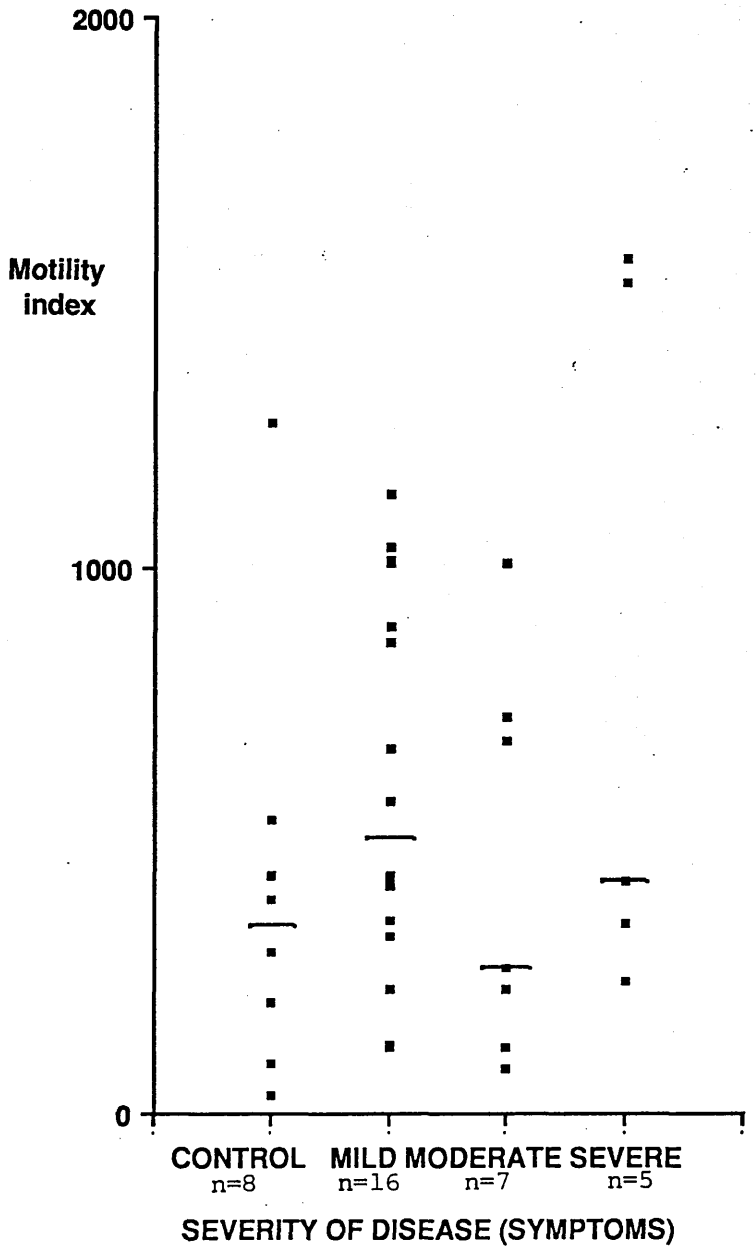


Figure 43.
Left colonic motility index and the symptomatic classification of disease severity.

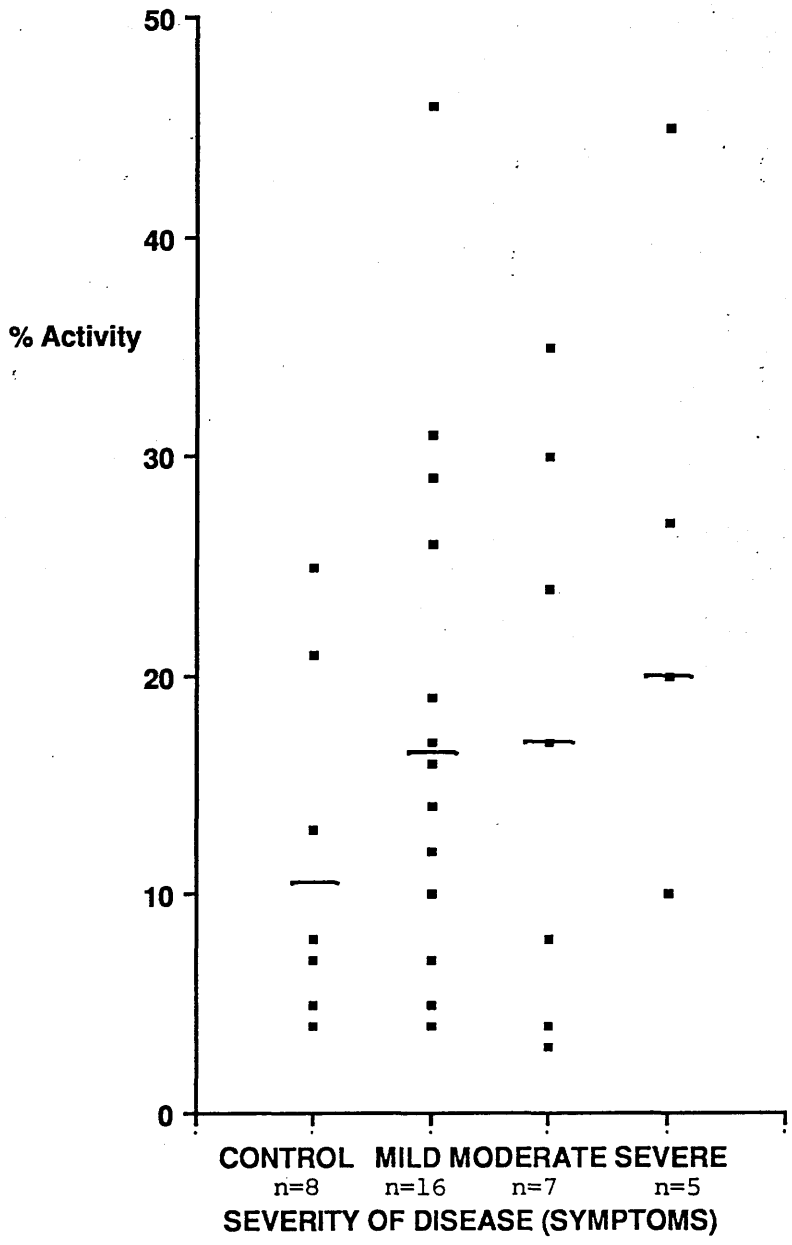


Figure 44.
Left colonic % activity and the symptomatic classification of disease severity.

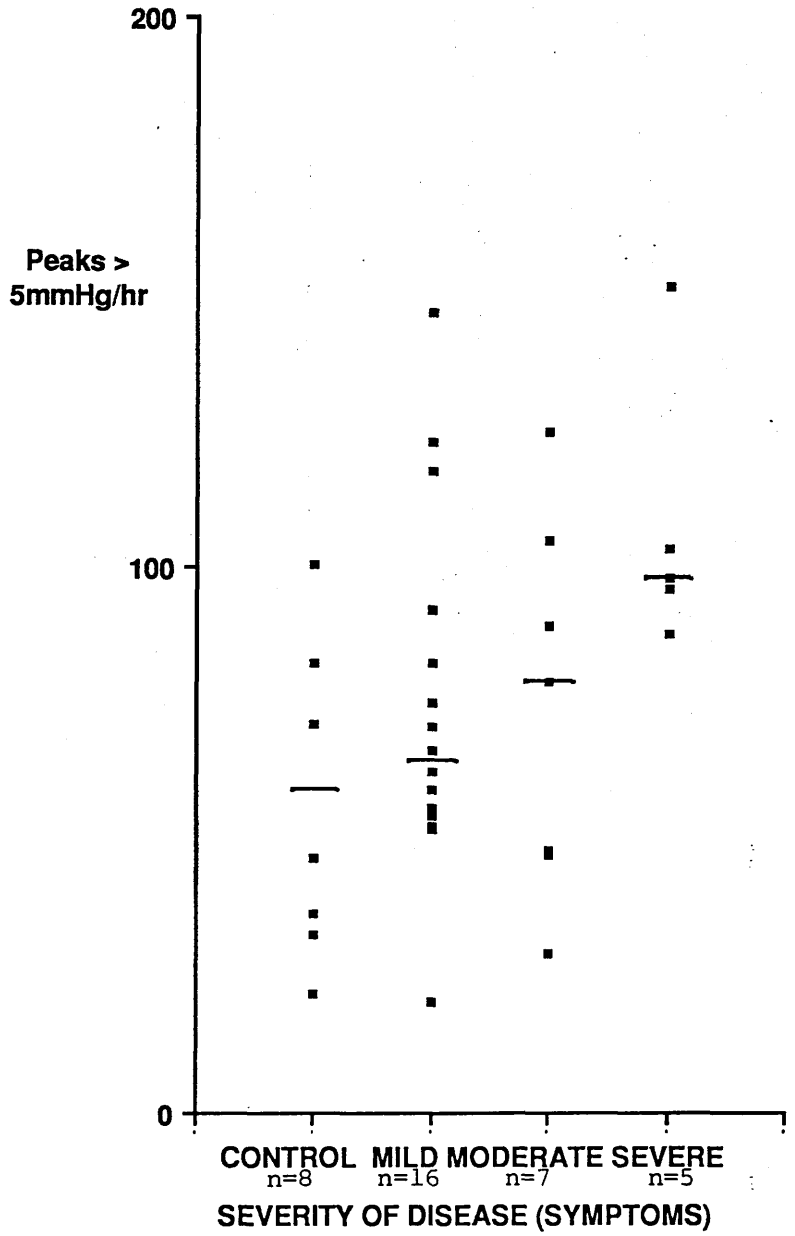


Figure 45.
Left colonic number of peaks >5mmHg/hour and the symptomatic classification of disease severity.

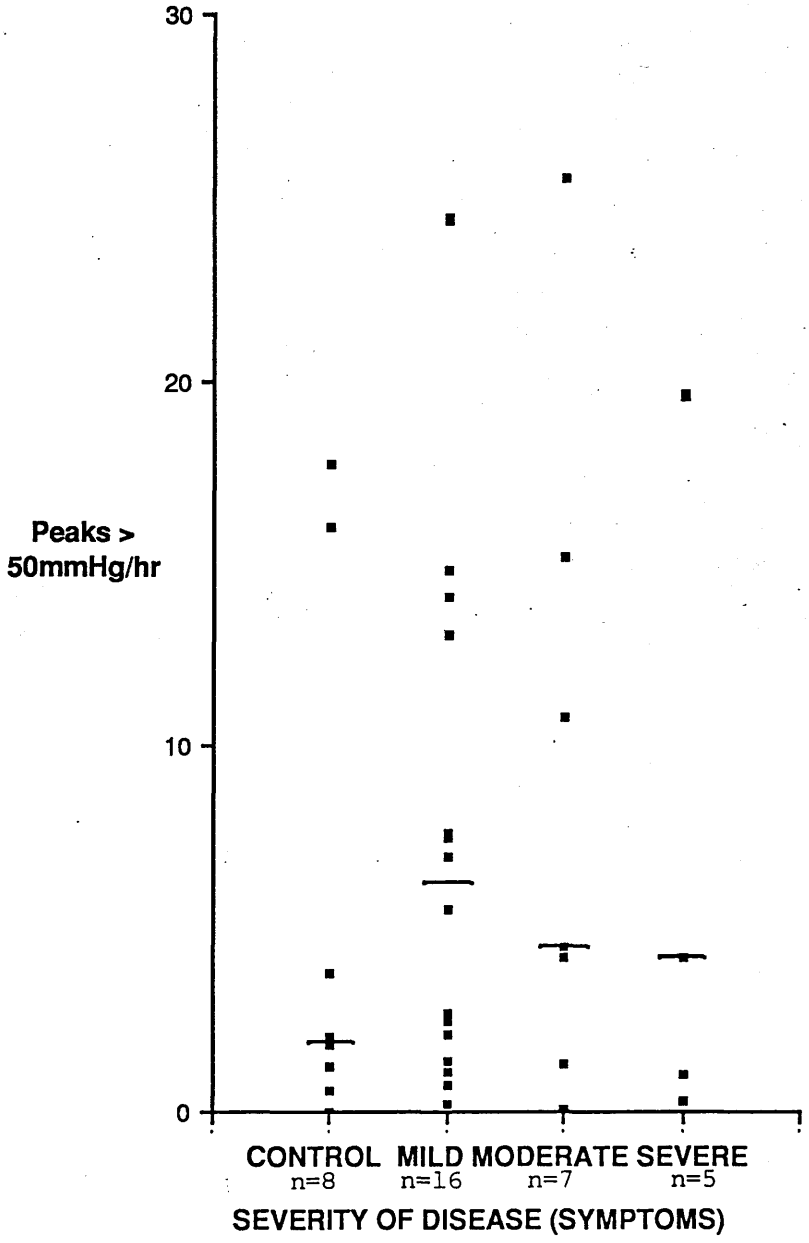


Figure 46.
Left colonic number of peaks >50mmHg/hour and the symptomatic classification of disease severity.

	CONTROL	MILD	MODERATE	SEVERE
Motility index				
median	344	502	267	425
range	32-1266	120-1132	80-1005	243-1566
% Activity				
median	10.5	16.5	17.0	20.0
range	4.0-25.0	4.0-46.0	3.0-35.0	10.0-45.0
Peaks >5mmHg/hr				
median	59.1	64.4	79.0	97.7
range	22.0-100.3	20.5-146.2	29.2-124.5	87.6-151.2
Peaks >50mmHg/hr				
median	1.9	6.25	4.5	4.2
range	0-17.7	0.2-24.5	0.1-25.6	0.3-19.7

Table 18.

Left colonic motility and the symptomatic classification of disease severity.

The whole of the left colon was selected for this study because from practical considerations, time of entry into and exit from this region was easily determined. This was not possible with the relatively small sigmoid colon. The net result was to give motility information on both diseased and undiseased bowel subjected to the periodic stimulus of eating. The prandial stimulus is likely to be minimal as eating occupied a small proportion of the study period which was usually longer than 10 hours. The prandial stimulus is of sufficient importance that it is dealt with in the next study (Patient Study 7).

The finding that there was no correlation between the symptomatic classification and motility parameters is contrary to the results reported by Weinreich and Andersen (1976b) who measured sigmoid motility in a wide spectrum of patients ranging from those with chronic diverticular disease to those with "sigmoid syndrome" and vague dyspepsia. They found that an elevated motility index in the sigmoid colon, as measured by open ended tubes, correlated with symptoms of abdominal pain. However, important differences exist between the two studies. Weinreich and Andersen (1976a & b) used an invasive technique on prepared bowel and measured the response of the sigmoid colon to a stimulus of 0.5mg intravenous neostigmine over half an hour. The combination of these

factors could influence their results and make comparison with this study difficult.

Although no statistically significant correlation was observed between symptoms and motility parameters, there was a trend in the percentage activity and the number of pressure peaks greater than 5mmHg/hour increasing with severity. It may be that frequent, low amplitude pressure waves represent segmental activity within the colon which may precipitate intestinal colic. Colicky lower abdominal pain in diverticular disease is thought to result from excessive segmentation of the colon leading to raised intracolonic pressures (Eastwood et al,1982). In this study, however, there was no significant increase in the number of pressure peaks above 50mmHg/hour which are thought to be responsible for some of the symptoms of diverticular disease (Eastwood, Smith et al,1978).

The important finding of this study is that motility index increased with the increasing number of colonic diverticula on the left side. The most important reason for this is the rising trend in the number of pressure peaks greater than 50mmHg/hour. These intergroup differences are likely to exist in untreated patients as it has been shown that ispaghula husk has minimal effect on the motility parameters of the left colon (Patient Study 2).

Since the radiological classification is an objective method of categorising patients and as this study has shown significant correlation between the number of diverticula and the motility index, it was decided to abandon symptomatic classification and use the radiological method for further analysis.

Patient Study 7: The effect of food on left colonic motility.

Prandial data was available on 21 of the 28 patients studied and on 5 control subjects. Motility parameters were calculated for the immediate pre-prandial hour and the first hour post-prandially when the radiopill was located in the left colon. Thus basal and stimulated activity were analysed separately.

Using the radiological method of patient classification, 7 patients were allocated to the mild group(median age 63yrs, range 57-73yrs), 6 to the moderate disease group (median age 74.5yrs, range 64-79yrs) and 8 were considered to have severe disease of the left colon (median age 68.5yrs, range 33-77yrs). The median age of the 5 control subjects was 41 years and ranged from 23-71 years.

Figures 47-50 illustrate the pre-prandial motility parameters for each group and Table 19 details the median values and ranges.

Use of the Kruskal-Wallis test demonstrated that there was a significant difference in the pre-prandial motility index between the four groups, KW = (9.298) 3 d.f., $p<0.05$.

In diverticular disease, a systematic rise was found in the median pre-prandial motility index with increasing severity of disease, rising from 271(57-478) [median(range)] in the mild group to 514(110-1024) and 891(156-1488) in the moderate and severe groups respectively, $r=0.632$, $p<0.01$, (Figure 47). The median pre-prandial motility index in the control group was 306 and ranged from 27-704.

Percentage activity and the number of pressure peaks greater than 5mmHg/hour and 50mmHg/hour did not differ significantly between the four groups. There was, however, a significant correlation between percentage activity and severity of diverticular disease in the pre-prandial period, $r=0.44$, $p<0.05$, (Figures 48,49).

The severe group demonstrated a large number of high amplitude waves (>50mmHg) in comparison to the other two groups. This difference, however, was not significant (Figure 50).

In the post-prandial period the motility parameters did not differ significantly between the four groups. However, a similar pattern of increasing motility index with increasing severity of disease was found, rising from 553(140-855) in the mild group to 788(224-1080) and 839(125-1280) in the moderate and severe groups respectively. This trend, however, was not statistically significant. The median motility index in the control group was 589 and ranged from 34-766 (Figure 51).

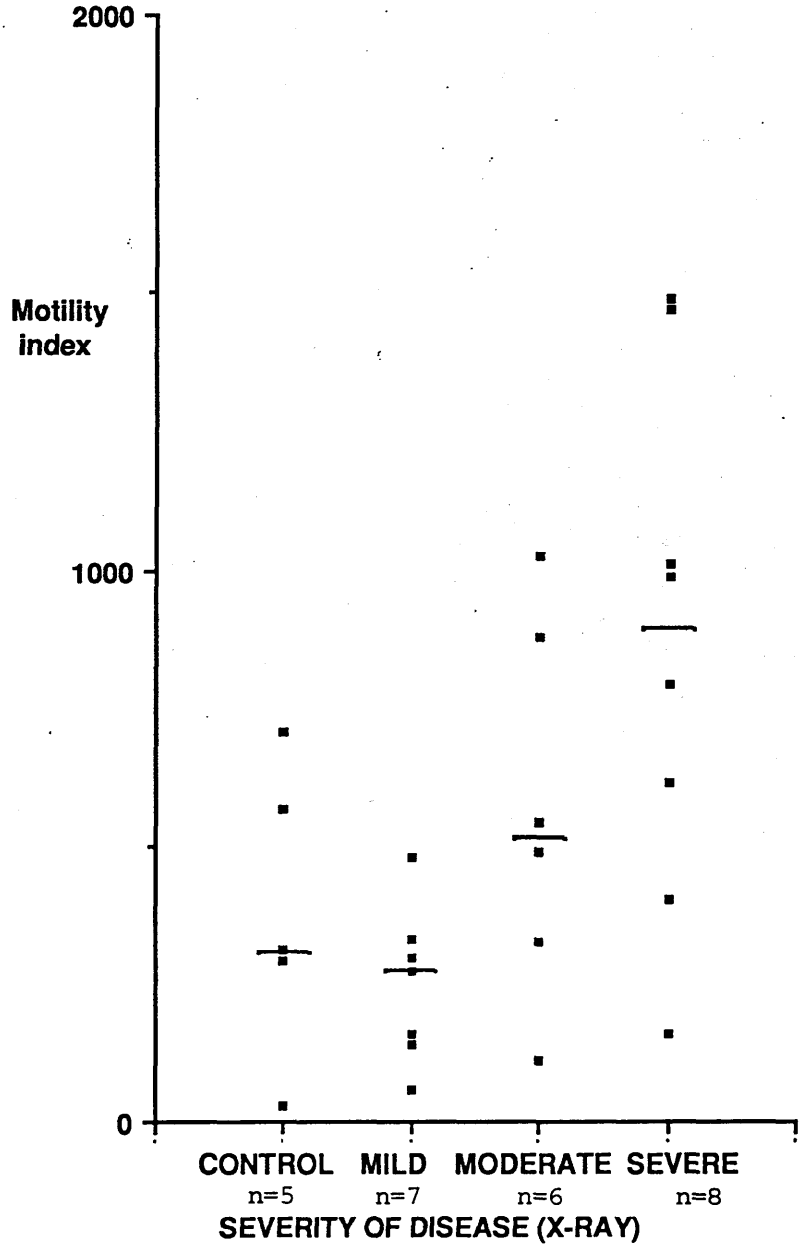


Figure 47

Pre-prandial motility index.

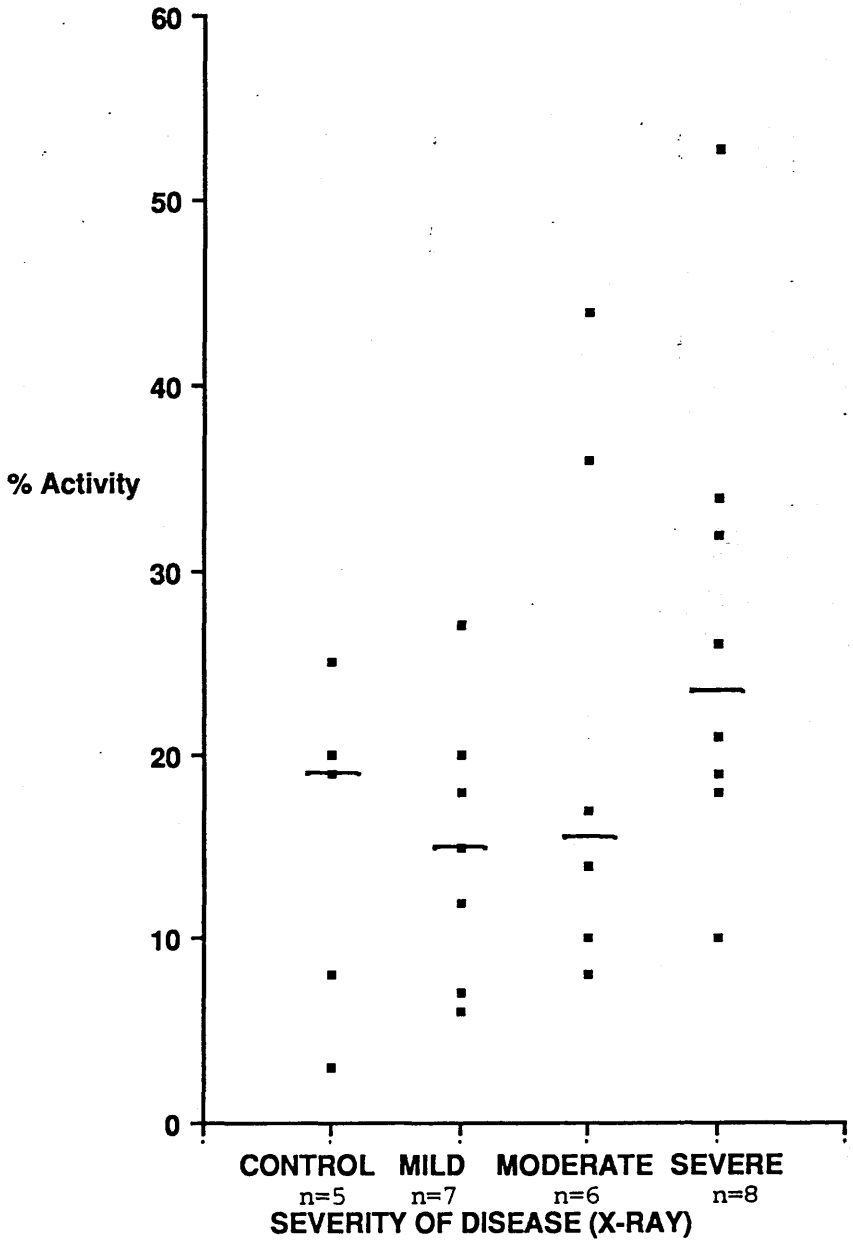


Figure 48

Pre-prandial % activity.

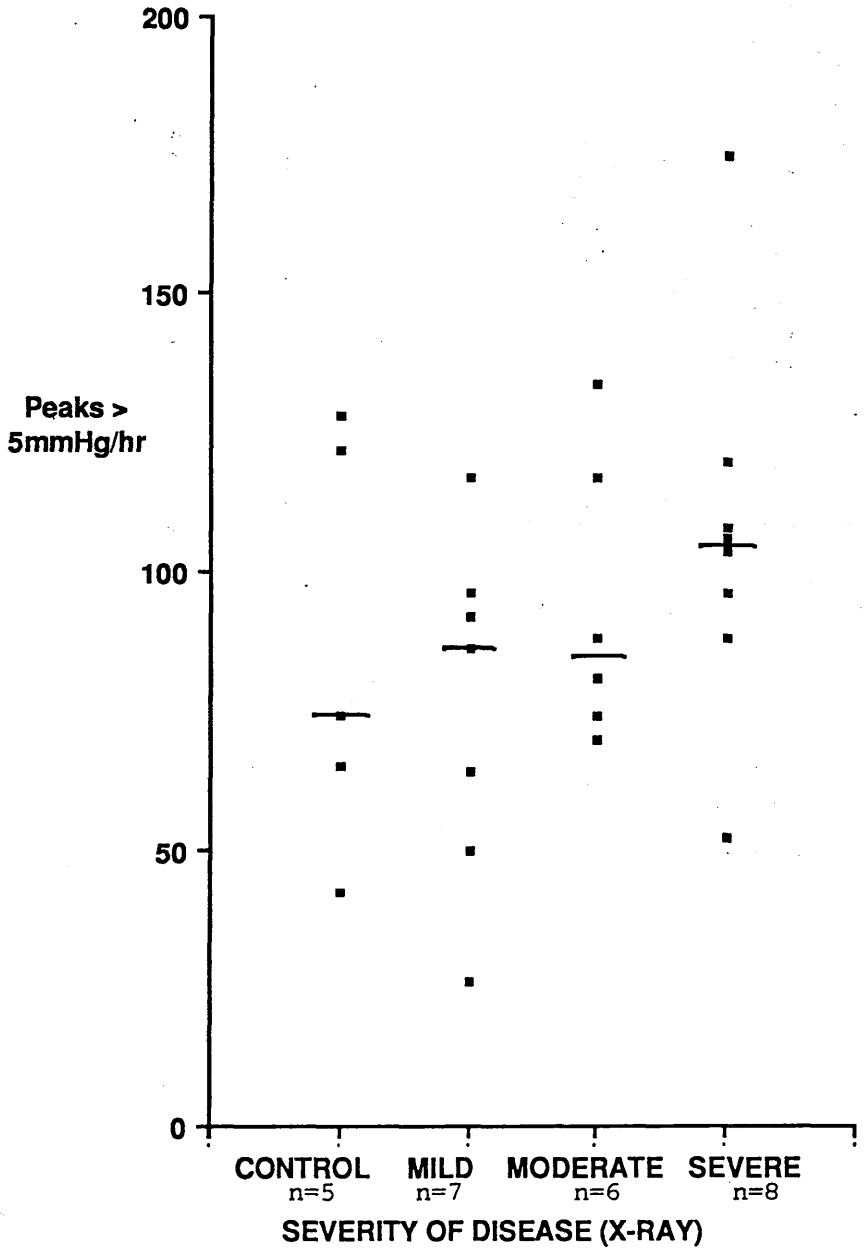


Figure 49

Pre-prandial number of peaks >5mmHg/hour.

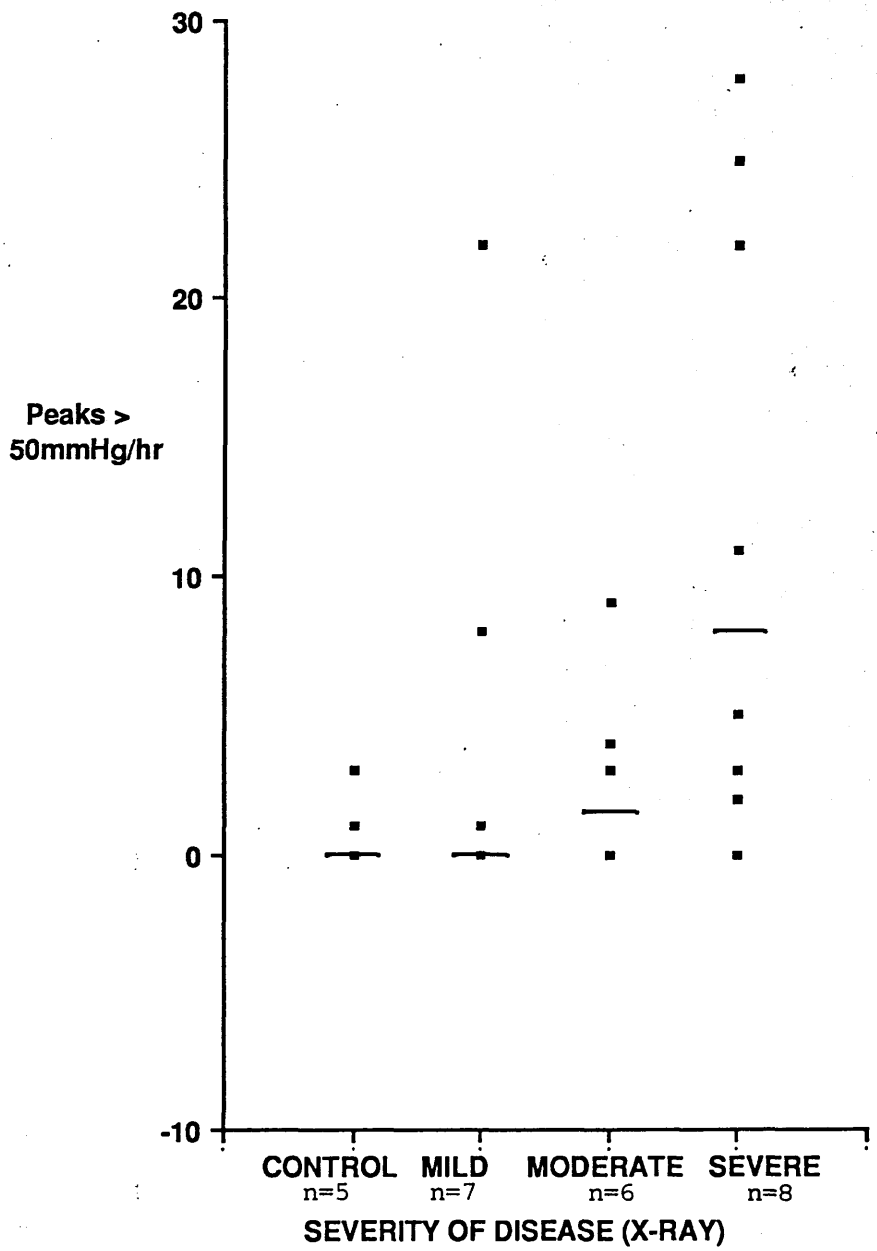


Figure 50

Pre-prandial number of peaks >50mmHg/hour.

	CONTROL	MILD	MODERATE	SEVERE
Motility index				
median	306	271	514	891
range	27-704	57-478	110-1024	156-1488
% Activity				
median	19.0	15	15.5	23.5
range	3-25	6-27	8-44	10-53
Peaks >5mmHg/hr				
median	74.0	86	84.5	105
range	42-128	26-117	70-134	52-175
Peaks >50mmHg/hr				
median	0.0	0.0	1.5	8.0
range	0.0-3.0	0.0-22.0	0.0-9.0	0.0-28.0

Table 19.

Pre-prandial motility parameters.

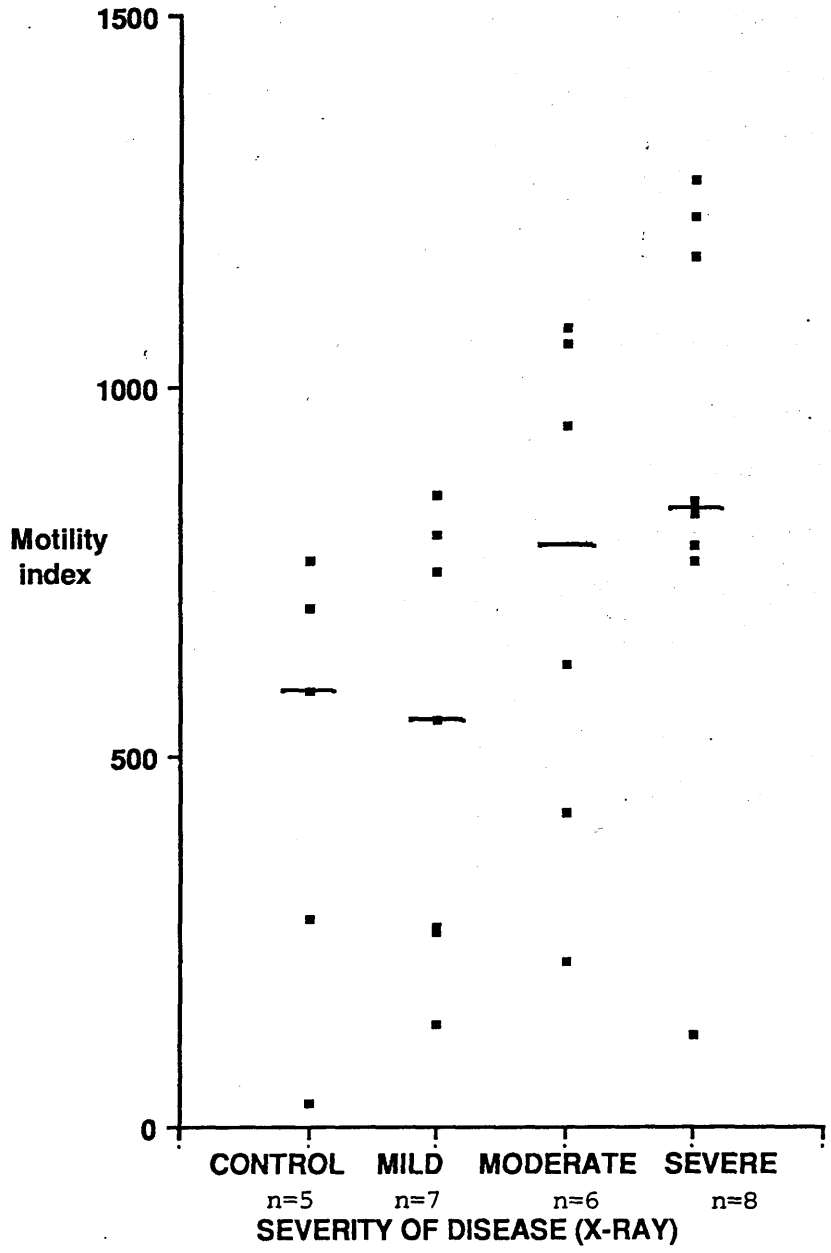


Figure 51

Post-prandial motility index.

In the post-prandial period, percentage activity and peaks greater than 50mmHg/hour again tended to increase with severity of disease although these trends were not significant. There was no correlation between increasing severity of disease and the number of peaks greater than 5mmHg/hour (Figures 52-54).

To demonstrate the significance of the prandial response within each group, the percentage change in motility index, percentage activity and the number of pressure peaks greater than 5mmHg/hour and the absolute change in the number of pressure peaks greater than 50mmHg/hour was calculated.

The motility parameters did not differ significantly between the four groups. In diverticular disease, however, the increase in motility index after the ingestion of food became less marked as the severity of disease increased, $r = -0.474$, $p<0.05$. (Figure 55). There was no correlation between the other motility parameters and disease severity (Figures 56-58). These results are summarised in Tables 20 & 21 and individual values are detailed in Appendix 7.

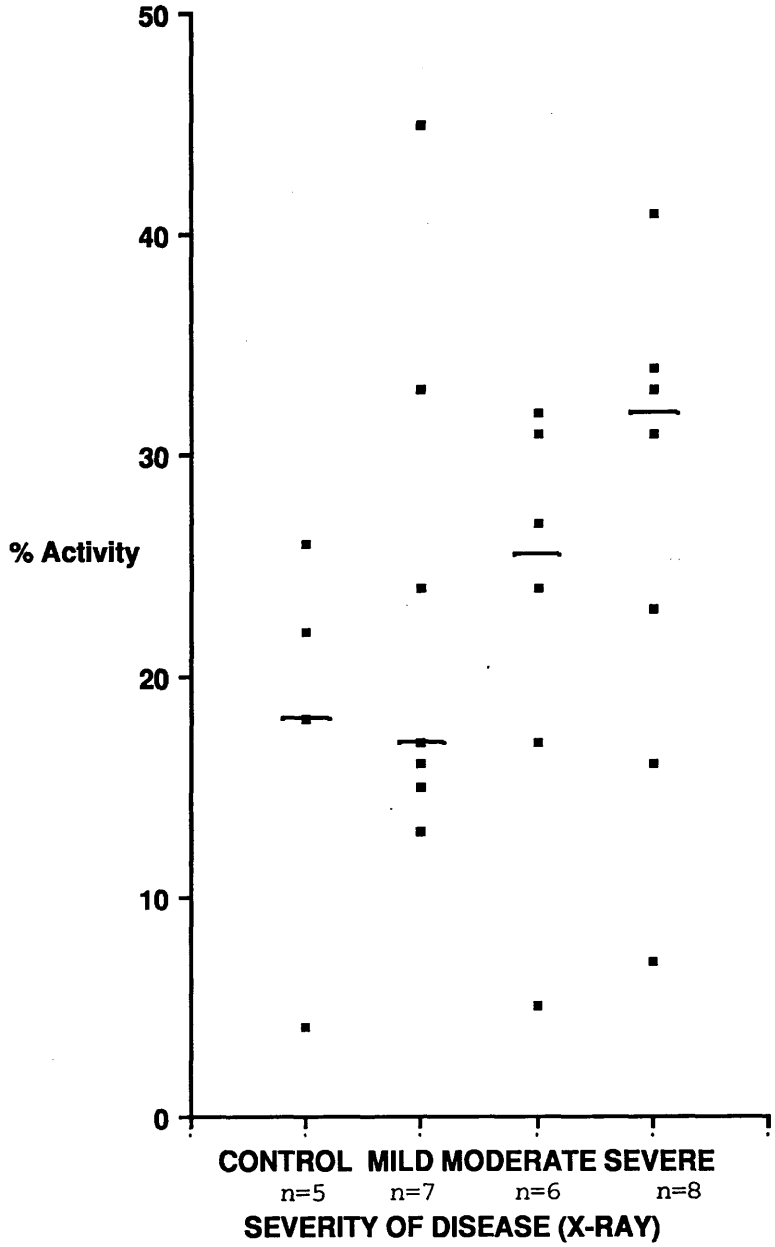


Figure 52.

Post-prandial % activity.

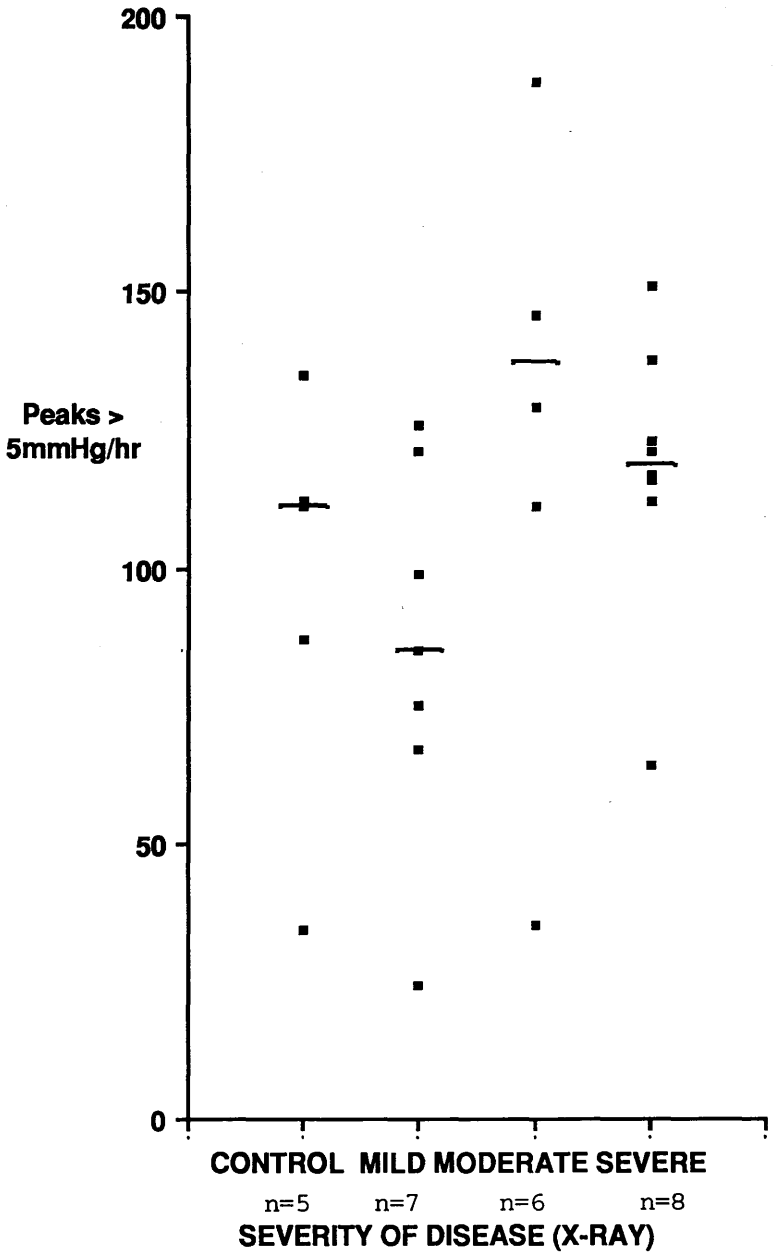


Figure 53.

Post-prandial number of peaks >5mmHg/hour.

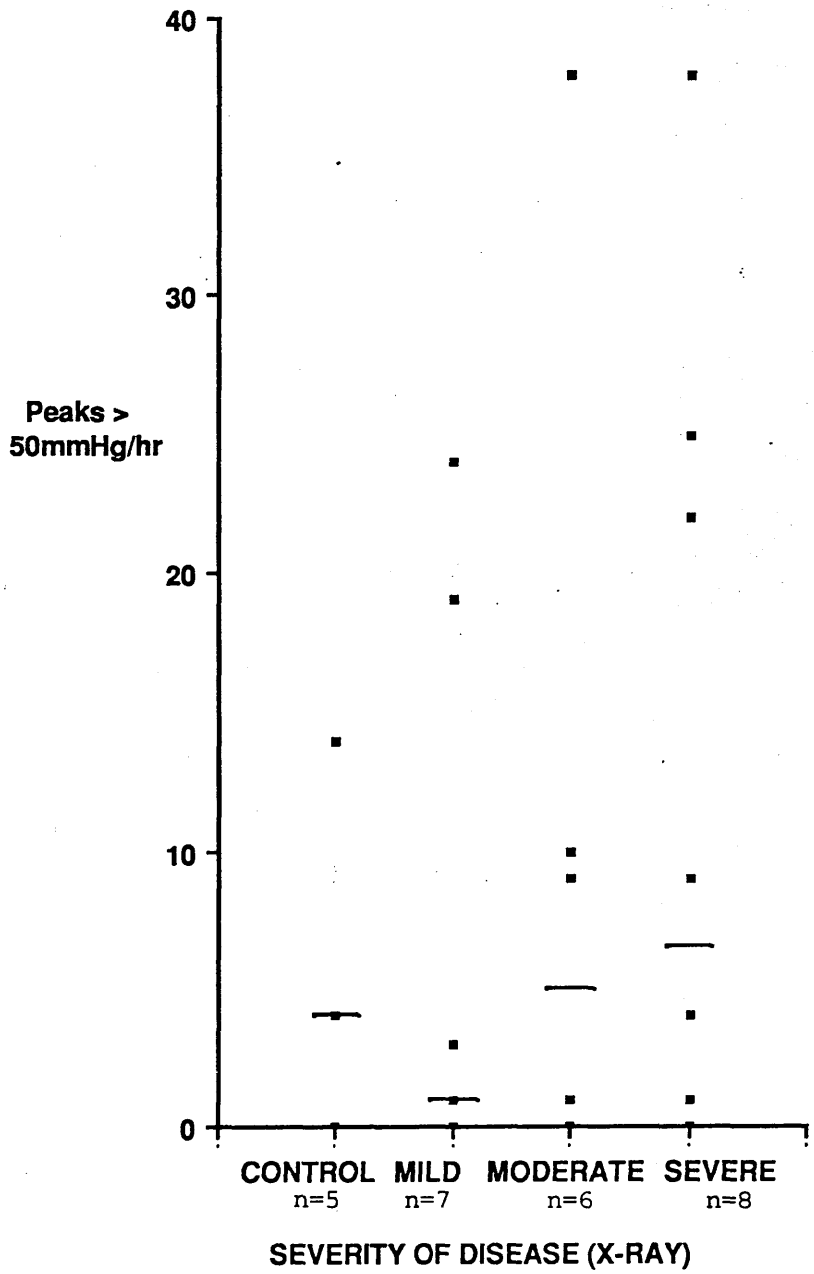


Figure 54
Post-prandial number of peaks >50mmHg/hour.

	CONTROL	MILD	MODERATE	SEVERE
Motility index				
median	589	553	788	839
range	34-766	140-855	224-1080	125-1280
% Activity				
median	18	17	25.5	32
range	4-26	13-45	5-32	7-41
Peaks >5mmHg/hr				
median	111	85	137.5	119
range	34-135	24-126	35-188	64-151
Peaks >50mmHg/hr				
median	4.0	1.0	5.0	6.5
range	0.0-14.0	0.0-24.0	0.0-38.0	0.0-38.0

Table 20.

Post-prandial motility parameters.

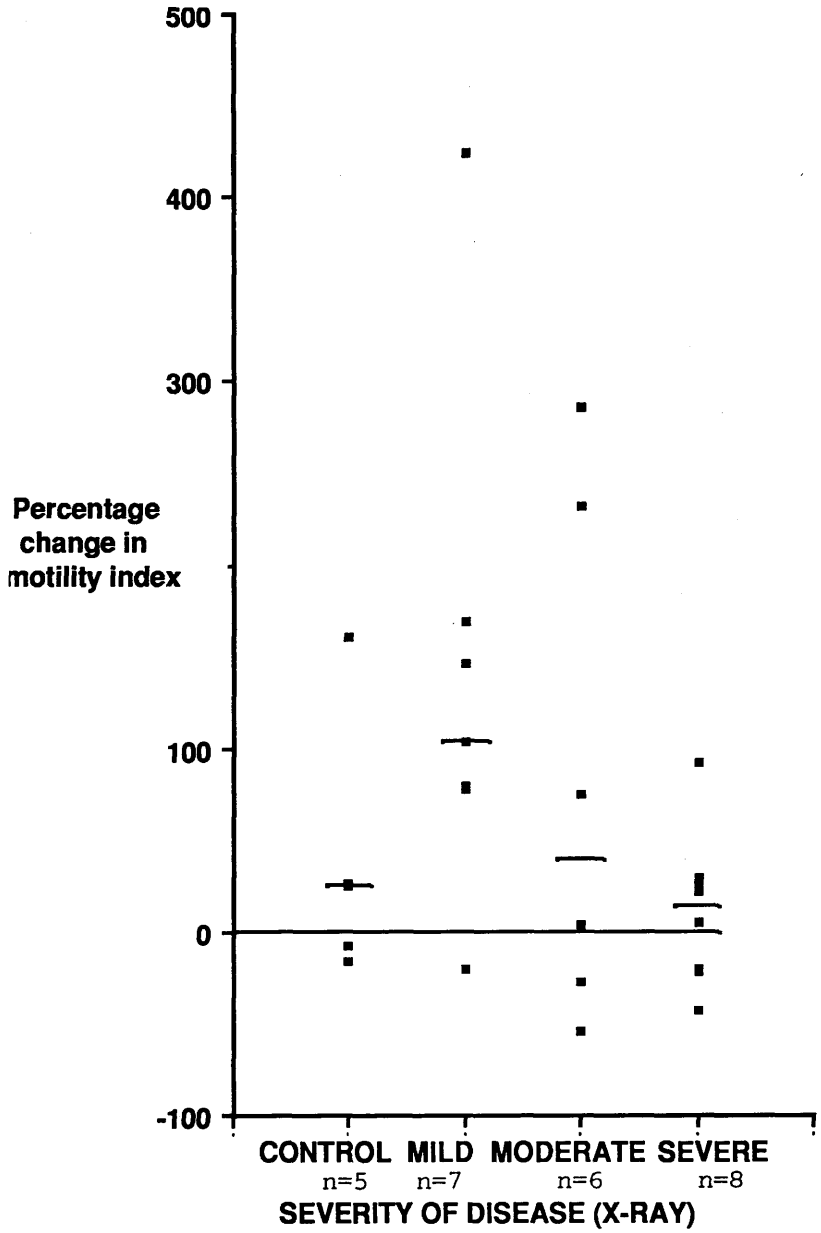


Figure 55.

The effect of eating on motility index.

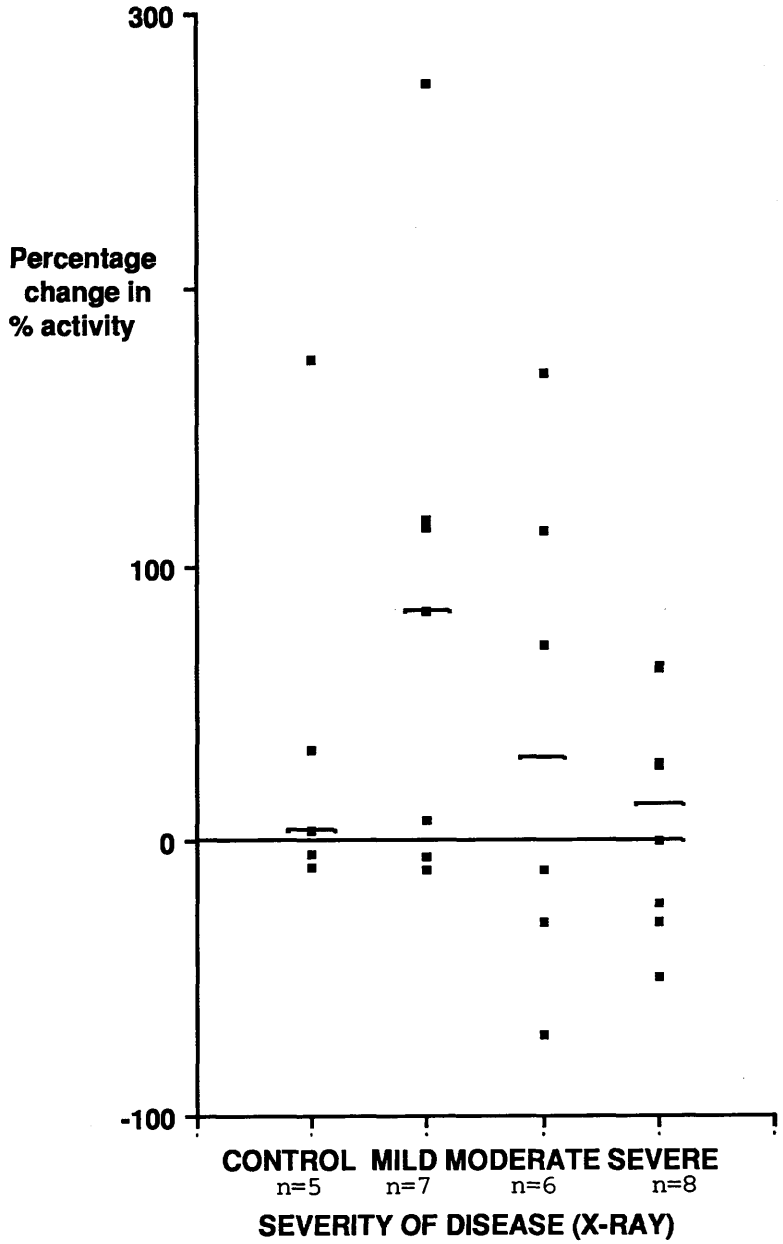


Figure 56.

The effect of eating on % activity.

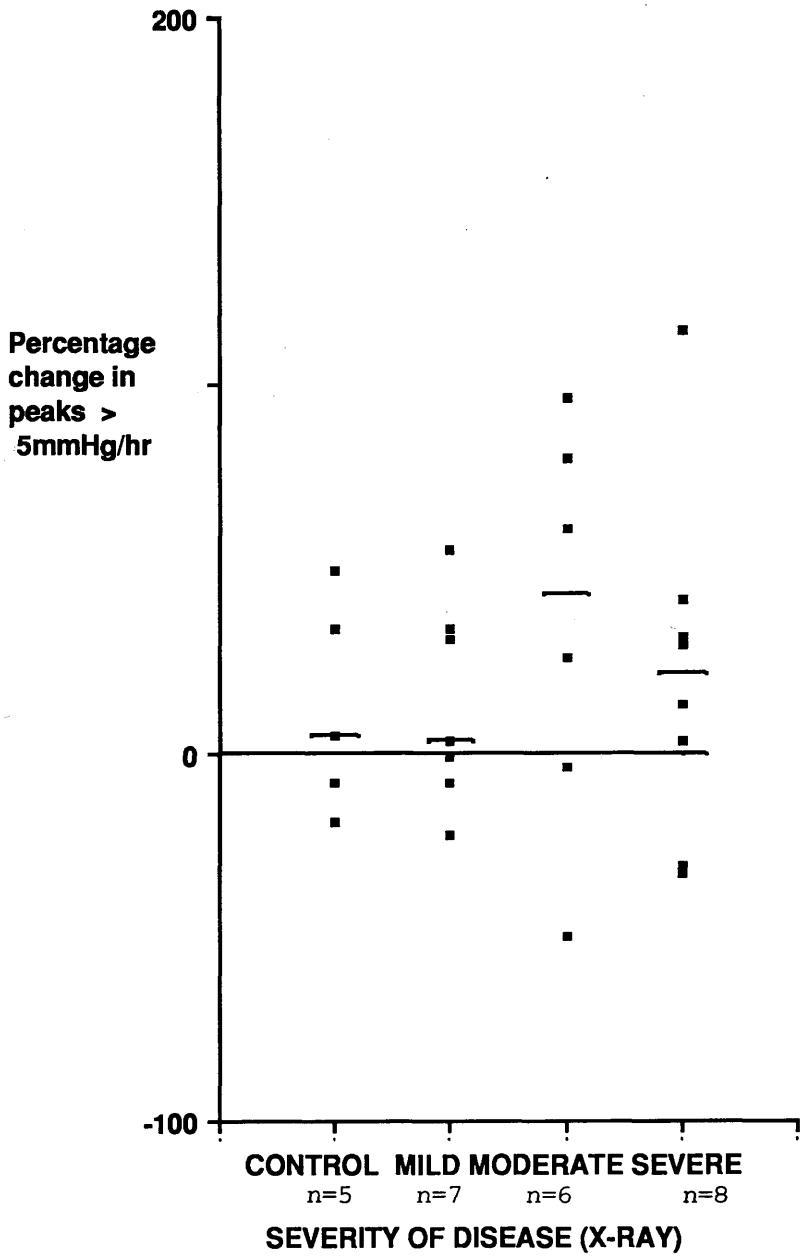


Figure 57.
The effect of eating on the number of peaks >5mmHg/hour.

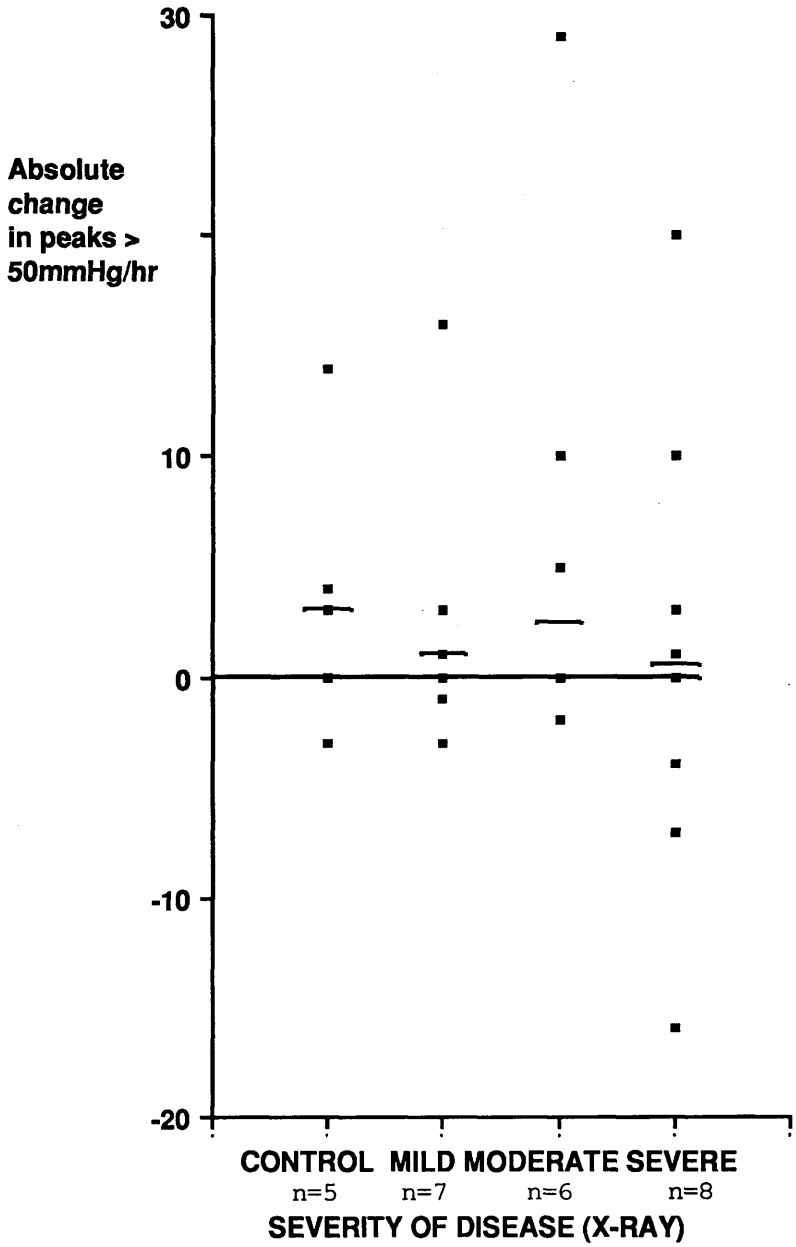


Figure 58.
The effect of eating on the number of peaks >50mmHg/hour.

	CONTROL	MILD	MODERATE	SEVERE
Motility index				
median	26	104	40	14
range	-16- 161	-20- 424	-54- 286	-43- 92
% Activity				
median	4	83	30	13.5
range	-10- 175	-11- 275	-71- 170	-50- 63
Peaks >5mmHg/hr				
median	5	3	43.5	21.5
range	-19- 50	-22- 55	-50- 97	-33- 115
Peaks >50mmHg/hr*				
median	3.0	1.0	2.5	0.5
range	-3- 14	-3- 16	-2- 29	-16- 20

Table 21.

Percentage change in motility parameters with eating.
(* absolute change)

Discussion

For the first time a link between basal motility index and severity of disease has been demonstrated. As the disease progresses, an increase in both the duration and strength of contractions occurs. It is unclear, however, why the diverticular colon in severe disease appears to be already hyperactive in the basal state. It may simply chart the progress of the disease; the motility parameters increasing with the number of diverticula. On the other hand, the narrowing of the lumen in severe cases due to thickening and infolding of the circular muscle (Morson, 1963; Williams, 1965; Hughes 1969b) increases its mechanical resistance. The colon may have to work harder in order to overcome this and hence increase the motility index.

The phenomenon of increased colonic activity after the ingestion of food in normal subjects has been recognized for almost a century (Hertz, 1909). In 1909, Hertz referred to this as the "gastrocolic reflex" and, using radiological techniques, demonstrated large displacements of colonic contents following a food stimulus. In diverticular disease, however, the colonic response to food is less certain. Using open-ended tubes, both Arfwidsson and Kock (1964) and Trotman and Misiewicz (1988) found that the motility index of the diverticular colon increased after eating. Painter and Truelove (1964b), using a similar

technique, found that only colonic segments bearing diverticula reacted excessively to a pharmacological stimulus of morphine and postulated that the effect of eating may be similar.

The philosophy behind the present study was to maintain as natural conditions as possible. As a result, uncontrolled stimuli such as subject movement and variations in dietary intake were present. The effect of movement is likely to be small since somatic activity has been shown to influence colonic propulsion post-prandially but not intracolonic pressure (Holdstock et al,1970).

There has been no previous research into the effect of the quantity of food on the magnitude of the gastrocolic reflex. In this study, the quantity of food consumed was unrelated to severity of disease, therefore there is no reason to conclude that the size of the meal significantly influenced the results.

Addressing the question of dietary composition, Snape et al (1979) found that ingestion of fat produced an immediate response in the distal colon similar to that provoked by a standard meal (40% carbohydrate, 40% fat, 20% protein) with an additional delayed peak of activity which occurred 70 minutes after eating. By choosing a post-prandial analysis time of 60 minutes, the possible effects of the variable dietary composition of meals were minimised.

The most interesting finding in this study is that food stimulates the colon in different ways. In the control group, the gastrocolic reflex is small. This is rather surprising and conflicts with earlier reports which show that the motility index of the normal colon exhibits a two to three fold increase following a food stimulus (Arfwidsson and Kock,1964; Trotman and Misiewicz, 1988). Closer examination of the control group reveals that it comprises five subjects who are not age-matched to the disease groups. Furthermore, diverticular disease cannot be excluded from this group as only two subjects had undergone barium enema examination. For these reasons, the control group response must be viewed with caution.

In the disease groups, the gastrocolic reflex diminishes with increasing number of diverticula. In mild disease, the gastrocolic reflex appears to be preserved; in moderate disease the response is limited, whilst in severe disease the already hyperactive colon seems unable to generate more energy when stimulated by food. These findings may explain some of the anomolies in previous studies where a bias in disease severity in a group of patients would influence the results.

In general, the pre and post-prandial motility indices in this study are lower than those found by other workers (Arfwidsson and Kock,1964; Trotman and Misiewicz, 1988).

This is likely to be due to their different measuring technique which used tubes on a prepared bowel. Tubes are prone to movement artifact resulting in higher pressures when they contact the bowel wall. Also the introduction of tubes per rectum may cause distress to the patient and stimulate colonic activity. Radiotelemetry is a more physiological method of measuring colonic pressures since no bowel preparation is required and the radiopill has no external connections to produce movement artifact.

Another factor which must be taken into account when comparing this study to other work is that the motility index was measured within the left hemicolon and not solely confined to the sigmoid. Trotman and Misiewicz (1988) have shown that an exaggerated prandial response in diverticular disease is obtained throughout the sigmoid colon but does not extend into the rectosigmoid region. In their examination of the sigmoid colon , Painter and Truelove (1964b) suggested from morphine studies that an excessive prandial response may be confined to the diverticular bearing segments.

The position of the radiopill within the colon was not controlled. Analysis of the records showed that there was a spread of radiopill position during the pre and post prandial periods. About two thirds of the recordings were

obtained before the pill entered the sigmoid. However, it was impossible to determine where the pill was in relation to diverticula although the likelihood of measuring pressures in diverticular bearing segments clearly increases with severity of disease. Evidence from this study suggests that the excessive prandial response in diverticular disease involves the whole of the left colon. Further work is required to determine what proportion of this response is due to the diverticular bearing segments.

Patient Study 8: The effect of sleep on left colonic motility.

Measurements during sleep when the radiopill was in the left colon were available on 17 patients and 3 controls. Motility parameters were calculated over a standard six hour period from 12 midnight to 6am.

Five patients (median age 64yrs, range 62-73yrs) showed mild disease on x-ray, 6 had moderate disease (median age 63.5yrs, range 39-79yrs) and 6 were considered to have severe diverticular disease (median age 73yrs, range 55-77yrs). The median age of the control group was 48yrs and ranged from 43-71yrs.

During sleep, motility index increased with increasing severity of disease from 104(61-253) [median(range)] in the mild group to 174 (58-526) and 436(220-1169) in the moderate and severe groups respectively, $r = 0.617$, $p<0.05$. The median motility index in the control group was 257 and ranged from 115-260 (Figure 59).

There was also a significant correlation between percentage activity and increasing severity of diverticular disease, $r = 0.512$, $p<0.05$ (Figure 60). During sleep, there was no significant difference in the number of low or high amplitude peaks between the groups (Figures 61,62). Table 22 details the results and individual values are documented in Appendix 8.

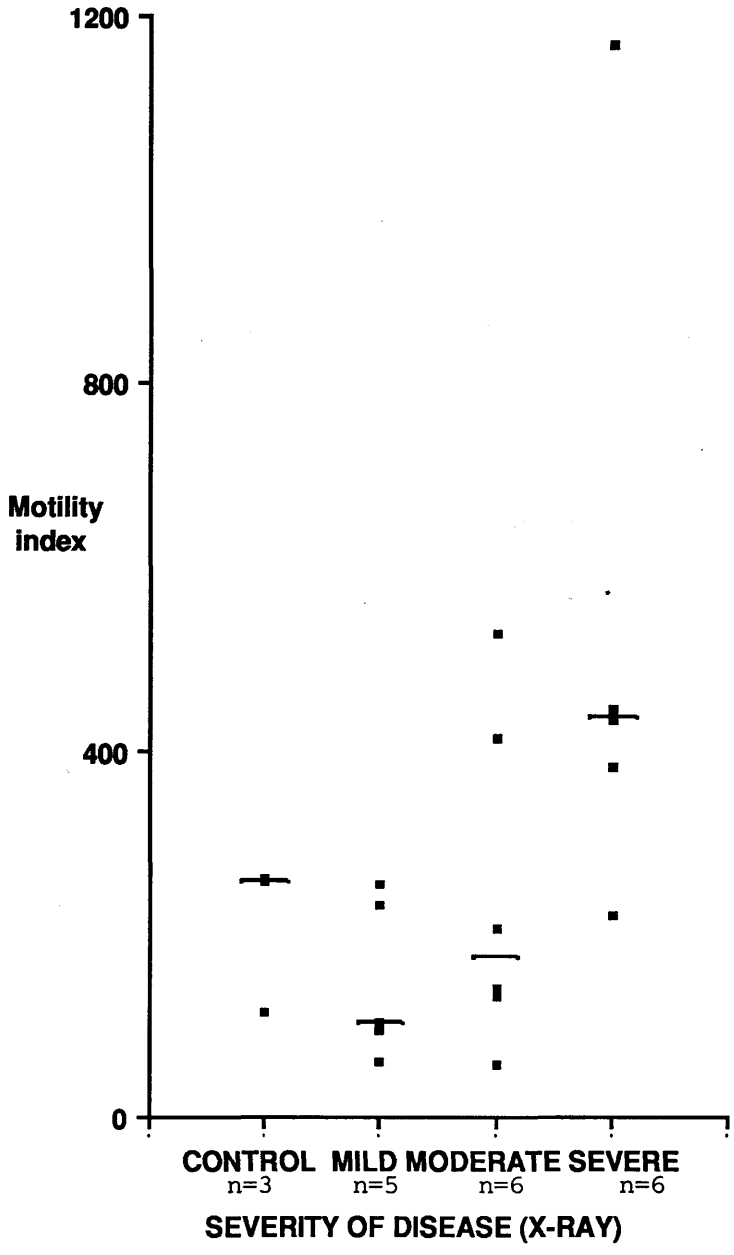


Figure 59.

Left colonic motility index during sleep.

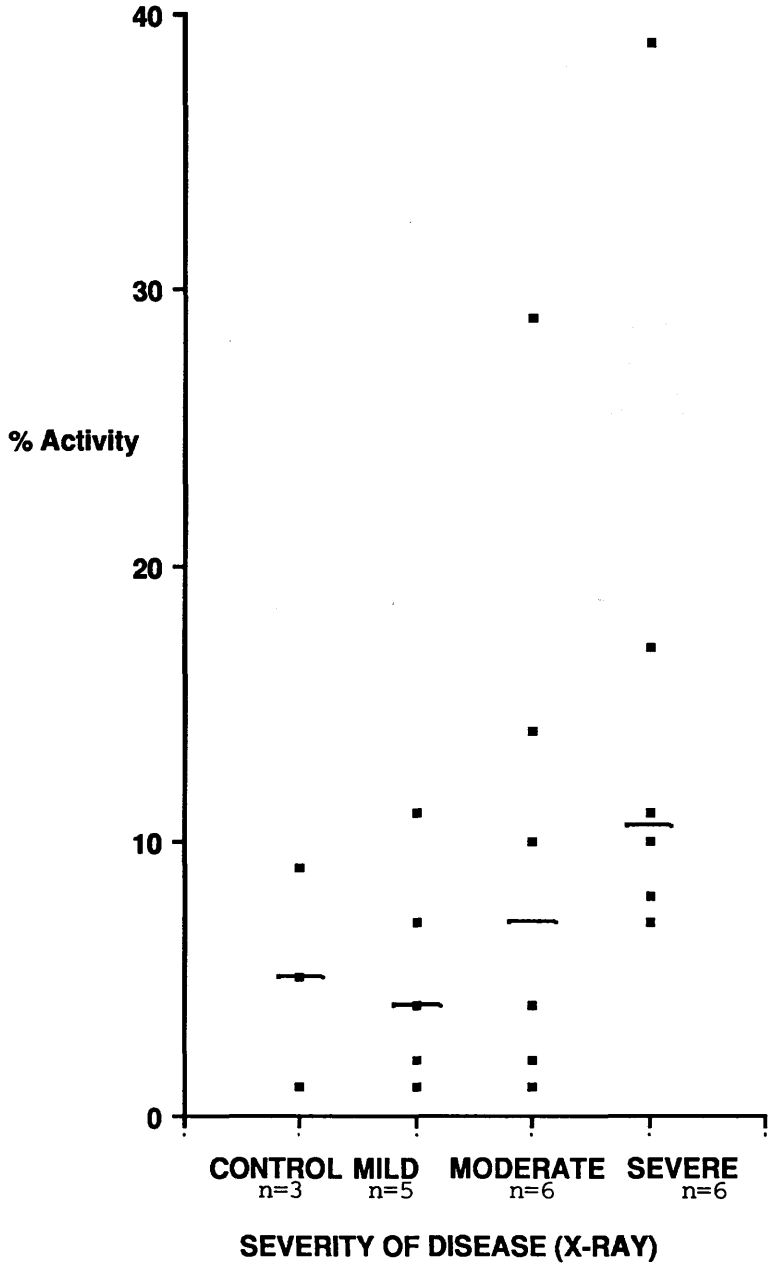


Figure 60.

Left colonic % activity during sleep

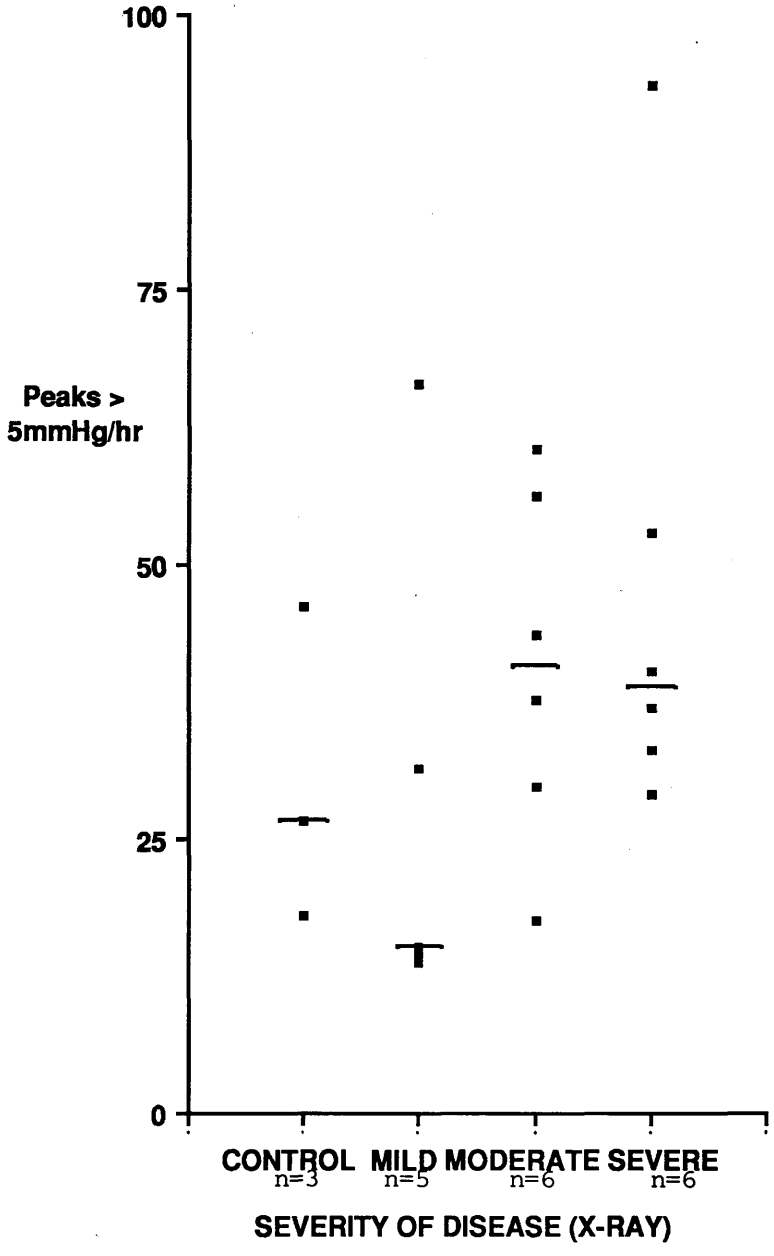


Figure 61.
Left colonic number of peaks >5mmHg/hour during sleep.

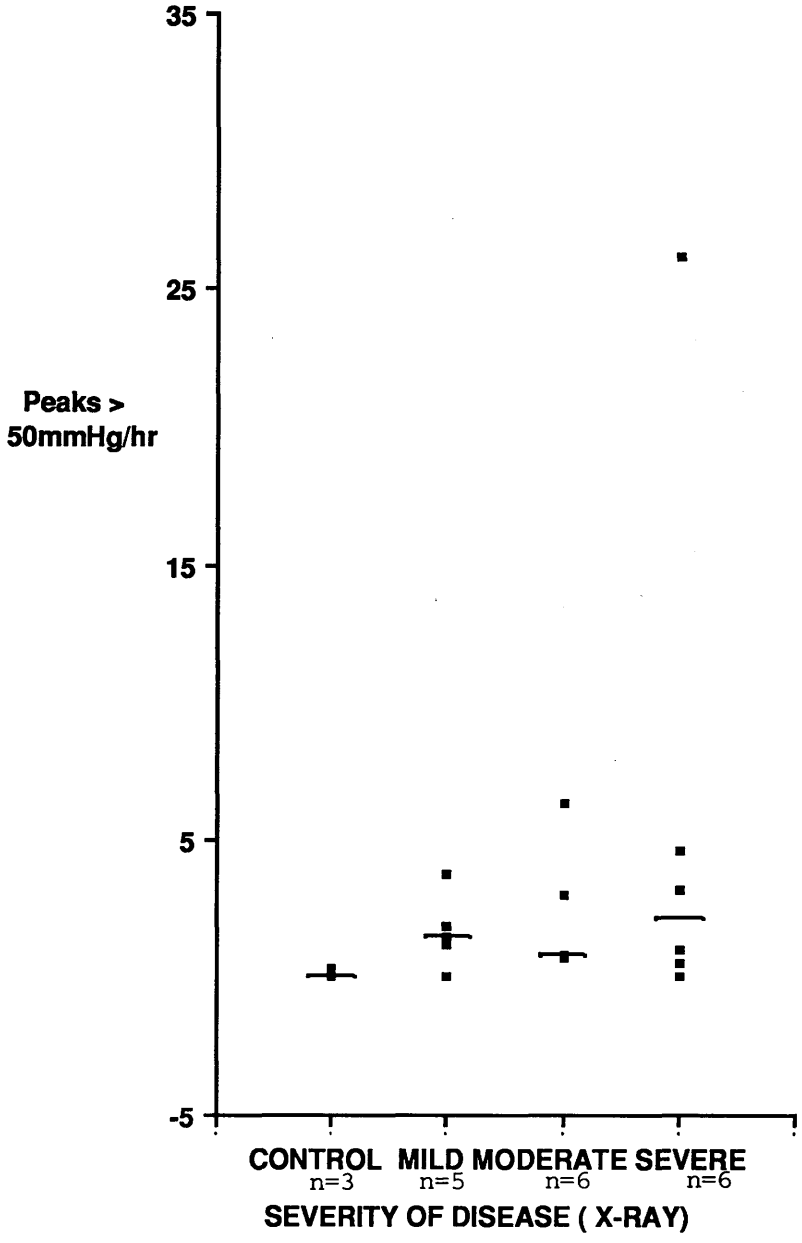


Figure 62.
Left colonic number of peaks >50mmHg/hour during sleep.

	CONTROL	MILD	MODERATE	SEVERE
Motility index				
median	257	104	174	436
range	115-260	61-253	58-526	220-1169
% Activity				
median	5	4	7	10.5
range	1-9	1-11	1-29	8-39
Peaks >5mmHg/hr				
median	26.7	15.3	40.6	38.7
range	18-46.3	13.7-66.5	17.7-60.4	29.0-93.5
Peaks >50mmHg/hr				
median	0.0	1.5	0.8	2.1
range	0.0-0.3	0.0-3.7	0.7-6.3	0.0-26.2

Table 22.

Motility parameters during sleep.

Discussion

The elevated basal motility index found in the previous study in diverticular disease raises the question - " Does sleep influence the diverticular colon? ". In normal subjects and in patients with irritable bowel syndrome, drowsiness and sleep depress colonic motor activity (Narducci et al,1987; Rosenblum and Cummins,1954).

Unfortunately, measurements during sleep were available in only three of the control subjects making it impossible for them to be included in statistical testing. They are, therefore, detailed for reference purposes only.

It was also disappointing that comparisons between sleep and pre-prandial measurements were not possible because different subjects were included in each group in order to give reasonable numbers. However, comparison of the different disease groups during sleep reveals a significant correlation between disease severity and motility index due to an increase in percentage activity.

Patient Study 9: Motility of the right and left colon.

Nineteen patients with diverticular disease confined to the left colon and 7 controls were included in this study. Of the 19 patients, 5 were allocated to the mild group (median age 62yrs, range 57-73yrs), 9 to the moderate group (median age 64yrs, range 39-79yrs) and 5 to the severe disease group (median age 72yrs, range 67-73yrs). The median age of the control subjects was 43 years and ranged from 23-71yrs. The transit times through the right and left colon determined the period of analysis of the other motility parameters.

Figures 63-70 illustrate the motility parameters of the right and left colon and Tables 23 and 24 detail the results. Individual values are listed in Appendix 9.

In the right colon, the motility index increased with increasing severity of disease on x-ray from 126 (81-168) [median (range)] in the mild group to 227 (30-528) and 682 (359-861) in the moderate and severe groups respectively. The median motility index in the control group was 274 (range 69-783). The Kruskal-Wallis test demonstrated a significant difference between the four groups, $p<0.05$. In the disease groups, there was also a significant correlation between increasing severity of diverticular disease and the motility index of the right colon, $r=0.689$, $p<0.01$. (Figure 63).

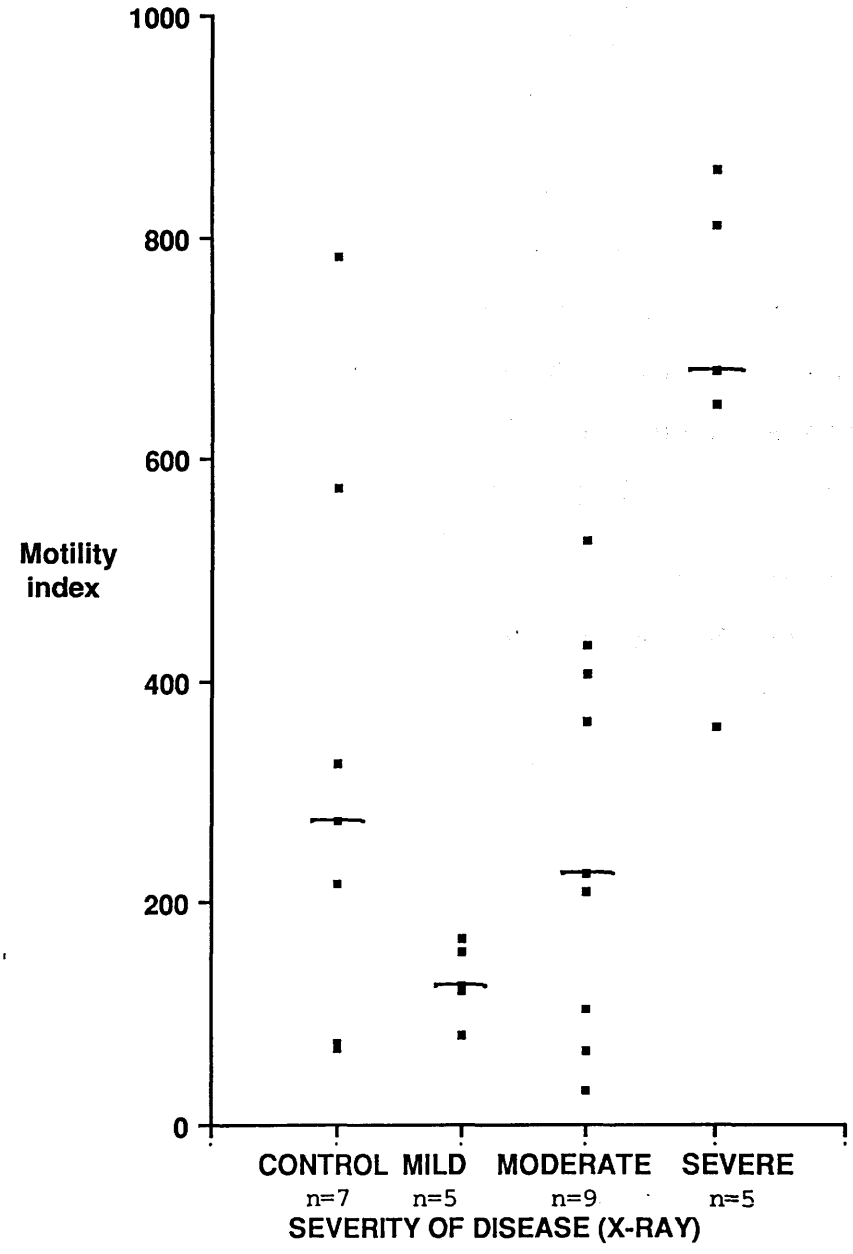


Figure 63

Right colonic motility index.

Percentage activity, peaks greater than 5mmHg/hour and peaks greater than 50mmHg/hour did not differ significantly between the patient groups (Figures 64-66).

In the left colon there was also a significant correlation between increasing severity of diverticular disease and the motility index of the left colon increasing from 227 (80-726) [median (range)] in the mild group to 425 (119-1013) and 1009 (431-1520) in the moderate and severe groups respectively, $r = 0.490$, $p<0.05$, (Figure 67).

The number of peaks greater than 50mmHg/hour also increased with disease severity although not significantly. Percentage activity and the number of peaks greater than 5mmHg/hour did not differ significantly between the patient groups, (Figures 68-70).

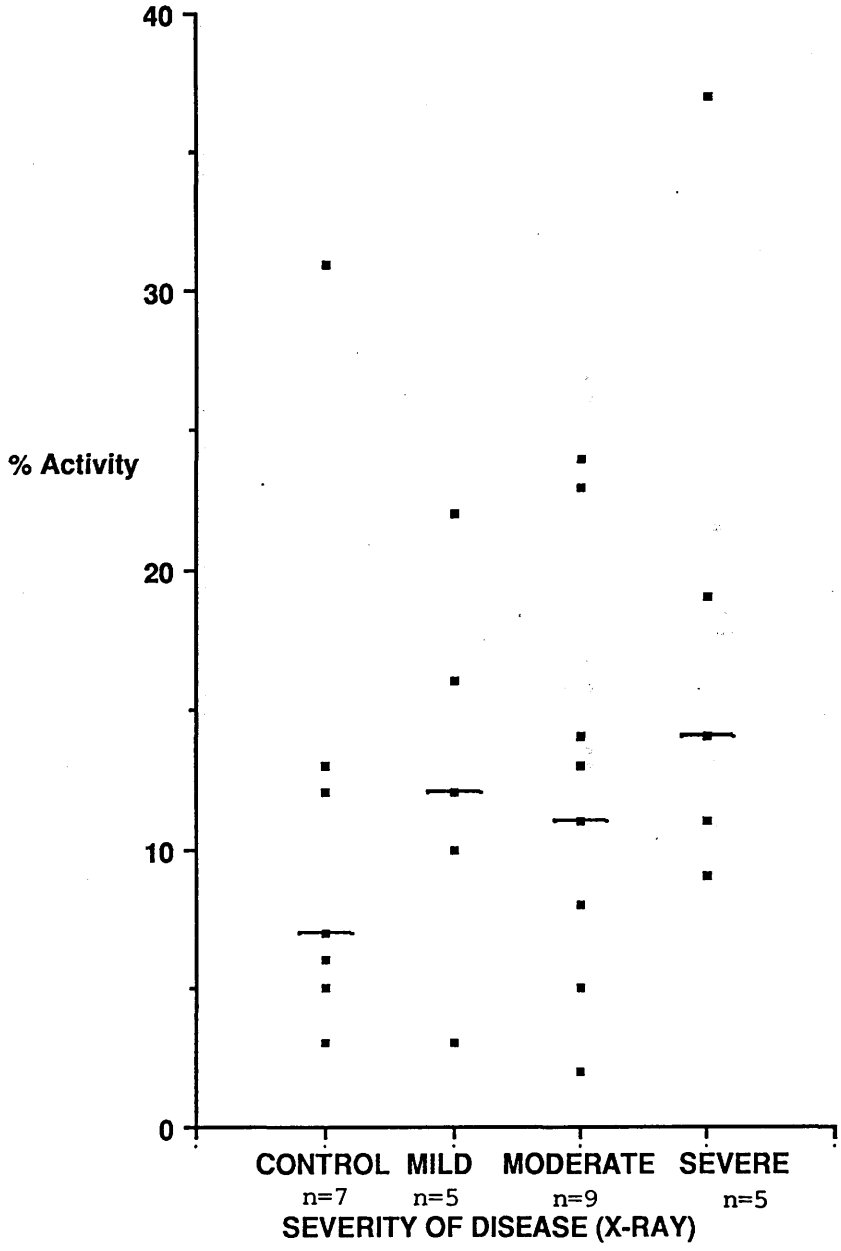


Figure 64

Right colonic % activity.

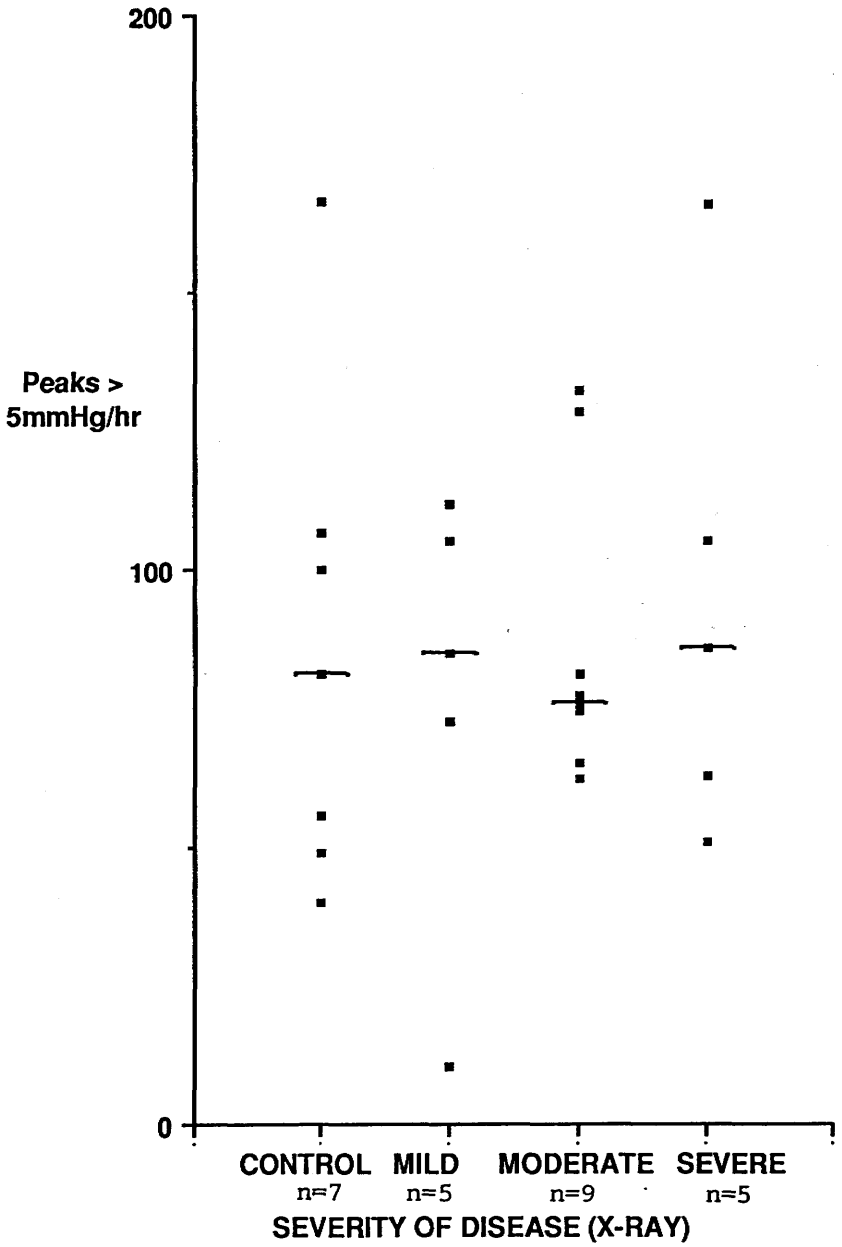


Figure 65

Right colonic number of peaks > 5mmHg/hour.

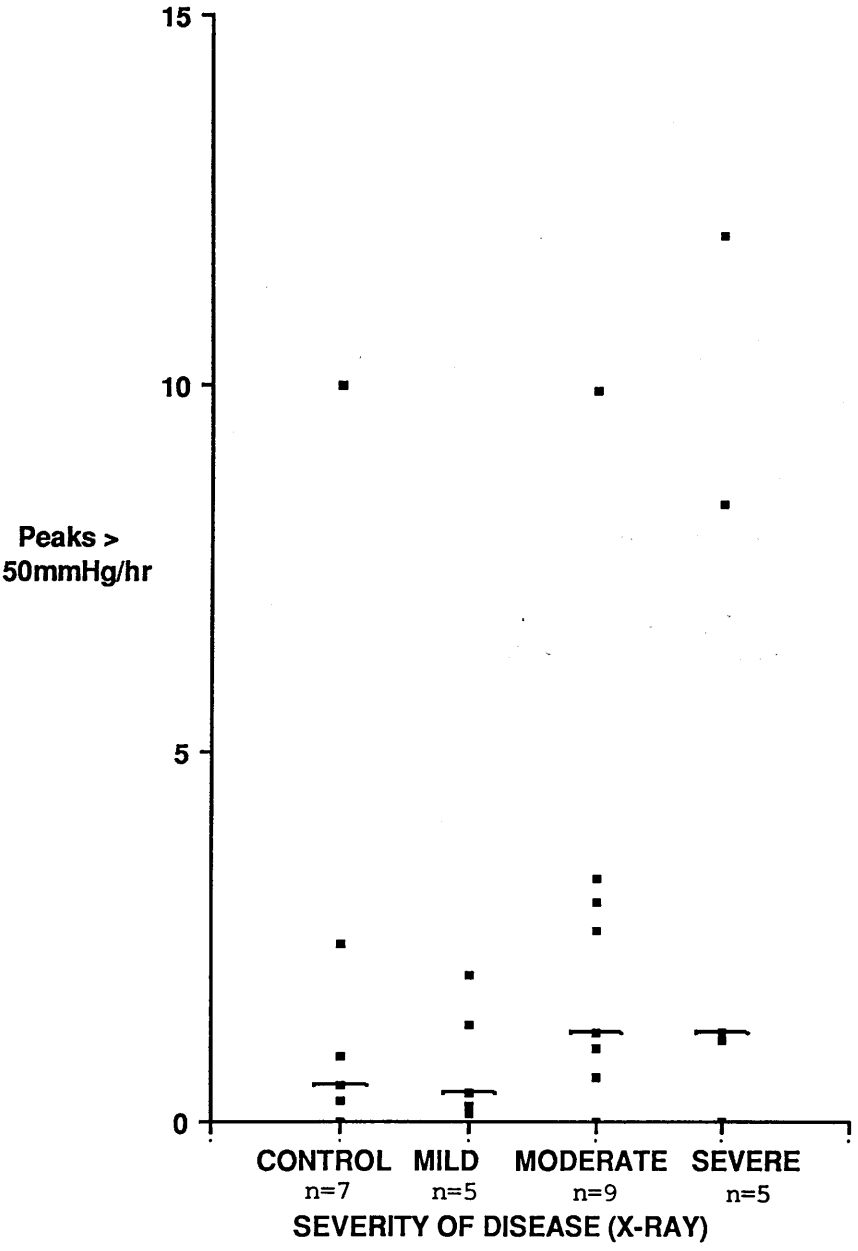


Figure 66

Right colonic number of peaks >50mmHg/hour.

	CONTROL	MILD	MODERATE	SEVERE
Motility index				
median	274	126	227	682
range	69-783	81-168	30-528	359-861
% Activity				
median	7	12	11	14
range	3-31	3-22	2-24	9-37
Peaks >5mmHg/hr				
median	81.3	85.3	76.2	86.0
range	40.1-166.3	10.3-112.2	62.3-132.4	51.1-166
Peaks >50mmHg/hr				
median	0.5	0.4	1.2	1.2
range	0-10	0.1-2	0-9.9	0-12

Table 23.

Right colonic motility parameters.

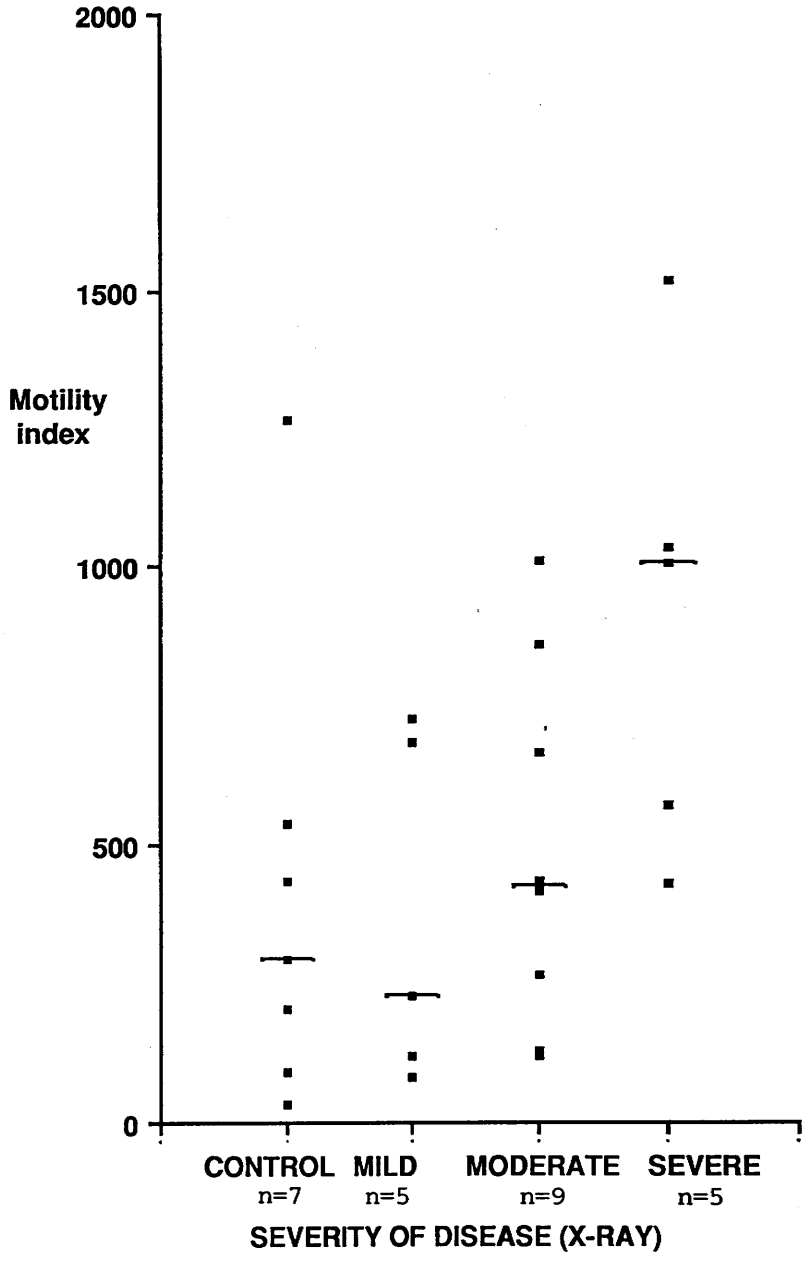


Figure 67

Left colonic motility index.

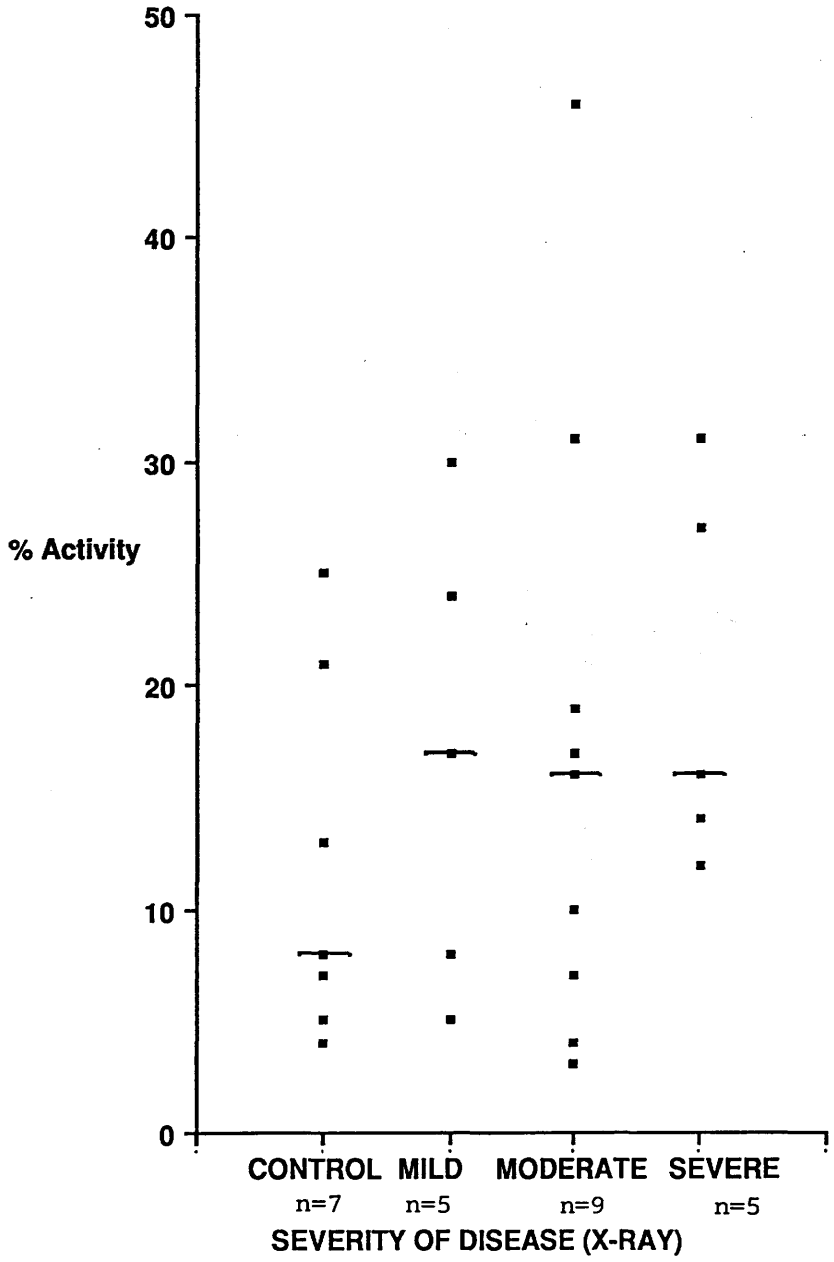


Figure 68

Left colonic % activity.

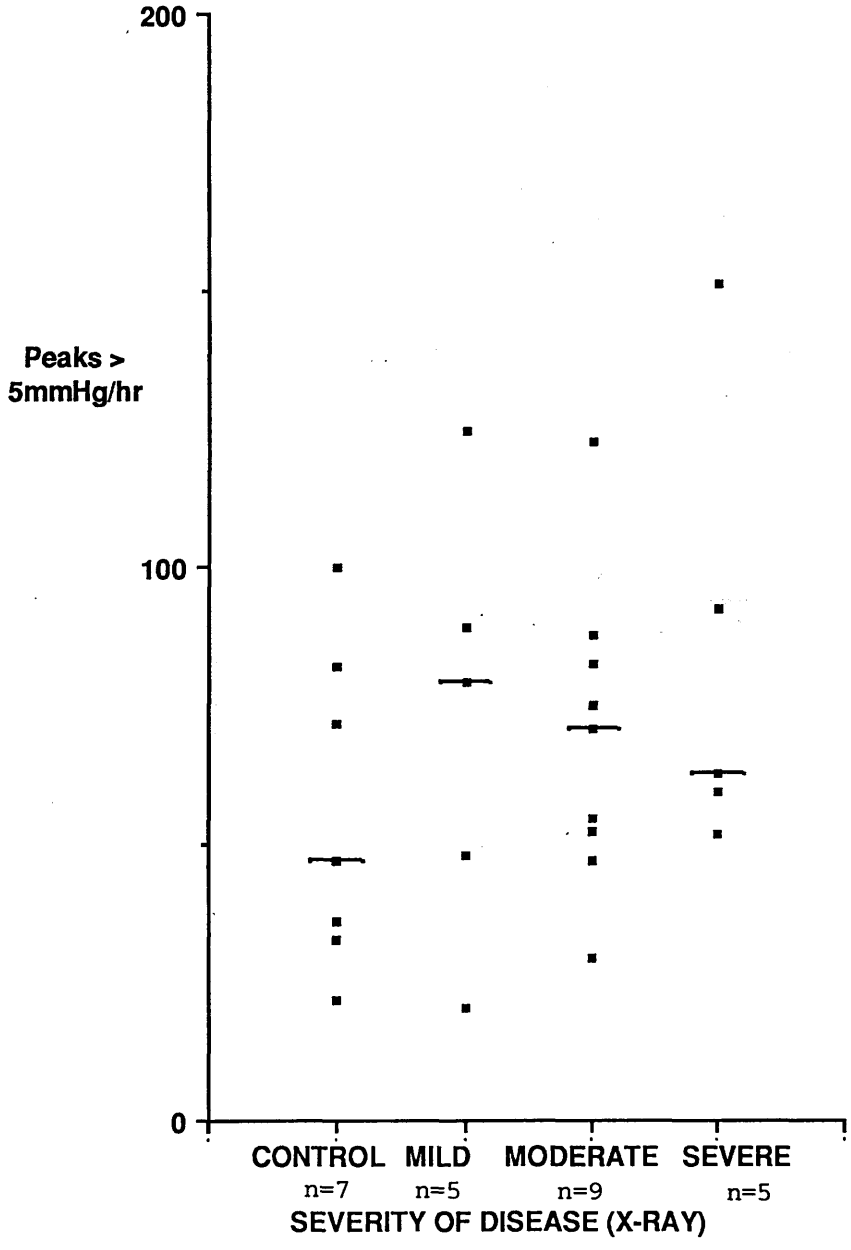


Figure 69

Left colonic number of peaks >5mmHg/hour.

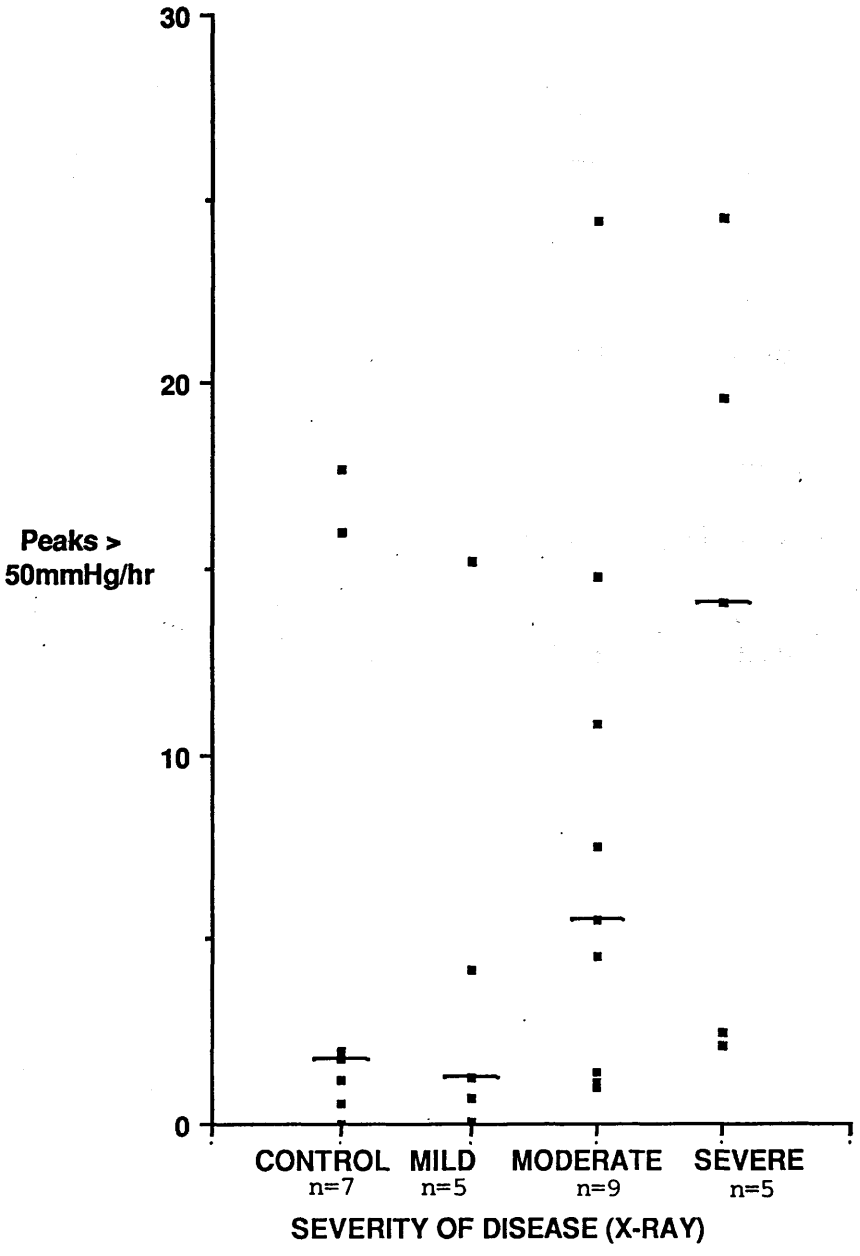


Figure 70

Left colonic number of peaks >50mmHg/hour.

	CONTROL	MILD	MODERATE	SEVERE
Motility index				
median	295	227	425	1009
range	32-1266	80-726	119-1013	431-1520
% Activity				
median	8	17	16	16
range	4-25	5-30	3-46	12-31
Peaks >5mmHg/hr				
median	46.7	79.0	70.8	62.5
range	22.0-100.2	20.5-124.5	29.2-122.6	51.7-151.2
Peaks >50mmHg/hr				
median	1.8	1.3	5.5	14.1
range	0-17.7	0.1-15.2	1.0-24.4	2.1-24.5

Table 24.

Left colonic motility parameters.

Discussion

The motility pattern of the right hemicolon has received little attention (Kerlin et al, 1983; Dapoigny et al, 1988). Most studies on colonic motility have confined their manometric measurements to the distal colon due to its easier accessibility by tubes or wires introduced per rectum (Painter and Truelove, 1964a & b; Weinreich and Andersen, 1976a & b; Eastwood, Brydon et al, 1978; Narducci et al,1987; Trotman and Misiewicz, 1988).

Untethered radiotelemetry capsules, however, allow pressure measurements to be recorded throughout the whole of the large bowel thus opening up analysis of motility data from the right side of the colon. Amongst the first workers to exploit this was Misiewicz et al (1966) who used a radiopill to record pressures from the right colon simultaneously with balloon-tipped tubes in the distal colon. They concluded that the pressure waves of the two colonic segments were generally similar in type and magnitude in a study which included healthy volunteers, subjects with spastic colon and those with diarrhoea.

This study was criticised by Kerlin et al, (1983) who pointed out that comparisons of motor activity in the proximal and distal colon may be influenced by the use of different recording techniques at different loci. In their study on healthy volunteers, a tube was introduced into the proximal colon by mouth and another per rectally into the

distal colon. However, they too found no difference between the motility index of the right and left colon in either the pre or post-prandial hour (Kerlin et al, 1983).

The present study differs from these earlier reports in that motility of the right and left colon was recorded in a serial fashion as the radiopill progressed through the large bowel. Nevertheless, the results obtained by serial measurement in the control group concur with those found simultaneously by failing to detect a significant difference between the motility index of the right and left colon.

The finding that there was a significant correlation between the motility index of the left colon and severity of radiological disease reiterates the results from a larger population study reported earlier (Patient Study 3).

The most interesting discovery from this study was that the increase in motility index found in the left colon is mirrored by the right colon. This is a surprising observation which has not been previously reported and raises some interesting questions. Is diverticular disease a pancolonic disorder, especially in its severe form ? Or, is the right colon simply responding to the effect of treatment with ispaghula husk which has been found to primarily influence the motility parameters of the right hemicolon (Patient Study 2)?

Clearly, this is an important area for further study which could have implications for clinical management of the disease. A large number of untreated patients in each of the three categories of disease and age matched controls would be required. This would allow the effect of ispaghula husk on disease severity to be assessed and also enable comparisons to be made between the right and left colon of each individual group.

6: CONCLUSIONS

Radiotelemetry is a non-invasive, physiological method of measuring colonic motility and transit time. The system validated in the present study was a considerable improvement on earlier telemetry systems with advances in microprocessing technology making colonic motility measurement easier. The receiver software guided the user carefully through the various steps in setting up the system during calibration and for clinical monitoring in the ward. The Atari 1040ST microcomputer was also particularly useful in providing a compact and automatic method for storing data and its subsequent analysis.

The new band aerial developed during the validation of the technique overcame the problem of directional sensitivity, making it ideal for detecting signals from the untethered radiopill as it progressed through the gastrointestinal tract. The improved field strength meter was also important to enable the position of the radiopill within the colon to be mapped on the anterior abdominal wall accurately and easily. This arrangement of monitoring and mapping the radiopill was well tolerated by the patients.

Patients who were studied before and after treatment demonstrated that ispaghula husk reduced total gut transit times and increased colonic motility, primarily by its effect on the right colon. It had no significant effect on

7: REFERENCES

7: REFERENCES

Ahran, P., Devroede, G., Jehannin, B. et al (1981) Segmental colonic transit time. Diseases of the Colon and Rectum, 24(8),625-29.

Almy, T.P. & Tulin, M. (1947) Alterations in colonic function in man under stress: experimental production of changes simulating the "irritable colon". Gastroenterology, 8,616-26.

Almy, T.P., Kern, F. & Tulin, M. (1949) Alterations in colonic function in man under stress: II Experimental production of sigmoid spasm in healthy persons. Gastroenterology, 12, 425-36.

Almy, T.P. & Howell, D.A. (1980) Diverticular disease of the colon. New England Journal of Medicine, 302 (1), 324-31.

Alvarez, W.C. & Freedlander, B.L. (1924) The rate of progress of food residues through the bowel. Journal of the American Medical Association,83,576-80.

Anders, G., Wangel, M.D. & Deller, D.J. (1965) Intestinal motility in man. (3) Mechanisms of constipation and diarrhoea with particular reference to the irritable colon syndrome. Gastroenterology,48, 69-84.

Archbold, A. & Parks, T.G. (1979) Fybogel; its effect on colonic motility and intestinal transit in diverticular disease.
Irish Journal of Medical Science,148(1), 27.

Arfwidsson, S. & Kock, N.G. (1964)Intraluminal pressure in the sigmoid colon of normal subjects and patients with diverticular disease of the colon.
Acta Chirurgica Scandinavica (supplementum 342).

Attisha, R.P. & Smith, A.N. (1969) Pressure activity of the colon and rectum in diverticular disease before and after sigmoid myotomy.
British Journal of Surgery, 56(12), 891-94.

Avery - Jones, F. (1981) Are fibre supplements really necessary in diverticular disease of the colon ?
British Medical Journal, 282, 1792.

Beighton,P.H., Murdoch,J.L. & Votteler,T. (1969) Gastro-intestinal complications of the Ehlers-Danlos syndrome.
Gut, 10, 1004-8.

BNF 1988a (no.16)
1.6.2.Stimulant laxatives,64-66, Eds. Prasad,A.B. et al.
Joint publication of the B.M.A. and the Pharmaceutical Society of Great Britain.

BNF 1988b (no.16)
1.6.1. Bulk-forming drugs,62-63, Eds. Prasad,A.B. et al. Joint publication of the B.M.A. and the Pharmaceutical Society of Great Britain.

Brodribb, A.J.M. & Humphreys, D.M. (1976) Diverticular disease: Three studies-Part II Treatment with bran. British Medical Journal, 1(1), 425-28.

Brodribb, A.J.M.(1977)Treatment of symptomatic diverticular disease with a high fibre diet.
Lancet,1(2), 664-66.

Brodribb, A.J.M., Condon, R.E., Cowles, V. et al. (1979) Effect of dietary fibre on intraluminal pressure and myoelectrical activity of the left colon in monkeys. Gastroenterology,77, 70-4.

Burkitt, D.P., Walker, A.R.P. & Painter, N.S.(1972) Effect of dietary fibre in stools and transit times and its role in the causation of disease.
Lancet,2, 1408.

Burkitt, D.P. (1975) Dietary fibre and "pressure diseases". Journal of the Royal College of Physicians, London. 9 (2), 138-47.

Carlson, A.J. & Hoelzel, F. (1949) Relation of diet to diverticulosis of the colon in rats.
Gastroenterology, 12, 108.

Chaudary,N.A. & Truelove,S.C.(1961a)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, 1-17.

Chaudary, N.A. & Truelove, S.C. (1961b) Human colonic motility: a comparative study of normal subjects, patients with ulcerative colitis and patients with the irritable colon syndrome. III Effects of emotions. Gastroenterology,40, 27-36.

Christensen, J. (1983) The colon. In: A Guide to Gastro-intestinal Motility. (eds.Christensen,J. & Wingate,D.L.) Chapter 7, p200; Bristol, Wright.

Code, C.F., Hightower, N.C. Jr. & Morlock, C.G. (1952) Motility of the alimentary canal in man; a review of recent studies. American Journal of Medicine, 13, 328.

Connell, A.M.& Rowlands, E.N. (1960) Wireless telemetering from the digestive tract. Gut,1, 266-72.

Connell, A.M. (1961) The motility of the pelvic colon (1) Motility in normals and in patients with asymptomatic duodenal ulcer. Gut,2, 175-86.

Connell, A.M., McCall, J., Misiewicz,J.J. et al. (1963) Observations on the clinical use of radiopills. British Medical Journal, 2, 771-74.

Connell, A.M., Avery-Jones, F.& Rowlands, E.N. (1965) Motility of the pelvic colon. Part IV Abdominal pain associated with colonic hypermotility after meals. Gut, 6, 105-12.

Connell, A.M. (1968) Problems of methodology and interpretation and analysis of records. American Journal of Digestive Diseases,13(5),397-409.

Connell, A.M. (1975) Applied physiology of the colon: factors relevant to diverticular disease. Clinics in Gastroenterology, 4 (1), 23-36.

Connell, A.M. (1977) Pathogenesis of diverticular disease of the colon. Advances in Internal Medicine,22, 377-95.

Cook, J.M. (1968) Spontaneous perforation of the colon. Report of two cases in a family exhibiting Marfan Stigmata. Ohio Medical Journal,64, 73.

Cummings, J.H. & Wiggins, H.S. (1976) Transit through the gut measured by analysis of a single stool. Gut,17, 219-23.

Dapoigny, M., Trolese, J-F., Bommelaer, G. et al. (1988) Myoelectric spiking activity of the right colon, left colon, and rectosigmoid of healthy humans. Digestive Diseases and Sciences, 33, 1007-12.

Davidson, M., Sleisenger, M.H., Almy, T.P. et al. (1956) Studies in distal colonic motility in children. I Non-propulsive patterns in normal children. Paediatrics,17, 807.

Eastwood, M.A., Brydon, W.G., Smith, A.N. et al. (1978) Colonic function in patients with diverticular disease. Lancet,1, 1181-82.

Eastwood, M.A., Smith, A.N., Brydon, W.G. et al. (1978) Comparison of bran, ispaghula and lactulose on colonic function in diverticular disease. Gut,19, 1144-47.

Eastwood, M.A., Watters, D.A.K. & Smith, A.N. (1982) Diverticular disease - Is it a motility disorder? Clinics in Gastroenterology, 11, 545-61.

Eastwood, M.A. (1987) Diverticular disease. In Oxford Textbook of Medicine Vol 1 (2nd Edition,eds.Weatherall, D.J., Ledingham, J.G.G., Warrell, D.A.)12.135-12.137; Oxford Medical Publications.

Edward, H.C. (1939) Diverticula and diverticulitis of the intestine. Bristol, Wright.

Evans, D.F., Foster, G.E., Hardcastle, J.D. et al. (1980) Studies of the human gastro-intestinal tract in the ambulatory subject using the pressure sensitive radiotelemetry capsule.
Proceedings of the third international symposium on ambulatory monitoring. (Eds. Stott,F.D., Raftery,E.B., Goulding, L. Academic press.

Evans, D.F., Pye, G., Bramley, R. et al.(1988) Measurement of gastrointestinal pH profiles in normal ambulant human subjects.
Gut, 29, 1035-44.

Farrar, J.T., Zworykin, V.K. & Baum, J. (1957) Pressure-sensitive telemetering capsule for the study of gastrointestinal motility.
Science,126, 975-76.

Findlay, J.M., Mitchell, W.D., Smith, A.N. et al. (1974) Effects of unprocessed bran on colon function in normal subjects and in diverticular disease.
Lancet,1(1), 146-49.

Finlay, J.G., Carter, K. & McLeod, I. (1986) A comparison of intrarectal infusion of gas and mass on anorectal angle and anal canal pressure.
British Journal of Surgery,73, 1025.

Gear, J.S., Fursdon, P., Nolan, D.J. et al. (1979) Symptomless diverticular disease and intake of dietary fibre.
Lancet,1(1), 511-14.

Heaton, K.W. (1981)Is bran useful in diverticular disease?
British Medical Journal, 283(2), 1523-24.

Hertz, A.F. (1909) Constipation and allied intestinal disorders. Oxford Medical Publications;London.

Hertz, A.F. & Newton, A. (1913) The normal movements of the colon in man.
Journal of Physiology,47, 57-65.

Hinton, J.M., Lennard-Jones, J.E. & Young, A.C. (1969) A new method for studying gut transit times using radio-opaque markers.
Gut,10, 842-47.

Hodgson, J. (1975) Animal models in the study of diverticular disease. 1 Aetiology and treatment.
Clinical Gastroenterology,4, 201-19.

Hodgson, W.J.B. (1977) The placebo effect. Is it important in diverticular disease?
American Journal of Gastroenterology,67(2), 157-62.

Hoelzel, F. (1930) The rate of passage of inert materials through the digestive tract.
American Journal of Physiology,92, 466-97.

Holdstock, D.J., Misiewicz, J.J. & Waller, S.L. (1969) Observations on the mechanism of abdominal pain. Gut,10, 19-31.

Holdstock, D.J., Misiewicz,J.J., Smith,T. et al. (1970) Propulsion (mass movements) in the human colon and its relationship to meals and somatic activity. Gut,11, 91-9.

Holzknecht, G. (1909) Die normale peristaltik des kolon. Munchener Medizinische Wochenschrift,56, 2401-03.

Horowitz, L. & Farrar, J.T. (1962) Intraluminal small intestinal pressures in normal patients and in patients with functional gastrointestinal disorders. Gastroenterology,42, 455-64.

Howell, D.A., Crow, H.C., Almy, T.P. et al. (1978) A controlled double blind study of sigmoid motility using Psyllium mucilloid in diverticular disease. Gastroenterology,74, 1046(Abstract).

Hughes, L.E. (1969a) Post mortem survey of diverticular disease of the colon. Part I Diverticulosis and diverticulitis. Gut,10, 336-43.

Hughes, L.E. (1969b) Post mortem survey of diverticular disease of the colon. Part II The muscular abnormality in the sigmoid colon. Gut,10, 344-51.

Jacob, R., Riddle, H. & Watson, B.W. (1973) Circuit for searching for a circle from a three aerial system during inductive loop telemetry.
Biomedical Engineering, 8, 292.

Jacobson, B. (1962) Tracking radiopills in the human body.
New Scientist,286, 288-90.

Johnson, H.C.L. Jr. & Block, M.A. (1985) Diverticular disease. Current trends in therapy.
Postgraduate Medicine, 78(3),75-9.

Karaus, M. & Sarna, S.K. (1987) Giant migrating contractions during defaecation in the dog colon.
Gastroenterology,92(4), 925-33.

Keith, A. (1910) Diverticula of the alimentary tract of congenital or of obscure origin.
British Medical Journal,1, 376-80.

Kerlin, P., Zinsmeister, A. & Phillips, S. (1983) Motor responses to food of the ileum, proximal colon, and distal colon of healthy humans.
Gastroenterology, 84, 762-70.

Kern, F. Jr., Almy, T.P., Abbot, F.K. et al. (1951) Motility of the colon in non-specific ulcerative colitis.
Gastroenterology,19, 492.

Kirwan, W.C. & Smith, A.N. (1974) Gastrointestinal transit estimated by an isotope capsule.
Scandinavian Journal of Gastroenterology, 9,763-66.

Leandro, P.A., Cecconello, I., Habr-gama, A., et al.(1984) Gastrointestinal motility in normal subjects and patients with diverticulosis of the colon.
Arquivos de Gastroenterologia, 21(4), 157-63.

Mackay, R.S. & Jacobson, B. (1957) Endoradiosonde.
Nature, 179, 1239-40.

Manousos, O.N., Truelove, S.C. & Lumsden, K.(1967) Transit times of food in patients with diverticulosis or irritable colon syndrome and normal subjects.
British Medical Journal,3, 760-2.

Metcalf, A.M., Phillips, S.F., Zinsmeister, A.R. et al. (1987) Simplified assessment of segmental colonic transit.
Gastroenterology,92, 40-7.

Misiewicz, J.J., Connell, A.M. & Pontes, F.A. (1966) Comparison of the effect of meals and prostigmine on the proximal and distal colon in patients with and without diarrhoea.
Gut,7, 468-73.

Misiewicz, J.J., Waller, S.L., Fox, R.H. et al. (1968) The effect of elevated body temperature and of stress on the motility of the stomach and colon in man. Clinical Science,34, 149-59.

Misiewicz,J.J., Waller,S.L., Healy, M.J.R. et al. (1968) Computer analysis of intraluminal pressure records. Gut,9, 232-36

Misiewicz, J.J., Waller, S.L., Kiley,N. et al. (1969) Effect of oral prostaglandin E1 on intestinal transit in man.
Lancet, 1,648-51.

Morson, B.C. (1963) The muscle abnormality in diverticular disease of the colon.
Proceedings of the Royal Society of Medicine,56,798-800.

Narducci, F., Bassotti, G., Gaburri, M. et al. (1987) Twenty four hour manometric recording of colonic motor activity in healthy man.
Gut,28, 17-25.

Ornstein, M.H., Littlewood, E.R., McLean Baird, I. et al. (1981) Are fibre supplements really necessary in diverticular disease of the colon? A controlled clinical trial.
British Medical Journal,282, 1353-56.

Painter, N.S. (1964) The aetiology of diverticulosis of the colon with special reference to the action of certain drugs on the bahaviour of the colon. Annals of the Royal College of Surgeons of England,34, 98-119.

Painter, N.S. & Truelove, S.C. (1964a) The intraluminal pressure patterns in diverticulosis of the colon. Part 1-Resting patterns of pressure. Gut,5, 201-6.

Painter, N.S. & Truelove, S.C. (1964b) The intraluminal pressure patterns in diverticulosis of the colon. Part II- The effect of morphine. Gut,5, 207-13.

Painter, N.S. & Truelove, S.C. (1964c) The intraluminal pressure patterns in diverticulosis of the colon. Part III- The effect of prostigmine. Gut, 5, 365-69.

Painter, N.S., Truelove, S.C., Ardran, G.M. et al. (1965) Segmentation and the localization of intraluminal pressures in the human with special reference to the pathogenesis of colonic diverticula. Gastroenterology,49, 169-77.

Painter, N.S. & Burkitt,D.P.(1971) Diverticular disease of the colon. A deficiency disease of Western civilization. British Medical Journal,2, 450-54.

Painter, N.S., Almeida, A.Z. & Colebourne, K.W. (1972) Unprocessed bran in treatment of diverticular disease of the colon.
British Medical Journal,2, 137-40.

Painter, N.S. (1975) Diverticular Disease of the Colon.
William Heinemann Medical Books,London.

Painter, N.S. (1981) Are fibre really necessary in diverticular disease?
British Medical Journal,283, 140.

Parks, T.G. & Connell, A.M. (1969) Motility studies in diverticular disease of the colon. Part 1. Basal activity and response to food assessed by open-ended tube and miniature balloon techniques.
Gut,10, 534-42.

Parks, T.G. (1970) Rectal and colonic studies after resection of the sigmoid for diverticular disease.
Gut,11, 121-25.

Posey, E.L. Jr., Dearing, W.H., Saver, W.G. et al.(1948) The recording of intestinal motility.
Proceedings. Mayo Clinic,23, 297.

Posey, E.L. Jr. & Bargen,J.A. (1951) Observations of normal and abnormal intestinal motor function.
American Journal of the Medical Sciences,221, 10.

Prior, A. & Whorwell, P.J. (1987) Double blind study of ispaghula in irritable bowel syndrome.
Gut, 28, 1510-1513.

Ramsey, G.S. (1965) Progress of a marker in the large intestine.
Diseases of the Colon and Rectum,8, 74-5.

Rees,B.I. & Griffin, P.J.A. (1977) Colonic diverticulosis in a child.
British Medical Journal,2, 1194.

Ritchie, J.A., Ardran, G.M. & Truelove, S.C. (1962) Motor activity of sigmoid colon of humans. A combined study of intraluminal pressure recording and cineradiography.
Gastroenterology,43, 642-68.

Ritchie,J.A. (1968)Colon motor activity and bowel function. Part 1. Normal movement of contents.
Gut,9, 442-56.

Ritchie, J.A., Truelove, S.C., Ardran, G.M. et al. (1971) Propulsion and retropulsion of normal colonic contents.
Digestive Diseases,16(8), 697-704.

Rosenblum, M.J. & Cummins, A.J.(1954) The effect of sleep and of amytal on the motor activity of the human sigmoid colon.
Gastroenterology,27(4), 445-50.

Ross, B., Watson, B.W. & Kay, A.W. (1963) Studies on the effect of vagotomy on small intestinal motility using the radiotelemetry capsule.
Gut,4, 77-81.

Rosswick, R.P., Stedeford, R.D. & Brooke, B.N. (1967) New methods of studying intestinal transit times.
Gut,8, 195-96.

Smith, A.N., Shepherd, J. & Eastwood, M.A. (1981) Pressure changes after balloon distention of the colon wall in diverticular disease.
Gut,21, 841-44.

Snape, W.J.Jr., Wright,S.H., Battle, W.M. et al. (1979) The gastrocolic response: evidence for a neural mechanism.
Gastroenterology, 77, 1235-40.

Spriggs, E.A., Code, C.F., Bargen, J.A. et al (1951) Motility of the pelvic colon and rectum of normal persons and patients with ulcerative colitis.
Gastroenterology,19, 480.

Thompson,D.G., Laidlow, J.M. & Wingate,D.L. (1979) Abnormal small bowel motility demonstrated by radiotelemetry in a patient with irritable colon.
Lancet,2, 1321-23.

Thompson, D.G., Wingate, D.L., Archer, L. et al. (1980) Normal patterns of human upper small bowel motor activity recorded by prolonged radiotelemetry. Gut,21, 500-06.

Thornton, J.R. (1981) Are fibre supplements really necessary in diverticular disease of the colon. British Medical Journal,282, 1546.

Trotman, I.F. & Misiewicz, J.J. (1988) Sigmoid motility in diverticular disease and the irritable bowel syndrome. Gut,29, 218-22.

Waller, S.L. (1975) Differential measurement of small and large bowel transit times in constipation and diarrhoea: A new approach. Gut,16, 372-78.

Watters, D.A.K., Smith,A.N., Eastwood,M.A. et al. (1985) Mechanical properties of the colon: comparison of the features of the African and European colon in vitro. Gut,26, 384-92.

Weinreich, J. & Andersen, D. (1976a) Intraluminal pressure in the sigmoid colon. 1 Method and results in normal subjects. Scandinavian Journal of Gastroenterology,11, 577-80.

Weinreich, J. & Andersen, D. (1976b) Intraluminal pressure in the sigmoid colon. II Patients with sigmoid diverticula and related conditions.
Scandinavian Journal of Gastroenterology,11, 581-86.

Whiteway, J.& Morson, B.C. (1985) Elastosis in diverticular disease of the sigmoid colon.
Gut,26, 258-66.

Williams, I. (1963) Changing emphasis in diverticular disease of the colon.
British Journal of Radiology,36, 393-406.

Williams, I. (1965) The resemblence of diverticular disease of the colon to a myostatic contracture.
British Journal of Radiology,38, 437-43.

Wingate, D.L. (1983) Methodology of Motility. In:A Guide to Gastrointestinal Motility (eds. Christensen, J. & Wingate, D.L.) Chapter 8, pp215-220. Bristol, Wright.

Wolff, H.S. (1961) The radiopill.
New Scientist,261, 419-21.

8: APPENDICES

8: APPENDICES

Appendix 1.

The effect of ispaghula husk on intestinal transit times.

(a) Mouth to anus transit times (hours)

Pre-treatment	Post-treatment
23.4	34.6
39.3	34.1
58.8	31.5
40.9	31.0
34.4	18.8
68.6	35.3
57.2	35.1
33.3	35.9
48.8	33.5
33.8	22.0
18.5	26.0
23.3	22.3

(b) Mouth to rectum transit times (hours)

Pre-treatment	Post-treatment
23.0	32.8
34.1	33.9
55.3	18.8
37.4	27.3
15.4	13.6
67.2	25.0
57.0	35.0
29.6	22.2
47.9	17.1
33.7	22.0
9.3	25.8
23.3	22.3

(c) Right colonic transit times (hours)

Pre-treatment	Post-treatment
6.3	8.5
19.0	15.3
38.8	0.5
21.0	13.4
4.6	3.0
35.6	7.5
36.5	13.6
13.8	11.7
26.0	2.3
15.4	9.2
1.1	10.5
1.4	2.8

(d) Left colonic transit times (hours)

Pre-treatment	Post-treatment
8.8	16.3
7.8	10.7
10.8	10.3
8.4	5.8
2.8	2.7
24.0	9.5
12.5	13.4
7.8	2.5
13.9	6.8
10.3	4.8
2.3	7.3
13.9	11.6

Appendix 2.

The effect of ispaghula husk on right and left colonic motility.

(a) Right colonic motility indices

Pre-treatment	Post-treatment
93	528
324	682
135	861
207	157
630	282
152	433
73	210
117	650
241	865
473	126
440	364
537	1016

(b) Right colonic percentage activity

Pre-treatment	Post-treatment
7	13
10	19
4	37
5	22
17	20
20	24
4	14
6	11
14	23
14	12
9	8
14	30

(c) Right colonic peaks > 5mmHg/hour

Pre-treatment	Post-treatment
85.6	128.8
43.5	105.6
22.2	166.0
35.4	72.8
89.3	78.0
26.0	132.4
41.9	77.5
56.5	86.0
66.4	132.0
119.3	105.6
18.2	75.2
107.1	188.3

(d) Right colonic peaks >50mmHg/hour

Pre-treatment	Post-treatment
0.4	1.0
0.9	1.1
1.4	12.0
2.6	2.0
0.6	0.0
0.6	2.6
0.9	3.3
4.1	8.4
0.1	6.0
0.9	1.3
10.0	3.0
1.4	6.7

(e) Left colonic motility indices

Pre-treatment	Post-treatment
249	667
382	570
1572	1036
524	726
1014	350
744	1013
136	434
830	1520
709	1132
305	685
368	267
960	1266

(f) Left colonic percentage activity

Pre-treatment	Post-treatment
14	16
10	14
29	31
4	24
19	20
37	31
11	17
24	27
22	26
8	30
12	4
19	38

(g) Left colonic peaks >5mmHg/hour

Pre-treatment	Post-treatment
108.0	82.9
56.4	51.7
59.2	92.8
31.0	79.3
95.7	98.5
61.1	122.6
42.2	54.3
136.6	151.2
92.0	146.1
45.4	124.5
21.3	29.2
152.6	105.4

(h) Left colonic peaks >50mmHg/hour

Pre-treatment	Post-treatment
1.0	1.1
0.3	2.1
27.3	24.3
4.6	14.9
13.2	4.1
11.5	24.4
0.6	7.5
21.9	19.6
14.0	7.3
0.6	4.2
7.4	4.5
10.9	24.7

Appendix 3.

Intestinal transit times and the radiological classification of disease severity.

(a) Mouth to anus transit times (hours)

CONTROL	MILD	MODERATE	SEVERE
40.5	31.0	35.1	81.2
21.5	18.8	34.6	42.0
22.5	56.5	35.2	31.5
87.8	40.0	18.9	32.0
92.0	44.7	41.2	34.1
34.7	62.2	33.5	35.9
35.4	82.7	44.7	43.2
33.4	22.0	54.0	65.3
		36.7	16.4
		26.0	46.0

(b) Mouth to rectum transit times (hours)

CONTROL	MILD	MODERATE	SEVERE
34.0	27.2	35.0	81.0
21.4	13.6	32.8	41.3
20.0	44.5	25.0	18.8
58.4	35.0	15.5	31.0
91.5	34.6	32.3	33.9
34.7	59.4	17.1	22.2
32.3	81.2	36.8	43.0
33.0	22.0	53.7	34.5
		19.0	16.2
		25.8	34.8

(c) Right colonic transit times (hours)

CONTROL	MILD	MODERATE	SEVERE
11.4	13.4	13.6	60.6
1.3	2.9	8.5	2.8
2.8	13.2	7.5	0.5
15.0	15.0	4.6	13.6
21.2	9.7	12.0	15.4
1.8	10.2	2.3	11.7
12.5	58.6	12.3	11.6
14.1	9.2	25.1	10.4
		4.9	5.5
		10.5	3.6

(d) Left colonic transit times (hours)

CONTROL	MILD	MODERATE	SEVERE
14.6	5.8	13.4	12.4
12.2	2.7	16.2	30.5
9.2	23.2	9.5	10.2
35.4	12.0	2.9	9.4
62.3	16.6	12.3	10.7
24.9	41.2	6.8	2.5
11.5	14.7	16.4	23.5
10.9	4.8	20.6	16.1
		6.1	2.8
		7.2	23.2

Appendix 4.

Intestinal transit times and the symptomatic classification of disease severity.

(a) Mouth to anus transit times (hours)

CONTROL	MILD	MODERATE	SEVERE
40.5	35.1	31.0	18.8
21.5	34.6	56.5	18.9
22.5	35.2	42.0	62.2
87.8	81.2	44.7	35.9
92.0	41.2	44.7	43.2
34.7	40.0	22.0	
35.4	16.4	26.0	
33.4	46.0		
	31.5		
	33.5		
	82.7		
	32.0		
	54.0		
	36.7		
	34.1		
	65.3		

(b) Mouth to rectum transit times (hours)

CONTROL	MILD	MODERATE	SEVERE
34.0	35.0	27.2	13.6
21.4	32.8	44.5	15.5
20.0	25.0	41.3	59.4
58.4	81.0	34.6	22.2
91.5	32.3	36.8	43.0
34.7	35.0	22.0	
32.3	16.2	25.8	
33.0	34.8		
	18.8		
	17.1		
	81.2		
	31.0		
	53.7		
	19.0		
	33.9		
	34.5		

(c) Right colonic transit times (hours)

CONTROL	MILD	MODERATE	SEVERE
11.4	13.6	13.4	2.9
1.3	8.5	13.2	4.6
2.8	7.5	2.8	10.2
15.0	60.6	9.7	11.7
21.2	12.0	12.3	11.6
1.8	15.0	9.2	
12.5	5.5	10.5	
14.1	3.6		
	0.5		
	2.3		
	58.6		
	13.6		
	25.1		
	4.9		
	15.4		
	10.4		

(d) Left colonic transit times (hours)

CONTROL	MILD	MODERATE	SEVERE
14.6	13.4	5.8	2.7
12.2	16.2	23.2	2.9
9.2	9.5	30.5	41.2
35.4	12.4	16.6	2.5
62.3	12.3	16.4	23.5
24.9	12.0	4.8	
11.5	2.8	7.2	
10.9	23.2		
	10.2		
	6.8		
	14.7		
	9.4		
	20.6		
	6.1		
	10.7		
	16.1		

Appendix 5.

Left colonic motility and the radiological classification of disease severity.

(a) Left colonic motility indices

CONTROL	MILD	MODERATE	SEVERE
32	726	434	355
393	350	667	1005
1266	80	1013	1036
295	323	425	431
92	227	126	570
537	243	1132	1520
434	120	119	1566
204	685	415	1009
		860	893
		267	227

(b) Left colonic percentage activity

CONTROL	MILD	MODERATE	SEVERE
4	24	17	19
21	20	16	35
25	8	31	31
13	4	10	12
7	17	7	14
21	20	26	27
8	5	3	45
5	30	19	16
		46	29
		4	10

(c) Left colonic peaks>5mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
32.5	79.0	54.3	66.2
100.3	97.7	82.5	104.4
82.2	48.1	122.6	92.2
71.4	52.1	87.6	62.5
46.7	89.0	51.9	51.7
100.2	103.0	146.2	151.2
22.0	20.5	46.9	95.8
36.1	124.5	75.0	59.2
		70.8	117.1
		29.2	55.8

(d) Left colonic peaks>50mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
0.0	15.2	7.5	0.2
3.8	4.2	1.1	25.6
17.7	0.1	24.4	24.5
1.2	13.1	1.0	2.5
1.8	1.3	1.4	2.1
2.0	0.3	7.6	19.6
16.0	0.7	10.8	19.7
0.6	4.2	5.5	14.1
		14.8	7.0
		4.5	2.7

Appendix 6.

Left colonic motility and the symptomatic classification of disease severity.

(a) Left colonic motility indices

CONTROL	MILD	MODERATE	SEVERE
32	434	726	350
393	667	80	425
1266	1013	1005	243
295	355	227	1520
92	126	119	1566
537	323	685	
434	893	267	
204	227		
	1036		
	1132		
	120		
	431		
	415		
	860		
	570		
	1009		

(b) Left colonic percentage activity

CONTROL	MILD	MODERATE	SEVERE
4	17	24	20
21	16	8	10
25	31	35	20
13	19	17	27
7	7	3	45
21	4	30	
8	29	4	
5	10		
	31		
	26		
	5		
	12		
	19		
	46		
	14		
	16		

(c) Left colonic peaks >5mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
32.5	54.3	79.0	97.7
100.3	82.5	48.1	87.6
82.2	122.6	104.4	103.0
71.4	66.2	89.0	151.2
46.7	51.9	46.9	95.8
100.2	52.1	124.5	
22.0	117.1	29.2	
36.1	55.8		
	92.2		
	146.2		
	20.5		
	62.5		
	75.0		
	70.8		
	51.7		
	59.2		

(d) Left colonic peaks >50mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
0.0	7.5	15.2	4.2
3.8	1.1	0.1	1.0
17.7	24.4	25.6	0.3
1.2	0.2	1.3	19.6
1.8	1.4	10.8	19.7
2.0	13.1	4.2	
16.0	7.0	4.5	
0.6	2.7		
	24.5		
	7.6		
	0.7		
	2.5		
	5.5		
	14.8		
	2.1		
	14.1		

Appendix 7.

Pre-Post prandial motility parameters.

(a) Pre-prandial motility indices

CONTROL	MILD	MODERATE	SEVERE
306	478	1024	1488
294	153	325	405
704	297	876	792
27	330	488	1474
564	143	110	1001
	57	540	990
	271		612
			156

(b) Post-prandial motility indices

CONTROL	MILD	MODERATE	SEVERE
282	855	1068	1177
766	273	1080	779
589	802	627	832
34	265	224	847
714	750	425	1232
	140	948	1280
	553		766
			125

(c) Pre-prandial percentage activity

CONTROL	MILD	MODERATE	SEVERE
19	18	44	53
8	15	10	21
20	6	36	18
3	27	17	32
25	12	8	34
	7	14	26
	18		19
			10

(d) Post-prandial percentage activity

CONTROL	MILD	MODERATE	SEVERE
18	17	31	41
22	16	27	34
18	13	32	23
4	24	5	16
26	45	17	34
	15	24	33
	33		31
			7

(e) Pre-prandial peaks>5mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
74	50	81	120
65	96	74	106
122	64	134	52
42	117	70	175
128	86	88	88
	26	117	106
	96		104
			96

(f) Post-prandial peaks>5mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
111	67	146	123
87	75	146	138
112	99	129	112
34	121	35	121
135	85	111	116
	24	188	151
	126		117
			64

(g) Pre-prandial peaks>50mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
0.0	8.0	9.0	28.0
3.0	0.0	0.0	2.0
1.0	22.0	4.0	11.0
0.0	1.0	0.0	25.0
0.0	0.0	0.0	22.0
	0.0	3.0	5.0
	0.0		3.0
			0.0

(h) Post-prandial peaks>50mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
4.0	24.0	38.0	38.0
0.0	1.0	0.0	22.0
4.0	19.0	9.0	4.0
0.0	0.0	0.0	9.0
14.0	3.0	10.0	25.0
	0.0	1.0	1.0
	1.0		4.0
			0.0

(i) Percentage change in motility indices

CONTROL	MILD	MODERATE	SEVERE
-8	79	4	-21
161	78	232	92
-16	170	-28	5
26	-20	-54	-43
27	424	286	23
	146	76	29
	104		25
			-20

(j) Percentage change in percentage activity

CONTROL	MILD	MODERATE	SEVERE
-5	-6	-30	-23
175	7	170	62
-10	117	-11	28
33	-11	-71	-50
4	275	113	0
	114	71	27
	83		63
			-30

(k) Percentage change in peaks >5mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
50	34	80	3
34	-22	97	30
-8	55	-4	115
-19	3	-50	-31
5	-1	26	32
	-8	61	42
	31		13
			-33

(l) Absolute change in peaks >50mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
4	16	29	10
-3	1	0	20
3	-3	5	-7
0	-1	0	-16
14	3	10	3
	0	-2	-4
	1		1
			0

Appendix 8.

Sleep motility parameters.

(a) Sleep motility indices

CONTROL	MILD	MODERATE	SEVERE
257	61	206	381
260	95	526	1169
115	104	132	439
	230	58	446
	253	413	432
		141	220

(b) Sleep percentage activity

CONTROL	MILD	MODERATE	SEVERE
5	1	10	17
9	1	14	39
1	11	4	10
	7	1	11
	4	29	8
		2	8

(c) Sleep peaks > 5mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
26.7	14.6	29.8	52.8
46.3	13.7	56.2	93.5
18.0	66.5	37.7	33.2
	31.4	43.5	40.3
	15.3	60.4	29.0
		17.7	37.0

(d) Sleep peaks>50mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
0.3	0.0	0.8	0.0
0.0	1.2	0.7	26.2
0.0	1.8	0.8	4.6
	3.7	0.7	0.5
	1.5	6.3	3.2
		3.0	1.0

Appendix 9.

Motility parameters of the right and left colon - classification into disease groups.

(a) Right colonic motility indices

CONTROL	MILD	MODERATE	SEVERE
69	157	210	812
574	121	528	682
326	168	433	650
74	81	406	359
783	126	104	861
274		66	
218		227	
		30	
		364	

(b) Right colonic percentage activity

CONTROL	MILD	MODERATE	SEVERE
3	22	14	14
13	10	13	19
7	16	24	11
5	3	11	9
31	12	5	37
12		2	
6		23	
		5	
		8	

(c) Right colonic peaks >5mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
40.1	72.8	77.5	51.1
107.0	85.3	128.8	105.6
81.3	112.2	132.4	86.0
49.1	10.3	74.8	63.0
166.3	105.3	65.4	166.0
100.0		81.2	
55.6		76.2	
		62.3	
		75.2	

(d) Right colonic peaks >50mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
0.0	2.0	3.3	7.5
0.0	0.2	1.0	1.1
0.9	0.1	2.6	24.4
0.3	0.4	1.0	1.0
2.4	1.3	0.6	1.4
10.0		9.9	10.8
0.5		1.2	5.5
		0.0	14.8
		3.0	4.5

(e) Left colonic motility indices

CONTROL	MILD	MODERATE	SEVERE
32	726	434	431
1266	80	667	570
295	227	1013	1520
92	120	425	1009
537	685	126	1036
434		119	
204		415	
		860	
		267	

(f) Left colonic percentage activity

CONTROL	MILD	MODERATE	SEVERE
4	24	17	12
25	8	16	14
13	17	31	27
7	5	10	16
21	30	7	31
8		3	
5		19	
		46	
		4	

(g) Left colonic peaks >5mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
32.5	79.0	54.3	62.5
82.2	48.1	82.5	51.7
71.4	89.0	122.6	151.2
46.7	20.5	87.6	59.2
100.2	124.5	51.9	92.2
22.0		46.9	
36.1		75.0	
		70.8	
		29.2	

(h) Left colonic peaks >50mmHg/hour

CONTROL	MILD	MODERATE	SEVERE
0.0	15.2	7.5	2.5
17.7	0.1	1.1	2.1
1.2	1.3	24.4	19.6
1.8	0.7	1.0	14.1
2.0	4.2	1.4	24.5
16.0		10.8	
0.6		5.5	
		14.8	
		4.5	