Colonic motility: practice or research?

Disorders of colonic motility are thought to play a part in several diseases, especially the irritable bowel syndrome, and also ulcerative colitis, diverticular disease, and constipation. The genesis of abdominal pain or disordered bowel habit is generally ascribed to abnormal colonic motor function. Despite research contributions from many countries the normal and pathological motor function of the colon remains poorly understood. This is due in part to the relative inaccessibility of the organ, its regional differences in structure and function, and to the capricious nature of motor events in the large bowel. It is difficult to measure colonic function simultaneously in its various parts and it is erroneous to extrapolate findings from one part to another. Ritchie hoped that manometry would prove a 'safe and reliable method of studying colonic movements' and in 1965 Deller and Wangel expressed the view that understanding of intestinal motility may progress if pertinent problems were recognised. They pointed out that motility patterns in normal subjects needed to be described in more detail, that the relation between pressure and transit needed to be further investigated, and that the analysis and classification of pressure waves had to be standardised and quantified. Although some of these points have been considered, our understanding of colonic function has not increased much and measurements of colonic pressures have not found their way into routine clinical practice; measurements of transit have a more practical value in selected patients.

Why is it that clinical usefulness of colonic pressure measurements remains elusive? The answer is partly methodological and partly dependent on the physiology of colonic smooth muscle. Colonic motility can be conveniently considered under two related aspects, intraluminal pressure activity and transit of intraluminal contents. The second has been measured by studying the movements of barium, or radio-opaque shapes and more recently radioactive isotopes. Radio-opaque shapes are clinically the most useful for quantifying colonic transit; movement of barium involves unacceptably high doses of radiation and radioisotope studies need access to imaging equipment and the patient has to be immobilised during the scans. Formulae have been devised to measure segmental colonic transit with radio-opaque shapes. The need for repeated abdominal radiographs can be avoided by a modification of this technique and segmental transit can be measured from a single x-ray film taken after the serial ingestion of radio-opaque shapes for three days. This minimises exposure of the patient to radiation. If the stools, rather than the patient's abdomen are screened for the shapes, there is no radiation risk but this approach is inconvenient. Slow transit constipation can be distinguished from outlet obstruction by the ingestion of a capsule containing 20 shapes followed by an abdominal x-ray film taken on the fifth day; 80% retention of the markers signifies slow colonic transit. These simple methods can be used clinically to help establish a diagnosis and to measure the effect of treatment; they are also useful in research.

Colonic pressures can be measured with balloons, continuously perfused catheters, freely mobile pressure sensitive radiotelemetry capsules, or solid state tube mounted strain gauges, each measuring different aspects of colonic motor function. Most studies use water perfused catheters. Solid state transducers have the important advantage that they can be used in the ambulatory patient and are becoming readily available. Hardware and software exist for prolonged computerised collection (including the ambulant patient) and analysis of data. The positioning of the recording devices in the colonic lumen and cleansing of the bowel before pressure measurements remain non-standardised. It seems logical to study unprepared bowel in an unsedated patient, but this limits studies to the distal colon or requires invasive and time consuming intestinal transubation.

Morphology of individual colonic pressure waves has eluded reliable classification. This has led to the concept of the motility index (area under the time pressure curve) to describe pressure activity. This has the advantage of being expressed as a number and is thus amenable to statistical analysis, but it does not recognise different types of colonic pressure waves. As pressure measurements obtained from colonic probes 5 cm apart can be very different, some workers have summed the pressure activity from adjacent channels to obtain a value for the colonic segment under study as a whole in an attempt to standardise analysis.

Colonic motor function has also been investigated with electromyography, the electrodes being attached to the mucosa in the intact human. A background slow variation in electrical potential has been described (basal electrical rhythm) with superimposed shorter duration, larger amplitude potentials (spike potentials or electrical response activity). The basal electrical rhythm controls the occurrence of the electrical response activity, which is thought to correlate with colonic smooth muscle contraction.

Normal motility of the small intestine in the fasting state is characterised by the cyclical appearance of the migrating motor complex. This is a high amplitude burst of contractions that start in the stomach and are propagated distally into the lower small bowel. After eating, this regular coordinated activity gives way to irregular, non-propagated pressure
activity (phase II), or periods of quiescence (phase I). Unfortunately in the colon the situation is far less clear. Instead of orderly motility patterns, which can be analysed relatively easily, irregular contractions occur that are apparently randomly distributed in location and time. Low amplitude segmenting contractions coexist with contractions of higher amplitude that can be present simultaneously at points up to 10 cm apart, but do not propagate proximally or distally. This type of segmenting pressure activity does not propel intraluminal contents over large distances and is probably responsible for the mixing of bowel contents. High amplitude (100 and 200 mm Hg) contractions, travelling distally over distances of at least 24 cm have also been recorded. These are termed high amplitude propagated contractions, or giant migrating contractions and differ greatly from the segmenting pressure activity that normally predominates. The high amplitude contractions travel over relatively long segments of the colon and appear consecutively in the more distal bowel, suggesting that this activity is coordinated and propulsive. These contractions occur infrequently, between four and five times a day,6 so that their recognition needs prolonged periods of intraluminal monitoring. Alternatively, they can be stimulated with contact laxatives such as dulcolax. They are thought to represent the manometric equivalent of colonic mass movements that were first described by radiologists at the turn of the century.6

The relation between segmenting or propagating pressure activity and transit can be investigated by simultaneously measuring intraluminal pressures and transit of intraluminal radioiodine markers with a gamma camera. The isotope most commonly used for measurement of colonic transit is 99mTc-DTPA in liquid form,9 or it may also be incorporated into ispaghula husk to simulate the physical properties of faeces more closely.9 In normal subjects in the fasted state segmenting pressure activity is low and little transit of marker is seen. After a meal segmenting pressure activity increases and antegrade and retrograde transit of marker occurs in association with this activity. Movement in these circumstances is over short distances and occurs down a pressure gradient. Giant migrating contractions are associated with transit of marker over larger distances in a distal direction.10 Insight into abnormalities of transit and pressure activity in constipation or diarrhoea has been obtained with these techniques. In functional diarrhoea there is more to and fro movement of intraluminal contents in the fasting state than in normal controls. After eating, although intraluminal pressure does not increase appreciably, the number of high amplitude propagating contractions is reduced and in patients with chronic constipation fasting transit of marker was not recorded. Moreover, there was no postprandial increase in segmenting colonic pressure activity, no propagating contractions, and no postprandial transit of marker.12 Patients with idiopathic chronic constipation have a decreased number and duration of giant migrating complexes than healthy controls.13 Measurements of colonic pressures are confounded by pronounced intra and interindividual variation of colonic motility indices14 depending on factors that are obscure and thus difficult to control. They probably include the nature of the intraluminal contents, the emotional and metabolic state of the patient, and the location of the recording devices. This situation makes it difficult to use basal colonic motility as a basis for comparisons and has led to the development of provocation tests in a controlled environment in an attempt to characterise differences between groups of patients. Appreciable variations between subjects, combined with the small numbers investigated in these invasive and time consuming studies, compound the difficulties of showing statistically significant differences and establishing a normal range of values.

Awakening stimulates colonic pressures, showing a link between the central nervous system and the bowel.12 Apart from awakening, the most powerful and reproducible physiological stimulus to segmenting colonic activity is a meal. The meal needs to contain 1000 kCal or more and have a relatively high fat content (>40%).16 High amino acid content in the meal abolishes the colonic response.17 It is not abolished by gastrectomy,18 is related to the entry of food into the upper small bowel,12 and has a neural component.17 A cephalic phase of this response has recently been described in normal subjects19 and in the irritable bowel syndrome,20 again emphasising the link between the ‘big brain’ (central nervous system) and the ‘little brain’ (myenteric and submucous plexuses) in the gut. Unfortunately the colonic response to a meal is not consistent even in normal subjects and its absence does not point to a specific lesion in the nervous system-colon axis. For example, it is absent in such diverse conditions as constipation,21 diabetes,22 multiple sclerosis,23 and thoracic spinal cord injuries.24 Experiments on the effects of various gastrointestinal polypeptide hormones and drugs on colonic motility have sought further clarification of normal motility patterns or effective treatments for motility disorders. Many hormones have been implicated in the colonic response to food, including cholecystokinin, gastrin, motilin, neurotensin, pancreatic polypeptide, and polypeptide Y. Cholecystokinin increases rectosigmoid segmenting pressure activity when administered exogenously, and the response can be reproduced by the administration of intraduodenal nutrients known to cause release of cholecystokinin.25 Motilin, administered exogenously at physiological doses, also increases the distal colonic motility index26 but these results were not confirmed with the motilin agonist erythromycin, which had no effect on segmenting sigmoid pressure activity or colonic transit.27 It is known that intravenous pentagastrin decreases rectal postprandial pressures28 when it is administered in the cephalic phase of this response has recently been described in normal subjects29 and in the irritable bowel syndrome,30 again emphasising the link between the ‘big brain’ (central nervous system) and the ‘little brain’ (myenteric and submucous plexuses) in the gut. Unfortunately the colonic response to a meal is not consistent even in normal subjects and its absence does not point to a specific lesion in the nervous system-colon axis. For example, it is absent in such diverse conditions as constipation,31 diabetes,32 multiple sclerosis,33 and thoracic spinal cord injuries.34 Experiments on the effects of various gastrointestinal polypeptide hormones and drugs on colonic motility have sought further clarification of normal motility patterns or effective treatments for motility disorders. Many hormones have been implicated in the colonic response to food, including cholecystokinin, gastrin, motilin, neurotensin, pancreatic polypeptide, and polypeptide Y. Cholecystokinin increases rectosigmoid segmenting pressure activity when administered exogenously, and the response can be reproduced by the administration of intraduodenal nutrients known to cause release of cholecystokinin.30 Motilin, administered exogenously at physiological doses, also increases the distal colonic motility index31 but these results were not confirmed with the motilin agonist erythromycin, which had no effect on segmenting sigmoid pressure activity or colonic transit.32 It is known that intravenous pentagastrin decreases rectal postprandial pressures33 when it is administered in the cephalic phase of this response has recently been described in normal subjects34 and in the irritable bowel syndrome,35 again emphasising the link between the ‘big brain’ (central nervous system) and the ‘little brain’ (myenteric and submucous plexuses) in the gut. Unfortunately the colonic response to a meal is not consistent even in normal subjects and its absence does not point to a specific lesion in the nervous system-colon axis. For example, it is absent in such diverse conditions as constipation,36 diabetes,37 multiple sclerosis,38 and thoracic spinal cord injuries.39 Experiments on the effects of various gastrointestinal polypeptide hormones and drugs on colonic motility have sought further clarification of normal motility patterns or effective treatments for motility disorders. Many hormones have been implicated in the colonic response to food, including cholecystokinin, gastrin, motilin, neurotensin, pancreatic polypeptide, and polypeptide Y. Cholecystokinin increases rectosigmoid segmenting pressure activity when administered exogenously, and the response can be reproduced by the administration of intraduodenal nutrients known to cause release of cholecystokinin.40
when given intravenously at doses of 2.5 to 10 mg (Amin Z, Misiewicz JJ, personal communication).

In line with these uncertainties measurements of colonic pressures in the irritable bowel syndrome produce contradictory data and no common underlying abnormality has been defined. Several years ago there was much interest in the finding of an apparently abnormal basal electrical rhythm in irritable bowel syndrome. In normal subjects there are two components to the basal electrical rhythm, a predominant rhythm at a frequency of 6 cycles per minute with some at 3 cycles per minute. In irritable bowel syndrome the 3 cycles per minute component was increased 45 but further work has not confirmed these findings. 46 Consistent differences in segmenting or propagating colonic pressures have not been identified between normal subjects and patients with irritable bowel syndrome. Responses to eating are variable, some but not all investigators reporting an exaggerated response. 44 45 These inconsistencies may be in part due to the heterogeneous nature of patients who are diagnosed as suffering from irritable bowel syndrome. Grouping patients according to gross, fairly imprecise symptoms such as predominant diarrhoea or constipation, is perhaps unlikely to uncover a common pathological abnormality. Classification of functional gut disorders is proliferating at present, 39 40 but there is much overlap of various functional symptom clusters and labelling these does not necessarily prove a common cause and may lend a false validity to the diagnosis.

Even when abnormalities of colonic motor function are identified, it is not clear whether they are responsible for the symptoms. This question is unlikely to be resolved in the non-ambulatory laboratory setting, with short recording periods. Indeed, it is reasonable to ask the question whether irritable bowel syndrome is a disease of the motor side of bowel motility at all; there is evidence that in some patients the abnormality is one of visceral sensation. Patients with irritable bowel syndrome experience pain induced by inflating a balloon in the colon at different and more numerous sites and at lower distending volumes than normal subjects. 34 35 That the decreased pain threshold is not a generalised feature in patients with irritable bowel syndrome was shown by Whitehead et al who confirmed the decreased tolerance to balloon distention but showed that their tolerance for hand immersion in ice cold water was not different from normal controls. 46 These differences between somatic and visceral pain thresholds were confirmed by others who showed that patients with irritable bowel syndrome and Crohn's disease had higher thresholds than normal controls for somatic pain. 47

These changes in perception of distension at the lower end of the gut seem to be mirrored in the stomach. Mearin et al have shown increased sensitivity to balloon distention of the stomach in patients with dyspepsia but without ulcers and the pain perception/distending volume relation in the stomach of such patients and in the rectum of patients with irritable bowel syndrome show a striking similarity. 36

The situation with respect to pressure changes and pain may be clarified by prolonged ambulatory measurements of colonic pressure activity, which allow the simultaneous recording of events such as abdominal pain and motor changes. This has been reported for clustered small intestinal contractions identified in patients with irritable bowel syndrome, 37 which seem to coincide with pain. 38 Indeed, it has been claimed that irritable bowel syndrome is primarily a small intestinal condition and that symptoms originate mainly from this site. Simultaneous records from the colon, however, have not yet been made, so that what happens to colonic pressures at the time clustered contractions are present in the small bowel is not known. It is possible that many patients with irritable bowel syndrome have a pancreatic motor disorder, and that extra-alimentary sites innervated by the autonomic nervous system, such as the bladder, are involved. 39 40

Areas of uncertainty extend to other conditions. Colonic diverticular disease is thought to occur in response to a combination of colonic wall weakness and high intraluminal pressures. Support for this hypothesis consists of high pressures recorded in the basal and postprandial period, and after prostigmine, but some investigators have challenged these findings. 41 42

There has recently been a revival of interest in changes in colonic motility in ulcerative colitis. Early studies showed decreased segmenting contractile pressure activity in this disease 43 with absence of the normal postprandial pressure response although the normal postprandial increase in myoelectric spike activity was retained, 44 suggesting some sort of electromechanical dissociation. These findings are consistent with decreased transit in the proximal and rapid transit through the sigmoid colon in patients with active colitis. 45 Studies with an animal model of colitis confirmed the decreased segmenting contractile activity and showed increased giant migrating complexes, which were often associated with defecation. 46 47

Thus research into colonic motor function remains a challenging and potentially rewarding area where progress has been facilitated by recent technological advances. More precise knowledge of control of colonic motor tone, coupled with basic research into the pathways that control colonic muscle, should eventually result in the development of drugs for modifying colonic motor function.

At present the use of colonic motility tests in clinical practice is limited and will remain so until normal ranges for colonic pressures can be defined and more effective treatments for the various motility disorders identified. In patients disabled by severe dysmotility syndromes, however, they sometimes provide the only objective evidence of abnormality. This can be useful in the management of persons driven to distraction by the relentlessly normal results of all conventional tests in the face of severe abdominal symptoms.

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