Intestinal motility and the irritable bowel

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Introduction

The second edition of Best and Taylor's textbook, *The Physiological Basis of Medical Practice*, was published in 1939 and can be taken as an example of the extent of knowledge about intestinal motility immediately preceding World War II. In this edition, a large amount of space was dedicated to discussion of the movements of the stomach, much less to the small intestine, and only a few relatively brief paragraphs to the colon. Segmenting activity and peristalsis were described. The gradient of activity throughout the intestine was noted. Cannon's descriptions of what we now call the interdigestive myenteric complex were presented. Knowledge of colonic motility was virtually nonexistent and based on inadequate data obtained from X-rays. In common with other texts of the time, the colon was described as presenting a picture of 'still life' (Barclay, 1935), interrupted only by the infrequent but climactic mass movements originally described by Holtznecht (1909). These movements were called the 'gastro-colic reflex'.

Elsewhere, conditions believed to result from disordered motility of the alimentary tract were clearly and well described, but almost entirely on the basis of clinical features with only minimal clarification from X-ray studies. Occasionally speculations about aetiology exist. Sir Arthur Hurst (1919) quoted Cherkewsky of St Petersburg in reference to spastic colon, 'the complaint does not so much consist in a defective power of contraction in the whole extent, as in a deficient freedom of relaxation in some part of the intestinal canal'. In fact, there had been little advance in knowledge over the previous century as a similar suggestion had been made in 1830 (Howship, 1830).

Diagnostic tools were limited in use. Hurst (1922) bemoans the fact that as late as 1922, the sigmoidoscope was rarely employed except by surgeons, especially those interested in diseases of the rectum. Contrast this with Sir Francis Avery Jones' instructions to his house staff and others that gastroenterolo-

gists should carry a sigmoidoscope in their pocket the way other persons carry a pen.

Research in the mid twentieth century focused largely on a small number of life-threatening conditions such as stroke, myocardial disease, and cancer. The amount or proportion of funds available for more common but less threatening syndromes, such as those associated with disorders of intestinal motility, has been much less. Sir Francis Avery Jones, however, was concerned not only with life-threatening disorders but perhaps even more so with those that impaired the quality of living. Progress in understanding the nature of some of the common clinical conditions in gastroenterology owes much to his initiatives in the 50s and 60s. Admittedly, in some areas, we seem to have progressed but little. For example, the nature and cause of many of the symptoms of bloating continues to elude us in spite of fascinating studies about the origin and elimination of intestinal gas (Levitt, 1983). For the most part, these disorders are still best described as 'burbulence'* (Avery Jones, 1967).

Advances in knowledge of intestinal motility

In other areas, however, considerable progress has been made. Knowledge of the movements of the small and large intestine and of their electrical analogues has greatly expanded. Recording of intraluminal pressures, pressure/volume relationships within the gut, the detection and analysis of electrical potentials from the gut, both *in vitro* and *in vivo*, has added to direct visualization and radiology of the gut and greatly enhanced our understanding of the physiology of alimentary movement. The intrinsic and extrinsic control mechanisms of gastrointestinal motility, the interaction of neural and humoral mechanisms and their coordination in local and

* How do I feel today? I feel as unfit as an unfiddle. And it is the result of a certain turbulence in my mind and an uncertain burbulence in the middle.—Ogden Nash (1964), *Marriage Lines* J.M. Dent, London. p. 64.

distant neuro-humoral responses have provided finer insights into the overall coordination of alimentary motility.

The recording of intraluminal pressures using open-ended tubes and small and large balloons, has resulted in a considerable body of knowledge, particularly of the oesophagus, the gastroduodenal area, and the distal colon. Knowledge of small intestinal motility in animals is fairly well advanced. Human small intestinal motility is less well studied but the existence of interdigestive complexes at all levels of the small intestine has been confirmed. However, marked inter- and intra-individual variations exist (Kerlin and Phillips, 1982). The right side of colon has had only limited exploration, probed by forays into inner space by radio telemetering capsules (Misiewicz, Connell and Pontes, 1966) or determined penetrations by peroral intubation (Fink and Friedman, 1960; Kerlin, Zinsmeister and Phillips, 1983).

Similarly, studies of the electrical activity of the alimentary tract have been pursued with vigour in animals and in isolated muscle preparations and significant understanding has been obtained of the electrical control activity (ECA) and its coordination at most areas of the alimentary tract. Recordings from man, however, have produced less clear results possibly due to differences in recording techniques and different methods of analysis of the complex analogues obtained. Variation among observers seems to be the rule. This is particularly true of recordings from the colon in man. Some earlier studies seemed to indicate that in the human subject two distinct frequencies of electrical control activity occurred, one at approximately three per minute and one at approximately six per minute (Snape, Carlson and Cohen, 1976; Taylor, Darby and Hammond, 1978). Both studies suggested that electrical control activity was present only part of the total recording time. However, it appears that colonic ECA is much more complex. Not only is it always present, but analysis of analogues shows it is highly irregular in frequency and amplitude. No one frequency is dominant (Latimer *et al.*, 1981; Sarna *et al.*, 1982). A number of studies have attempted to show changes in electrical control activity and other aspects of the electrical responses of the colon in patients with irritable colon or constipation (Sullivan, Cohen and Snape, 1978; Friere *et al.*, 1983). No clear picture, however, has yet emerged from these studies. However, a study of the effects of eating and stress with a careful experimental plan and analysis of recordings has shown that the frequency spectrum and the organization of the electrical control activity is not significantly different between normals and IBS patients in the resting state. Some changes from normal may occur in IBS patients under stress (Sarna *et al.*, 1982).

In the thirties and forties, lack of knowledge of the physiological basis of disordered motility resulted in much ineffective or ill-advised therapy. For example, in the belief that diarrhoeal conditions resulted from excessive motor activity of the alimentary tract, belladonna, an antispasmodic, was frequently used in treatment. In 1962, the use of the expression 'paradoxical motility' (Connell, 1962) highlighted the observation that diarrhoeal conditions were frequently associated with the absence of segmenting contractions of the colon whereas excessive contraction was often associated with slow transit and constipation. Belatedly, Howship's observation (1830) was substantiated experimentally as multi-channel recorders churned out the convincing motility analogues. Therapy can thus be more rationally assessed as the known pharmacological effects of drugs on intestinal motility are matched with the physiological variants underlying clinical symptoms.

Irritable bowel

Irritable bowel, so familiar to gastroenterologists, is a name given to a symptom complex associated with the passage of scybala with straining, possibly with excess mucus, abdominal cramping, bloating, distension, and sometimes intermittent diarrhoea. Combinations of these, but without radiological, biochemical or bacteriological abnormality, are syndromes only too well known to all physicians. We are now aware that many of those individuals have fairly well-defined abnormalities. Recognition that some had small intestinal disaccharidase deficiencies permitted the separation of this aetiological group. Others in older age groups are known to be chronic laxative users who may have neurological disturbances in the colon. Whether these disturbances are primary or secondary to the laxative usage remains unsettled. Other individuals have chronic infections, while yet others with so-called post-dysenteric irritable colon have no recognizable active infection but are known to have had one in the past. With the passage of time, the type and nature of the pathogens has changed and in the United States organisms such as shigella or salmonella are being replaced in frequency by campylobacter, chlamydia and giardia.

a. Post-prandial syndromes

A group of patients commonly seen at Central Middlesex Hospital were those with irritable colon-type symptoms made worse after eating. Such patients were shown to have exaggerated sigmoid motility after meals (Connell, Avery Jones and Rowlands, 1965). This increased segmentation could be presumed to result in inhibition of the passage of flatus or faeces with resulting distension and discomfort felt often in the mid-abdomen (Fig. 1). Some-

times the discomfort was referred to the upper left quadrant or even to the lower thorax, sometimes referred to as 'wind around the heart' (Avery Jones, 1967). On occasion, such patients were badly treated because of failure to recognize the mechanisms. Surgery, always unsuccessful, was sometimes attempted. The recognition of this syndrome not only led to some understanding of the mechanics of its causation but also prompted a quest for underlying altered physiological mechanisms.

FIG. 1. Segmental hypermotility of the sigmoid causes distension proximally: a possible explanation of upper abdominal discomfort in irritable bowel syndrome. (Reproduced from *Handbook of Physiology*, Section 6, Volume IV, 2086, 1968, by permission of Williams and Wilkins, Baltimore.)

Existing literature from animal studies had indicated that gastrocolonic segmenting responses could occur after the interruption of all known neural connections. In man, gastrocolonic responses were shown to occur after vagotomy (Connell and McKelvey, 1970), after transection of the spinal cord, or even after destruction of the lumbo-sacral cord (Connell, Frankel and Guttmann, 1963) elevating the possibility that a humoral effector existed. Gastrin was the first candidate hormone and high doses of gastrin result in increased colonic segmenting activity; however, it is unlikely that gastrin by itself is the normal mediator of this response. The finding that

the response could occur in patients with total gastrectomy established that it did not require the presence of stomach acid or antral gastrin, and that possibly a hormone from the upper small intestine was a factor (Holdstock and Misiewicz, 1970). Cholecystokinin, administered intravenously (Dinoso *et al.*, 1973), or released indirectly (Harvey and Read, 1973), results in an increase in distal colonic motility of a magnitude similar to that of eating. Cholecystokinin appears a potential candidate although the exact nature of the response and the importance of neural connections in the intact person remains unclear.

Following eating, a large number of neuro-humoral responses occur, some stimulatory, some inhibitory, and the exact nature and extent of the colonic response will depend on the resultant of these. It is likely, therefore, that different foodstuffs elicit different responses. Thus, a recent study indicates that fatty acids increase spike activity of the colon whereas amino acids decrease it although this result awaits confirmation (Levinson *et al.*, 1983). A meal which stimulates release of a large amount of cholecystokinin, a motor active hormone for the distal colon, could be expected to have a different effect from a meal which stimulates a large amount of glucagon, an inhibitory hormone. Future research should look more specifically at the motility responses elicited by the various materials in food. If a more precise knowledge of the effects of different nutrients on intestinal motility can be obtained, it should be possible to tailor therapeutic advice for the individual with a functional disorder in order to control symptoms better.

Nor have the Holtznecht 'mass movements' been overlooked. Propulsive activity has also been shown to occur in the human colon after eating. Interestingly, however, such propulsive activity rarely occurs in the resting patient but is prominent in physically active subjects (Holdstock *et al.*, 1970). The fact that somatic activity is an important factor in the control of colonic transit in health and disease seems to have been strangely overlooked in the current climate of enthusiasm for 'wellness'. This observation is well worth further exploration.

b. Relationship to emotion

Patients with irritable colon are assumed to have exaggerated responses to cholinergic stimuli but the motility data are conflicting. Early data suggested on the one hand that the colon in patients with irritable bowel responded in an exaggerated way to cholinergic stimuli particularly when symptoms were present (Chaudhary and Truelove, 1961). However this is not a universal finding (Parks and Connell, 1972). Any relationship between the colonic response to cholin-

ergic stimuli and the effects of stress or emotion on the colon has not been defined and is probably distant. However, the overall weight of the evidence is that, at certain times, certain individuals show an exaggerated motility response to emotion (Almy and Tulin, 1947). An interesting feature is that approximately the same percentage (between 25% and 33%) of normal individuals, persons with irritable colon, and patients with ulcerative colitis show an exaggerated colonic response to emotion (Chaudhary and Truelove, 1961). Altered small bowel motility probably also results from prolonged stress (McRae *et al.*, 1982). Interestingly there are no differences in responses to emotion of patients with irritable colon compared with individuals who are psychoneurotic but without bowel symptoms (Latimer *et al.*, 1981). Similarly in response to both physical and mental stress, pulse rate and blood pressure may show exaggerated rises in about one quarter of individuals tested. More precise documentation of both the strength and nature of the stressful stimuli as well as the intestinal or other somatic responses which result will be necessary before these observations can be sufficiently refined to be helpful clinically.

c. Sensitivity of colon

One distinction between patients with irritable colon and normals is believed to be in the tonic response to distention of the colon or small intestine. Most persons with irritable colon complain of discomfort or pain with distending volumes which in normal persons are well tolerated or not perceived at all (Ritchie, 1973; Whitehead, Engel and Schuster, 1980). Here again, contradictory results exist and another careful study of patients with irritable bowel was unable to determine colonic hyperalgesia (Latimer *et al.*, 1979). However many clinicians believe that the tender left colon palpated on examination and the more than usual discomfort experienced by many patients on sigmoidoscopy are characteristic of the syndrome.

d. Relationship to normal populations

While a great deal has been learned about the physiology of the motor activity of the colon and to a lesser extent of the small intestine, the amount of this information which has been transferable to clinical practice remains disappointingly small. This leads to some reflection on the nature of so called functional gastrointestinal disorders.

Two studies are instructive in demonstrating the wide range of variability in abdominal symptomatology which exists in healthy populations. In apparently healthy British individuals, one-fifth of the population studied had experienced abdominal pain more than six times in the previous year. Those

interviewed were naval technicians, nurses, individuals being screened for coronary disease, hospital clerical staff, and an elderly retired population. Although these persons were not complaining of any disturbance of the abdomen or of bowel habit, more than 13% could have been regarded as patients with an irritable colon had they presented complaining of symptoms (Thompson and Heaton, 1980). Another study involving a sampling of medical and graduate students and employees of the North Carolina Memorial Hospital, came up with very similar results. One-fourth reported abdominal discomfort more than six times a year and 25% reported alternating bowel dysfunction at least 25% of the time (Drossman *et al.*, 1982). There exists, then, a large number of people in an apparently normal population who have symptoms which might result in their being labelled as having an irritable colon. Many such persons present at physician's offices but it is evident that, fortunately, many more do not. Individuals with an altered bowel habit may not seek support either because they are phlegmatic persons, because they have been fortunate enough to avoid stressful life situations which overwhelm their tolerance levels, or because they do not have the economic means to afford support. This may explain why irritable colon is recognized mainly in more affluent communities.

Clearly the dividing line between health and disease in this area is a fine one and from time to time some individuals who have variations in bowel habit and intermittent abdominal pain choose to place themselves in the social role of being a patient. It can be assumed that this decision occurs at times of increased stress as there is ample evidence that patients who present and are labelled as having irritable colon are more anxious, depressed and neurotic than normals (Hislop, 1971; Esler and Goulston, 1973; Latimer, 1979). It can also be assumed that at times of anxiety and tension, additional stresses, such as bodily discomfort, are irritants less well tolerated, and add to the need of the patient to seek external support. There does not seem to be any distinct pattern of abnormal mobility during those periods of stress and it is more likely that the changes which occur are expressions of exaggerated physiology.

e. Therapy

These considerations have altered therapy for irritable bowel. Therapy directed to affecting the altered physiological patterns may have limited value and the use of extra dietary fibre to increase faecal bulk has had wide publicity and high level of acceptability. Fibre also alters the humoral response to eating, another way of affecting alimentary motil-

ity (Connell, McCarroll, and Chen, 1980). Controlled therapeutic trials of the use of fibre to treat IBS have been notoriously difficult to undertake and to date have been less than convincing (Soltoft *et al.*, 1976; Manning *et al.*, 1977). Other clinical trials have shown that mebeverine, hyoscine, ispaghula, lorazepam and combinations of these drugs may be helpful in relieving symptoms (Ritchie and Truelove, 1979, 1980). However, the possible unwanted effects of long-term use of these drugs should be considered. A recent study has suggested that nifedipine might be helpful (Blume, Schuster and Tucker, 1983). However, considering the reasons why individuals with altered bowel habit and abdominal discomfort present in a physician's office, treatment should be directed primarily to reassurance, psychological support, maybe with limited and temporary symptomatic relief using medications.

Sir Francis Avery Jones saw a large number of patients with irritable colon. Following his history, physical examination, and appropriate laboratory investigation, he would routinely explain to the patient the nature of the complaint. As he noted (Avery Jones, 1954), 'the doctor can do much to help the patient to get his personal difficulties in better perspective and to appreciate how the symptoms developed'. As the patient rose to leave the room, he would sometimes say, 'I am not going to lose any sleep over your condition'. This, the ultimate reassurance, rarely failed to be effective and the now smiling and relieved sufferer left to rejoin the ranks of the well.

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