

M.D. Thesis (University of London).

My M.D. Thesis was divided into two parts. The first part dealt with the technological developments concerning studies of colonic motility. This difficult area had been hampered in the past by a variety of methodological problems, some of which were solved by the new developments in the Thesis. For example, access for intubation with pressure-measuring assemblies in the unprepared descending and sigmoid colon was impossible until a technique was perfected to allow data collection under near physiological conditions. The problems posed by the laborious, time consuming and subjective nature of manual colonic pressure trace analysis was overcome by the application of computer technology. The second part of the Thesis was concerned with colonic responses to physiological stimuli in health and disease and studies which addressed the problem of the pathways that modulate colonic pressure and transit activities. These studies are described in detail below.

Research Work related to M.D. Thesis

Human colonic pressure activity in the unprepared sigmoid colon.

Methodology and techniques.

1. Development of the technique of colonic intubation of the true unprepared sigmoid colon, using fibreoptic endoscopy for the insertion of the manometric tubes. One immediate new finding generated by this technique has been the demonstration that intracolonic pressure in normals are much higher than previously described.
2. A study was done to establish which pressure variables were important in the investigation of colonic pressure activity. The results arrived at by distribution and correlative analysis of motility variables have generated a method for a quantitative description of colonic pressure activity which allows discrimination between different patient groups and precision to the description of abnormalities of colonic motility.
3. The design, development and validation of fully automated computer system for the objective analysis of colonic pressure activity has considerable implications. The release of valuable research time presently expended on labour-intensive manual analysis; complete objectivity and uniformity of analysis of serial studies; repeatability of analysis using new criteria as new ideas develop and the exchange of data between different centres, have all become possible as a result of this technique.

Normal colonic pressure activity.

1. Using the technique which allows the accurate location of pressure sensitive tubes in the descending colon and the sigmoid, I have demonstrated the existence of a high pressure zone in the normal sigmoid colon. This original observation suggests a physiological role for the sigmoid colon as a brake to colonic transit.
2. To characterise in more detail the nature of the colonic response to food experiments were done in which food and food constituents were administered in a variety of ways. The results confirmed that eating a meal has a stimulatory effect on sigmoid colonic pressure activity but the response varies according to the constituents and route of administration. This experiment also indicated a cephalic phase of the colonic response to food.
3. Using the cephalic phase of gastric acid secretion as a model I have demonstrated the existence of a cephalic phase of the colonic response to food. This original observation will now have to be taken into account in descriptions of the control pathways that affect colonic motility.
4. I have characterised the nature of the cephalic-colonic response by investigating the relationship between the cephalic phase of colonic response to food and gastric acid secretion. Analysis of the data suggests that the cephalic phase of the colonic response to food is independent of gastric acid secretion.

5. The cephalic phase of the colonic response to food has been characterise further by measuring the release of gut polypeptide hormones during cephalic stimulation. Preliminary analysis of these data suggest that there may be a relationship between hormone release and colonic motor response.
6. The investigation of the relationship between colonic pressure activity and transit in the sigmoid colon showed that in the majority of normal subjects food induced increase in pressure activity does not cause propulsion and adds to the evidence that the sigmoid colon is a brake to colonic transit.
7. Distension of the right colon influences sigmoid colonic pressure activity suggesting that there are reflex mechanisms co-ordinating the function of the colon.
8. The study of the effect of rectal distension on sigmoid colonic pressure activity gave further evidence of reflex control mechanisms co-ordinating colonic function. These last two studies point to the existence of complex integrating mechanisms modulating colonic motility in response to caecal and rectal filling with colonic contents.

Colonic pressure activity in IBS and Diverticular disease.

1. Studies of patients with IBS show that segmental pressure activity in the sigmoid colon is increased, the difference from normals being characterised by increased amplitude, and not by increased duration of pressure activity.
2. There is normal pressure activity in the sigmoid colon of patients with sigmoid diverticular disease, an interesting finding in view of the accepted views on the pathogenesis of this disease.

Research work unrelated to M.D. Thesis.

Anorectal physiology

I have done extensive experimental work in anorectal physiology. This evolved through my interest in coloproctology and particularly in the physiology of the continence mechanism.

I have established and used extensively the techniques of anal manometry, pudendal nerve electromyography, concentric needle and single muscle fibre electromyography, and mucosal electrostimulation.

The studies of anorectal physiology have been varied and have produced some interesting results. In a study of normals and patients with incontinence I was able to demonstrate that a combined sensory and motor neuropathy exists in the pelvic floor of patients with idiopathic faecal incontinence. This suggested that it was possible for decreased sensory awareness in the anal canal to contribute to the pathogenesis of faecal incontinence in addition to the accepted view of motor weakness of the sphincter muscles. In a study of diabetic subjects with peripheral neuropathy I discovered an asymptomatic sensorimotor pelvic floor neuropathy. This finding was of great interest as it suggested a possible mechanism for the development of faecal incontinence, which may occur in up to twenty percent of diabetic patients. I have also studied the risk to pelvic floor function in women undergoing hysterectomy. The results of this study showed no deficit in pelvic floor function after operation.

I also designed two studies, which assessed some aspects of the basis of anorectal physiology. The first study was designed to test the methods and techniques of anorectal physiology. The results of this study showed a high degree of repeatability for all the standard tests of anorectal motor and sensory function used in the clinical assessment of patients with anorectal disorders. In a subsequent study, the hypothesis of the importance of anorectal temperature sensation in the continence mechanism was disproved. This was done by measuring the anorectal temperature gradients between rectum and anal canal in normals and comparing the gradients with the thresholds for sensation of temperature change.

Small intestinal absorption and motility.

These experiments have been performed to investigate the effect of the formulation of enteral diets on the absorption of nutrients and small bowel motility. The first series of studies showed that intraduodenal infusion of energy dense diets converted small bowel motility from a fasting to a fed pattern and that the rate of colonic inflow did not exceed the normal absorptive capacity of the colon. These studies were performed in collaboration with Drs Ana H. Raimundo and D.B.A. Silk.

Technical innovation

I designed and developed the Synectics PC-polygram computer system for the automatic analysis of colonic pressure records. I developed a disposable pudendal nerve stimulator, and tested it under clinical conditions. I also devised and tested the oil-fill modification to the radiotelemetry capsule manometry system, enabling the capsule to record colonic pressure activity over the pressure range encountered in the unprepared colon. I also developed the computer software for a fully ambulatory computerised system of motility recording and analysis.