Progress report

Motility of the ileocolonic junction

Located between two ecologically and physiologically distinct segments of gut, the ileocolonic junction determines how intestinal contents move between the two. The region presumably contributes to gut homeostasis by optimising retention of chyme in the small intestine until digestion is largely complete; ileal contents should then be programmed to empty into the large bowel in a manner which does not compromise the colon's capacity to absorb.¹ Conversely, to safeguard the small intestine from the deleterious effects of bacterial overgrowth, reflux of colonic contents should be minimised. Certain anatomical characteristics and physiological properties which facilitate these functions have been identified. The relative contributions of a mechanical 'valve', a physiological sphincter, however, or integrated motor patterns in the distal ileum and proximal colon are still uncertain.

Mechanical barriers at the junction: the ileocaecal valve

One of the earliest descriptions, which equated the ileocolonic junction with a passive, mechanical barrier to retrograde flow, was that by Gaspard Bauhin, the Swiss anatomist.² His concept of a simple 'flap-valve' remained largely unchallenged until this century. Indeed, considerable clinical importance was attributed to competence of this valvular mechanism,^{3–5} and techniques for its surgical reconstruction were described. Based on more precise descriptions of the anatomy^{6–9} and on the early physiological studies of Elliot,¹⁰ however, a muscular sphincter was also proposed. Direct observations of the junction in man^{11–15} described a papillary protrusion into the lumen of the caecum, rather than two flat lips of a valve (Fig. 1); it seems probable that earlier interpretations of the junction as a simple slit were influenced by post mortem artifact. The papillary protrusion of the sphincter, conferred in life by active muscular action, was lost post mortem; a labial opening persisted and was probably exaggerated by fixation.^{13 14 16 17} In other species, distinct labia incorporating muscular elements were described in the dog,¹⁸ pig, cat, and monkey.¹⁹ As will be discussed later, physiological observations clearly defined a specialised segment of muscle, justifying the designation of 'ileocolonic sphincter'.

Presence of a sphincter, however, does not negate a role for a mechanical barrier. Narrow membranous ridges, or frenula, formed by the coalescence of the labia at their lateral margins, continue for a short distance around the circumference of the colon. One hypothesis was that increased intracaecal pressure stretched the frenula, causing the sphincter to become a slit, the orifice of which was progressively reduced by increasing intracaecal pressures.²⁰ Our interest in a mechanical barrier to reflux was sparked by observations that severance of external ligaments, which maintain the angle

Fig. 1 (a) Barium filling the terminal ileum and proximal colon during examination of the small intestine. Note the two finger like filling defects protruding into the lumen at the colocolic junction. These represent muscular 'lips' of the papillary eminence of the ileocolonic junction. (b) Air and barium filling the caecum during retrograde passage by enema. Note the 'duck-bill' stretching of the ileocolonic papilla.

at which the ileum and colon converge, facilitated retrograde flow from colon to ileum in human autopsy specimens.²¹ Other possible mechanisms have also been proposed. A greater density of elastic fibres has been noted at the human ileocaecal 'valve',²² and stereoradiographic techniques have shown an enlargement of the venous bed in the ileocaecal 'papilla', as a result of an increased density and size of submucosal veins. This enlarged venous bed may even operate as a 'compressible venous cushion' and facilitate closing of the ileal outlet.²³

Recent studies in our laboratory used fresh human tissue from autopsies. When a pressure head of up to 80 cm water was applied to the proximal colon, most specimens were competent, and coloileal reflux did not occur.²¹ On close inspection, two ligamentous bands were seen to maintain an acute angulation between the ileum and colon and, when these were severed, all specimens became incompetent to a retrograde head of pressure. Reconstruction of the angle by sutures restored competence.²¹ The valvular mechanism was not dependent *ex vivo* on the mucosa or the circular layer of the tunica muscularis. These findings on human autopsy tissues prompted creation of a canine model *in vivo*; simple dissection of the ileocolonic ligaments led to free reflux of colonic contents (Fig. 2) which could be documented and quantified by gammascintigraphy.²⁴ The interim conclusion is that mechanical factors opposing reflux deserve further study.

Evidence for a physiological sphincter at the ileocolonic junction

The concept of a muscular sphincter at the ileocolonic junction, although prompted initially by the demonstration of a discrete thickening of the circular muscle layer in several species,^{6-9 25} was confirmed by physiological studies. In man and dog, the junctional zone exhibited an intraluminal pressure greater than that found in the adjacent ileum or colon,^{18 26 27} and distension of the ileum reduced the raised pressure^{26 28} whereas colonic distension augmented the tone.^{26 28} Moreover, muscle from the ileocolonic sphincter (ICS) responded to nerve stimulation and pharmacological agents

Fig. 2 (a) Gamma camera scan of the canine ileocolonic junction, with the colon filled with ^{99}Tc DTPA from above. The ascending colon is outlined but there is little reflux into the ileum. (b) Gamma camera scan after division of the ileocolonic ligaments. The caecum is filled incompletely and colonic contents reflux freely into the ileum (bottom right). From reference 24, with permission.

in a manner different from that of adjacent, non-sphincteric muscle.^{29,30} These properties satisfy the usual criteria for a gastrointestinal sphincter.

IN VITRO PROPERTIES OF ICS MUSCLE

In vitro studies further support the presence of 'sphincter-type' muscle in several species. Thus, intracellular recordings from guinea pig ICS³⁰ revealed a low resting membrane potential in comparison with those of circular muscle cells from adjacent ileum or caecum. Electrotone potentials were recorded at distances up to 3 mm beyond the stimulating compartment, suggesting that ICS smooth muscle was an electrical syncytium.³⁰ In keeping with other sphincters, ICS muscle strips showed isometric tone *in vitro*,^{31,32} but in contrast with lower oesophageal muscle, the ICS exhibited spontaneous phasic contractions.³² Whereas these phasic events were closely related to spike bursts, ICS tone was spike independent.³² Alterations in tone and excitability of ICS muscle strips by agents known to influence transmembrane fluxes of calcium and potassium^{30,32} further supported the role of membrane potentials in determining the specialised muscle function of this area. Tone was oxygen dependent³¹ and persisted after tetrodotoxin,^{29,33} further evidence for a myogenic origin. Inhibition of myogenic activity with a calcium antagonist did not completely abolish tone, however, suggesting at least some contribution from elastic factors in the cat.³³ Ileocolonic sphincter muscle strips also showed a greater resistance to stretch than strips from adjacent terminal ileum and colon.^{29,33}

IDENTIFICATION OF SPHINCTER TONE IN VIVO

Single observations in patients in whom the area had been exteriorised surgically suggested the presence of sphincter which may be contracted^{11,13} or relaxed.^{12,34,35} Closure of the ICS was thought to depend on arrival of a propulsive wave from the adjacent ileum.³⁵ Animal studies also indicated a barrier to the reflux of colonic contents,³⁶ and a means whereby chyme could be retained in distal ileum.³⁷ Using modern manometry, fluctuating tone has

been directly recorded from the canine, feline, and human^{18, 38-44} ileocolonic junctions. Whether derived from acute pull through experiments in defunctioned loops,²⁷ under anaesthetic¹⁸ or during prolonged studies in conscious animals^{40, 41} recordings of tonic pressures at the canine ileocolonic junction have been remarkably uniform, 30-40 cm H₂O. At the canine ICS, the high pressure zone was centred on the anatomical sphincter¹⁸ but was, on average, 1.5 cm longer than the discrete zone of thickened smooth muscle, which measured only 0.5 cm. It appeared, therefore, that adjacent segments of distal ileum and proximal colon were also capable of generating tone.

In contrast, tone has not been identified consistently at the human ICS.^{26, 42, 43} Using the pull through technique in defunctioned bowel, Cohen and colleagues outlined a 4 cm zone of high pressure between the ileum and colon; mean pressure was 20 mm Hg.²⁶ Prolonged recordings from a catheter assembly placed at the ileocolonic junction in normal volunteers⁴² or from repeated pull throughs in patients with defunctioning loop ileostomies,⁴³ however, failed to identify a segment exhibiting consistent tone. Occasionally, tonic rises were recorded in association with bursts of phasic contractions.⁴³

Role of ileal and colonic contractions

As sphincteric tone in man is not consistently high, specialised contractile patterns in the distal ileum and proximal colon may contribute importantly to function. Certainly, ileal smooth muscle appears to possess certain special motor properties. In comparison with the proximal small intestine, the ileum contracted rather than relaxed after administration of alpha-adrenergic agonists^{44, 45} and, in the rat, was significantly less sensitive to cholinergic agonists.⁴⁶ Ileal muscle also exhibited distinctive responses to electrical stimulation.⁴⁷

Functionally, the distal ileum has unique propulsive properties; Weems showed that feline ileal segments were capable of spontaneously propelling fluid loads in an aboral direction.⁴⁸ Comparable ability to produce net fluid transport could not be shown in duodenal and jejunal segments⁴⁸ and was evident in colonic segments only when intraluminal pressures were raised.⁴⁹ Evidence to date suggests that these propulsive properties of the ileum are dependent on its neural connections, rather than being caused by the presence of specially adapted longitudinal or circular muscle. Distinctive anatomical features of the distal ileum and ileocolonic junction include a greater density of ganglia within the myenteric plexus,^{50, 51} and a relative prominence of non-adrenergic nerves in the muscularis mucosa.⁵²

Recordings of ileocolonic motility from conscious animals also imply that functional motor properties are integrated within the region. Thus, the progressive reduction of slow wave frequency^{40, 42, 53, 54} and the slowing of aboral migration of migrating myoelectric complexes⁴⁰ might be expected to retard flow of chyme, increase contact time, and promote absorption. Coordinated function is further suggested by the presence of ileal type slow waves at the feline^{55, 56} and canine⁴⁰ ICS and by participation of the sphincter in the interdigestive cycle.⁴⁰

Two specialised patterns of contraction have been recorded from the distal ileum. Prominent bursts of rhythmic phasic activity ('discrete clustered contractions' or DCC's) propagate through distal ileum, across the ICS and

into the proximal colon.^{41,42} Although resembling phase 3 'fronts' of the interdigestive cycle, they are distinct from these myoelectrically, and are more likely the ileal equivalent of 'minute rhythms' described in the proximal small bowel.⁵⁷ Phase 2 of the interdigestive cycle in the ileum thus appears to be organised more into such 'bursts' than is phase 2 in the jejunum. The other phenomenon, 'prolonged propagated contractions' (PPC's), might best be considered as a peristaltic equivalent. Pressure waves as recorded from intraluminal sensors,⁴¹ or muscular contractions as recorded by strain gauges,⁵⁸ span the duration of two or more slow waves; they are therefore 'prolonged', and appear not to be dependent upon the slow wave. The contractions propagate rapidly through the ileum and can progress into the proximal colon of man⁴² and the dog.^{41,58} Comparable contractions have been elicited in the canine jejunum,⁵⁹ although ileal musculature appears to be programmed more sensitively for this phenomenon.

Both DCC's and PPC's empty the terminal ileum (Fig. 3), and should therefore be considered as propulsive events.⁵⁸ Prolonged propagated contractions appear to correspond to high amplitude pressure waves recorded from a human ileostomy.⁶⁰ Using a tandem balloon assembly introduced through the stoma, Code identified waves which were longer in duration than the usual phasic waves in the small intestine; when present in rhythmic sequence, the terminal ileum functioned as a 'rhythmically contracting pump, which cleared the lower small bowel of its contents by expelling them distally'.⁶⁰ Similar, large amplitude, prolonged waves have been recorded from the distal ileum in patients who have undergone endorectal ileoanal anastomosis, and their occurrence coincides with emptying of the pouch and, in some patients, with leakage of stool.^{61,62}

One striking difference between the motilities of the canine and human

Canine ileum: high pressure wave and ileal effluent

Fig. 3 Strain gauge recordings from a canine ileal loop showing three prolonged propagated contractions (PPC's); distances are the position of each strain gauge, proximal to the ileocolonic junction. Each PPC induces a bolus of flow into the proximal colon (see reference 58 for details).

Fig. 4 Distribution of interdigestive cycles in the human small bowel. Most MMC's are recorded in the proximal jejunum, (J_1), few progress into the ileum (I_1 , I_4) with less than 10% reaching the ileocaecal junction (I_4). O is oesophagus, B and A body and antrum of stomach. Reproduced from reference 63, with permission.

ileum is that, in man, phase 3 of the interdigestive cycle (MMC) infrequently reaches the distal ileum. Less than 20% of jejunal MMC's reach the proximal ileum and only half of these reach the terminal ileum (Fig. 4). Ileal MMC's may pass into the colon and, although this is not unusual in the dog, it is rarely seen in man.^{42, 63} In this regard, the physiology of the pig is more like that of man; only two-thirds of porcine MMC's propagate to the distal ileum.⁶⁴

The role of motility in the caecum and proximal colon in determining antegrade and retrograde flow across the ICS has received little attention. As described above, ileal motor patterns are sometimes transmitted to the proximal colon and the human ascending colon is capable of generating high pressure waves⁶⁵ which propel contents even more distally. In these experiments, we attempted to reproduce the diarrhoea of malabsorption by perfusing the caecum with long chain fatty acids; under these conditions materials reaching the caecum were moved on rapidly. Occasionally, large caecal contractions appeared to progress back into the terminal ileum,⁶⁵ but their potential for establishing retrograde flow was not evaluated.

Another potential property of the proximal large bowel is a propensity to relax, a phenomenon which could influence the capacity of the caecum and colon to accommodate flow from the ileum. When long chain fats were again infused into the human caecum, simulating steatorrhoea, the volume of the right colon decreased.⁶⁶ Pretreatment with morphine relaxed the caecum and ascending colon, however, the proximal colon was able to accommodate larger volumes and distal transit of contents was slowed.⁶⁶

The ileocolonic region should then be considered as having properties that are determined not only by its anatomy and the function of the ICS but also by motility of the adjacent distal ileum and proximal colon. Transit may depend as much on coordinated motor patterns between these adjacent segments of bowel as on properties localised more sharply to the junctional zone.

Regulation of ileocolonic motility

NEURAL CONTROL

Integrity of the extrinsic nervous supply is not essential for ICS tone, which persisted after vagal and splanchnic nerve section.^{10 38 67} To judge by the results of nerve stimulation, however, vagal and sympathetic inputs both modify tone. Thus, in several species, stimulation of the distal end of the cut splanchnic nerve caused the ICS to contract.^{10 37 38 68 69} This response was inhibited by alpha-adrenergic blockers but not by beta blockade, ganglion blockers or atropine, suggesting excitatory alpha-adrenergic innervation of the ICS.^{38 69} Evidence also exists for an excitatory, vagal (cholinergic) innervation.^{10 37 67-70} Pharmacological studies *in vivo* and *in vitro* support these findings; the ICS contracted consistently after administration of alpha-adrenergic agonists^{10 38 44 67 69} and cholinergic agents,^{67 68 71 72} and responded by an inhibition of tone when beta-adrenergic receptors were stimulated.^{38 69} The excitatory alpha-adrenergic response at the ICS contrasts with inhibition of motor activity in the adjacent distal ileum and proximal colon.

A tonic inhibitory innervation, apparently mediated by intrinsic nerves, has been consistently shown at the ICS.^{29 30 33 73} This pathway, which may be an important regulator of tone, is mediated by an unidentified non-adrenergic, non-cholinergic neurotransmitter.^{30 73} Similar inhibitory innervation has been identified at the lower oesophageal sphincter⁷⁴ and pylorus,⁷⁵ suggesting that comparable neural mechanisms exist at other sphincters. In view of its high tissue concentration in the area⁷⁶ and of its known role as an inhibitory neurotransmitter elsewhere,⁷⁷ VIP is a logical candidate. Of other neurotransmitters, the effects of serotonin (5-hydroxytryptamine) on the feline ICS were biphasic; the contrasting effects were thought to be mediated by different serotonin receptors on smooth muscle.⁷⁸ Prostaglandins generally suppress the ICS and indomethacin evoked rhythmic spontaneous contractions, suggesting that derivatives of arachidonic acid could play a role in regulating tone.^{79 80} The feline ICS also possesses a delta-type opiate receptor, and opiate agonists induced tonic and phasic contractions.³⁹ Substance P induced tonic contractions in the ileum by acting on receptors in the myenteric plexus to release acetyl choline,⁸¹ a similar excitatory effect on the ICS has been demonstrated;⁸² indeed, the feline ICS was more sensitive than was adjacent ileum and also displayed dose dependent biphasic responses.

HUMORAL REGULATION

The possibility that gastrin mediates the ileal and/or colonic response to eating⁸³ led to the hypothesis that this hormone might also relax the ICS. The effects of exogenous and endogenous gastrin on ICS activity *in vivo* and *in vitro* have been inconclusive; different reports described relaxation,⁸⁴ stimulation,⁸⁵ and no response³³ after gastrin. Little information is available regarding other hormones; stimulation of the ICS being reported after administration of posterior pituitary extract³⁵ and glucagon.⁸⁵ *In vitro* studies on ICS muscle strips by Cardwell,³³ however, failed to elicit any response to secretin, gastrin, glucagon, or cholecystokinin.

ILEAL AND COLONIC MOTILITY AFTER THE INTAKE OF FOOD

Early observations consistently described a dramatic efflux of chyme from

the distal ileum after the ingestion of food.³⁵⁻³⁷ Although whether this efflux was mediated by an increase in ileal motor activity or sphincteric relaxation was unclear. Distal ileal motor activity increases after food – the ‘gastroileal reflex’,⁸⁶⁻⁸⁸ but the nature of this postprandial response is unclear. Some have described an increased incidence of irregular phasic contractions,⁴² while others report development of more discrete patterns.^{53 89-91} After food, myoelectrical spiking^{40 55} and phasic contractions^{40 92} increased in the immediate vicinity of the ileocolonic sphincter; relaxation, or a decrease in tonic pressure at the ileocolonic sphincter did not appear to be part of the response.^{42 92} In man, feeding increased ileal contractile activity slightly^{93 94} and this has been suggested as a mechanism whereby the terminal ileum may be cleared of residue from previous meals.⁹⁵ Based on the rather scanty evidence available it seems more likely that the response to food is an increase in coordinated phasic contractile activity in the distal ileum rather than sphincteric relaxation. Relationships among postprandial motility and propulsion at the ileocolonic junction deserve further study.

INFLUENCE OF LOCAL STIMULI

The relative independence of the ICS and distal ileum from extrinsic neural control, together with the region’s special patterns of motility raise the possibility that function may be influenced importantly by local conditions. Studies early in the century showed contraction of the sphincter in response to local stimuli such as pinching up a fold of caecum¹¹ or inserting a finger into the orifice.^{11 12 35}

Colonic distension was followed consistently by contraction of the human and canine ICS,^{18 26 28 37 96} but the response to ileal distension has been less consistent. Some have described relaxation,^{26 28} while others noted contraction of the sphincter to be the more usual response.^{18 37} Regional differences may explain these contradictory results; those investigators reporting relaxation distended the ileum close to the ICS, whereas those who reported an increase in tone stimulated in the more proximal ileum. The effect of intraluminal distension on phasic pressures at the ICS has also been reported.^{18 43} Both studies noted inhibition of phasic activity during ileal distension, but found either no change¹⁸ or an increase⁴³ in such contractions during distension of proximal colon. Ileocolonic sphincter tone increased after instillation of food into ileocolonic loops⁹⁷ and myoelectrical patterns at the junction were disrupted by perfusion of the region with an iso-osmotic solution.⁵⁸

One class of local stimuli which may shed light on the region’s function are the short chain (volatile) fatty acids (SCFA). Initially, instillation into the canine ileum of a suspension of stool was noted to provoke ‘peristalsis’ and empty the ileum.⁵⁸ Short chain fatty acids appeared as potential chemical mediators of this response, as they are small, hydrophilic molecules which reflect the metabolic activity of the faecal flora on carbohydrate residues.⁹⁷ Thus, they could be considered as ‘markers’ of colonic contents. We then instilled small boluses of a physiological mixture of SCFA (total concentration 108 mM; 66% acetic, 24% propionic, 10% butyric acids) into the canine ileum.⁹⁸ Discrete motor patterns were evoked in a predictable fashion (Fig. 5); the response was not due to the pH at which SCFA were instilled. All of this suggests that the ileum can ‘sense’ the presence of colonic contents, and that SCFA stimulate chemoreceptors by a mechanism that

Fig. 5 Stimulation of propagated bursts of ileal motility when 15 ml boluses of short chain fatty acid (SCFA) solution were instilled into the lumen. Tracings are from pressure catheters at sites indicated to the left (see reference 98 for additional details).

is sensitive to local anaesthesia and involves opiate receptors and prostanoids.⁸⁰ Thus, ileal peristalsis, mediated by SCFA, could be a mechanism for restricting or correcting, coloileal reflux. The response was also inhibited by pretreatment with prostacyclin, partially blocked by atropine and was unaffected by α and β -adrenergic blockade.⁸⁰

Motility-transit relationships across the ileocolonic sphincter

Transit of chyme from ileum to colon could be modified by changes in contractile activity of the distal ileum and/or proximal colon, by alterations in tone or patency of the ICS, by changes in the flow rate of chyme or by combinations of these factors.

Flow rates of chyme in the human ileum were low and variable during fasting; maximal flow coincided with, or just preceded, phase 3 of the MMC;⁹³ however, 50% of flow occurred during phases 1 and 2 of the interdigestive cycle. Flow increased promptly after a meal and usually fluctuated markedly, but by the return of the fasting motor pattern (several hours postprandially), 90% of a liquid meal had reached the terminal ileum.⁹³

Radionuclide scanning techniques have been used to quantify ileal emptying. In the fasting dog, ileocolonic transit of secretions was episodic;⁹⁹ most bolus movements of isotope were associated with passage of phase 3 (MMC) through the ileum, though each 'front' emptied less than one-half the contents from the ileum. Thus, more than one complete cycle – that is, two MMC's – was required to empty the ileum. The remainder of the emptying profile was a more steady trickle and was unrelated to specific

motor patterns.⁹⁹ After food, rates of ileal emptying were initially slow, and they did not increase until the fourth postprandial hour, a time at which flow of chyme was greatest.⁹⁷ Bolus movements of chyme were also seen postprandially, but, in most instances, caecal filling could not be related to specific motor patterns. In fasting man,¹⁰⁰ ileocolonic transit was also episodic, but it was not related to phase 3 of the interdigestive cycle, as few MMC's reach the human ICS.⁴²⁻⁴⁶ Chyme emptied from the human ileum faster after a meal than did secretions in the fasting state and, again, spurts of emptying could not be related to specific motor patterns; the addition of guar to the meal did not alter the $t_{1/2}$ of ileocolonic transit.¹⁰⁰ Although the propulsive potential of ileal PPC's has been established for crystalloid solutions in isolated canine loops,⁵⁸ their role in the transit of viscous fluids and solids has not been reported.

The role of the sphincter itself in regulating transit and flow across the junction remains controversial. While direct observations in animals and man have suggested that efflux of ileal contents is an active process, involving coordination of propulsive activity with opening of the ICS^{11, 35, 37} studies of transit or flow across the ileocolonic junction have yielded conflicting results. Studying intestinal propulsion and ileocaecal passage of a radiolabelled test meal in rats, Johansson and Nylander found that the ileocaecal sphincter offered no obstruction, or at most a constant resistance, to onward propulsion.¹⁰¹ Indeed, surgical excision of the rat ileocaecal junction resulted in a moderate delay rather than an acceleration of ileocolonic transit.¹⁰² Lundquist used a similar rat model but used a continuous dynamic evaluation of ileocolonic transit; in contrast, he concluded that the ICS was an important regulator of ileal emptying.¹⁰³

The role of the canine ICS in influencing transit of fluids and absorption of water was assessed in loops with or without an ICS.¹⁰⁴ Loops without an ICS propelled crystalloid fluids by steady, continuous flow at all rates of perfusion; loops with the ICS in place had irregular flow at low rates and steady transit only at high rates of perfusion. Transit was slower when the ICS was present, loops contained larger volumes of fluid and rates of electrolyte and water absorption were greater.¹⁰⁴ These observations need to be repeated with viscous and solid materials, and under postprandial conditions.

Clinical pharmacology of ileocolonic junctional motility

Alpha-adrenergic agonists such as phenylephrine, adrenaline, and noradrenaline and cholinergic agonists such as bethanechol contracted the ICS; pure beta-adrenergic agonists such as isoproterenol caused relaxation.^{10, 33, 38, 67, 68, 105} The response to atropine was more variable^{67, 72} and may have been influenced by the level of pre-existing 'cholinergic tone'. In healthy man, atropine did not appear to tighten the ICS, but it induced phase 3 type complexes in distal ileum;¹⁰⁶ flow rates in the ileum did not decrease, though sporadic contractile phenomena were virtually abolished.

The effects of opiates on the ileocaecal sphincter are of particular interest as the constipating effect of these drugs could, in part, be mediated through an increase in ICS tone. Opiates agonists, including morphine sulphate, increased ICS tone in a feline model³⁹ but, when analgesic doses of morphine were given to normal human volunteers, tone at the ICS did not increase.¹⁰⁶

The constipating effects of opiates could, alternatively, be caused by inhibition of propulsive forces. In support of this hypothesis, opiates decreased propulsive activity in terminal ileum^{35 107} and others noted a prolonged spasm of the ileum after morphine.⁵³ Both motor effects could retard transit through the region, and ileal flow was reduced by therapeutic doses of morphine.¹⁰⁶

This explanation of the reduced propulsion after opiates needs to be reconciled with the induction by morphine of 'MMC-like fronts' in the distal ileum.¹⁰⁶ Despite stimulation of such 'fronts', type 2 activity became less apparent and the total number of contractions was unchanged. In view of general notion that MMC's are propulsive, it was surprising that the 'phase 3-like' activity provoked by morphine did not stimulate flow.¹⁰⁶ Whether the antitransit effects of morphine are exerted principally in the proximal intestine, as suggested by Schiller,¹⁰⁸ whether they occur in the distal ileum but only at higher doses, or whether the retardation of flow is because of the abolition of phase 2-type activity is still unclear. The effects of morphine on the proximal colon may also be important in the overall slowing of transit.⁶⁶

Clinical significance of the ileocolonic junction

Attention has already been drawn to the early surgical contexts within which the functions of the ICS were considered.³⁻⁹ It is current surgical thinking, however, not to reconstruct a 'valve' routinely after right hemicolectomy, without obvious ill effects. Nevertheless, surgical barriers to coloileal reflux have been suggested in the management of short bowel syndrome, and several approaches have been described.¹⁰⁹ Experimental valves have been shown to prevent colonisation of the ileum with anaerobic flora.¹¹⁰

Whether disorders of ileocolonic motility are associated with symptoms in persons with an intact ICS is an even more intriguing question. We studied patients with well documented irritable bowel syndrome.^{111 112} Powerful pressure waves (PPC's) were recorded more frequently from the ileum of

Fig. 6 Basal, fasting intraluminal pressures from the canine ileum in a dog with chronic coloileal reflux. The ileum shows increased motility which features prolonged bursts of phasic waves. Reproduced from reference 24, with permission.

patients with irritable bowel syndrome (IBS), and were more often accompanied by cramping abdominal pain than they were in controls.¹¹¹ In IBS, infusions of cholecystokinin were more likely to provoke ileal PPC's than they were in controls.¹¹² We concluded that the distal small bowel should be implicated in the genesis of symptoms in some patients with IBS; moreover, PPC's must be considered as being potentially symptomatic. Might the generation of PPC's be related to coloileal reflux? The question seems worthy of exploration, especially since induction of chronic coloileal reflux in the dog²⁴ is associated with an abnormal pattern of ileal motility (Fig 6).

Conclusions

That the junction between the small and large bowel represented an ecological and physiological transition of considerable biological importance was apparent to the early anatomists and was widely written on by surgeons of the late 19th and early 20th centuries. The consensus has fluctuated somewhat between the relative importances of a mechanical valve and a functional sphincter, and now appears to encompass both concepts. Hurst¹¹³ crystallised many of these ideas, by terming the ileocolonic junction an 'intestinal stomach'; he proposed that the ileum stored and mixed chyme until distension initiated a wave of contraction which emptied the contents into the colon.

Taking this further, and drawing an analogy with other junctional zones, such as the gastric cardia and pylorus, a general hypothesis can be developed. Function of these crucial intestinal 'gates' is too important to be relegated to only one mechanism of control. Thus, the physiology of these regions appears to depend not only on intrinsic sphincters but is also determined by specialised motility in the adjacent bowel; the ileocolonic junction (ICJ) appears to fit this mode.

That a sphincter exists at the ileocolonic junction is clear, but equally apparent is the variable magnitude of the high pressure zone among species. In man, the sphincter must be judged to be poorly developed anatomically and functionally. Even a low pressure barrier, however, may be able to compartmentalise the ileum from the colon against weak propulsive forces. On the other hand, our hypothesis is that anatomical mechanisms are also mechanical barriers to reflux, and they may help resist greater heads of colonic pressure. In these terms, a 'flap-valve' at the ileocolonic junction would be useful, and this possibility deserves further testing. A third protection against coloileal reflux may be a means whereby the breaching of competence is sensed and, thereafter, an effective mechanism of cleansing the ileum is initiated. In this regard, the analogy between SCFA in the ileum and HCI in the oesophagus, as chemical stimuli for 'secondary peristalsis', is appealing.

Propulsive forces which empty the ileum are less clear. Coordination between fasting (or postprandial) ileal motility, tone at the ICS and colonic receptivity of the bolus seems likely, but the mechanisms mediating these processes are largely unexplored.

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