Pharmacology of colonic muscle

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The pharmacology of colonic muscle covers a wide range of topics. In this short review the subject has been restricted to a discussion of the intrinsic innervation of human colon, the type of response to substances occurring in the gut wall or reaching the muscle through the bloodstream, and drugs used therapeutically to affect motility by an action on the colon wall.

The Intrinsic Innervation of Human Colon

The intrinsic innervation of the colon is complex since there appear to be two types of excitatory nerves (one cholinergic and one non-cholinergic) and two types of inhibitory nerves (one adrenergic and one non-adrenergic). Evidence for these nerve pathways, which has come from different types of experiments *in vitro* on strips of taenia or circular muscle cut from operation specimens, has been discussed in detail by Stockley and Bennett (1974).

CHOLINERGIC EXCITATORY NERVES

Experiments with electrical stimulation have shown that cholinergic excitatory nerves are present: contractions are produced which are antagonized by cholinergic antagonists, potentiated by anticholinesterases, and accompanied by release of acetylcholine (Bucknell, 1966; Crema, Del Tacca, Frigo, and Lecchini, 1968; Del Tacca, Soldani, Selli, and Crema, 1970; Stockley and Bennett, 1974). Furthermore, cholinesterase-positive nerves, which are thought to be cholinergic, have been shown histologically (Garrett, Howard, and Nixon, 1969). Surprisingly, however, their demonstration with ganglion-stimulating drugs is much less convincing, even when adrenergic responses are prevented and an anticholinesterase is present (Bucknell, 1966).

NON-CHOLINERGIC EXCITATORY NERVES

Electrical stimulation has also revealed non-cholinergic excitatory nerves in the circular muscle of the sigmoid colon, and occasionally in the taeniae. Some contraction persists at low rates of stimulation in the presence of anticholinergic drugs, but is prevented by selective block of nerve conduction with tetrodotoxin (Stockley and Bennett, 1974). There is some indication that contraction of guinea-pig proximal colon due to stimulation of non-cholinergic excitatory nerves is mediated by 5-hydroxytryptamine (5-HT) (Furness and Costa, 1973) but this is unlikely to be so in human colon since 5-HT usually causes relaxation.

ADRENERGIC NERVES

Adrenergic nerves have been demonstrated histologically in the gut using catecholamine fluorescence microscopy. Most of the nerves terminate round the myenteric ganglia, and a few enter the muscle layers, but no adrenergic ganglia have been seen (Baumgarten, 1967; Bennett, Garrett, and Howard, 1968a; Capurso, Friedmann, and Parks, 1968). An important function of these nerves may be to control the amount of acetylcholine released from the preganglionic cholinergic nerves (see later). Adrenergic nerves have been demonstrated pharmacologically by several workers using ganglion stimulants (Fishlock and Parks, 1963; Bucknell and Whitney, 1964; and others). These drugs predominantly cause relaxations which appear to be neurally mediated because they are blocked by substances which prevent nerve conduction, and which are adrenergic because they are prevented by adrenergic antagonists.

NON-ADRENERGIC INHIBITORY NERVES

Non-adrenergic inhibitory nerves also exist as shown by relaxations to electrical stimulation of nerves which are unaffected by adrenergic antagonists (Bucknell, 1966; Crema *et al.*, 1968; Bennett and Stockley, 1973; Stockley and Bennett, 1974). The responses resemble those first seen in the gut from laboratory animals which might involve adenosine triphosphate (Burnstock, 1972). Ganglion stimulants do not seem to excite these nerves in human tissue, since no inhibitory response remains after blockade by adrenergic antagonists. For a reason which is not yet clear, electrical excitation (pulses of 1 msec used) has no demonstrable effect on non-adrenergic nerves. This is shown by the resistance of such responses to adrenergic antagonists (Crema *et al*, 1968; Bennett and Stockley, 1973; Stockley and Bennett, 1974).

The part played by these four types of innervation in the control of gut motility and the way they are integrated are not yet understood. One striking aspect is that the dominant response of the colon to

nerve stimulation is inhibitory, whereas excitatory innervation dominates in the small intestine. This shows a gradient of innervation down the gut which correlates with function—the high motor activity of the intestine correlates with its ability to mix and propel intraluminal contents, and the lower motility of the colon is consistent with its function as a 'reservoir' (Bennett and Whitney, 1966; Bennett and Stockley, 1973).

Responses to Naturally Occurring Substances

ACETYLCHOLINE AND NORADRENALINE

Many substances which can affect muscle activity occur naturally in the wall of the colon and might therefore have a role in motility. The responses of isolated muscle strips and of the gut *in vivo* following intravenous administration are usually similar, so validating the use of *in-vitro* studies to help to understand motility *in vivo*. Furthermore, isolated preparations seem preferable in many ways for studying substances released in the gut wall rather than reaching the muscle through the bloodstream (Bennett, 1968). Obviously, first on the list of substances are the transmitters acetylcholine and noradrenaline which are released from pre- and postganglionic cholinergic nerves, and from postganglionic adrenergic nerves respectively. Acetylcholine added to strips causes muscle contraction by stimulating cholinergic receptors on the muscle whereas noradrenaline causes relaxation by an action on α- and β-adrenoceptors on the muscle.

Theoretically it would seem that noradrenaline could also relax the tissue by acting on cholinergic nerves to inhibit the release of acetylcholine. However, little of the tone of isolated muscle strips seems to be mediated by intrinsic release of acetylcholine, since atropine causes little fall in tone. It also seems likely that an effect of noradrenaline on the muscle cells would swamp any relaxation mediated indirectly by inhibiting acetylcholine release. Some evidence also exists for α-excitatory receptors since in the presence of β-receptor blockade by oxprenolol adrenaline causes contraction of human colonic strips (Gagnon, Devroede, and Belisle, 1972). The noradrenaline released normally in the tissue might, as indicated by the anatomical arrangement of adrenergic nerves and discussed earlier, cause relaxation mainly by reducing the release of acetylcholine. Noradrenaline has been shown to inhibit the electrically induced release of acetylcholine in human colon (Del Tacca *et al*, 1970). The transmitter of non-cholinergic excitatory nerves is not known and it remains to be proven whether ATP or another purine nucleotide mediates non-adrenergic inhibitory nerve activity.

5-HYDROXYTRYPTAMINE AND HISTAMINE

Other biogenic amines in the colon wall include 5-HT and histamine, but neither appear to play a role in normal gut motility, whereas a role for 5-HT has been suggested in other species. In contrast to acetylcholine and noradrenaline, many other substances produce various responses of human colonic muscle in different preparations. With 5-HT and histamine colonic strips either relax or contract. Relaxation is more commonly seen with 5-HT whereas either response occurs to about the same extent with histamine (see Bennett and Whitney, 1966). 5-Hydroxytryptamine has a markedly different effect on the small bowel, which responds with strong contractions (Bennett, 1965; Fishlock, Parks, and Dewell, 1965; Misiewicz, Waller, and Eisner, 1966). A similar pattern of small intestine stimulation and colonic inhibition is seen with 5-HT infused intravenously *in vivo* (Misiewicz *et al*, 1966). 5-Hydroxytryptamine is an example, too, of a substance which can reach the gut through the bloodstream and it can cause diarrhoea in certain conditions, eg, the carcinoid syndrome. The fact that 5-HT inhibits colonic motility might at first sight argue against a role in diarrhoea, but Connell (1962) found that the colonic pressure waves were reduced in diarrhoea and increased in constipation.

PROSTAGLANDINS E AND F

Prostaglandins of the E and F type probably occur in human colon, but a firm statement cannot be made because they have not been fully characterized (unpublished data). As in the rest of the human gut prostaglandins (PGs) of the F series usually contract both muscle layers whereas PGE compounds contract the longitudinal muscle but relax the circular layer (Bennett, Eley, and Scholes, 1968; Fleshler and Bennett, 1969; Bennett and Fleshler, 1970; Bennett and Posner, 1971). No role has been established in motility, and no vital role seems likely since inhibitors of prostaglandin synthesis, eg, aspirin (Vane, 1971) have no marked effect on bowel function. However, care must be taken in reaching this conclusion. Although it is known that aspirin-like drugs inhibit synthesis of PG-like material by human colonic mucosa *in vitro* (Bennett *et al*, 1973), it has not been shown that the synthetase in the muscle is antagonized; nor is it known whether small amounts of PGs synthesized in the presence of inhibitors are sufficient to maintain normal gut activity. If PGs do play a role, the effect obtained would presumably depend on the types of prostaglandin involved and their relative amounts. As with 5-HT, PGs released into the bloodstream are thought to contribute to the diarrhoea of certain conditions, eg, medullary carcinoma of the thyroid

(Sandler, Karim, and Williams, 1968), but this may well be an effect on secretion rather than on muscle activity (see Bennett, 1973).

POLYPEPTIDES

Among the polypeptides in the gut, substance P has received little attention, although its presence was reported in human colon many years ago (Ehrenpreis and Pernow, 1953). Preliminary data indicate that small amounts contract the circular muscle of human sigmoid colon by an action on the muscle at a site which is unaffected by antagonists of acetylcholine histamine and 5-HT (unpublished).

BRADYKININ

Bradykinin occurs in inflamed tissues, but it is not known whether it is released normally. Low concentrations of the polypeptide relax both muscle layers of the distal colon but a biphasic response or contraction occurs in longitudinal muscle strips with higher concentrations (Fishlock, 1966). Apart from release in inflammation, bradykinin reaching the colon through the bloodstream in the carcinoid and dumping syndromes might contribute to the disordered motility. Other polypeptides, such as motilin (Brown, 1971), remain to be studied in human colon.

UPPER GASTROINTESTINAL HORMONES

Hormones of the upper gastrointestinal tract reach the colon through the bloodstream and they might have an important function in coordinating gut activity. Gastrin heptadecapeptide and its synthetic analogue pentagastrin have little or usually no stimulant effect on isolated colonic strips (Bennett, Misiewicz, and Waller, 1967), and in most studies (eg, Misiewicz, Holdstock, and Waller, 1967) no effect has been recorded on colonic motility with intravenous infusions. These studies indicate that gastrin is unlikely to be involved in the gastrocolic reflex, but it is now known that gastrin molecules larger than the heptadecapeptide are secreted (Berson and Yalow, 1971), and the question of their participation in the reflex must await further studies.

With the exception of cholecystokinin (CCK) which stimulates the colon (Harvey and Read, 1973) other upper gastrointestinal hormones, including secretin, insulin, and glucagon, do not appear to have been studied on human colon. Nor have hormones from the thyroid, adrenals, etc, been investigated. Perhaps some of these have clinical relationships—such as the diarrhoea seen in hyperthyroid patients. Low concentrations of angiotensin cause contraction of both muscle layers of the colon, apparently by an action directly on the muscle (Fishlock and Gunn, 1970). Might elevated levels of angiotensin in the circulation, due to renal or hepatic causes, affect the colon?

Drugs Used to Treat Disordered Colonic Motility

Many of the drugs used to treat disordered motility of the gastrointestinal tract are aimed specifically at the colon. Others affect the colon in addition to an action directed primarily at the other regions. These have been discussed in detail by Bennett and Misiewicz (1973), and only an outline is given here. As far as the colon is concerned, the drugs can be divided into laxatives, antidiarrhoeal agents, spasmolytics, and drugs in ileus.

SPASMOLYTICS

Spasmolytics are probably the easiest to understand. Those which are anticholinergic, such as atropine, antagonize the stimulant effect of acetylcholine released from postganglionic nerve endings. Some within this group, such as propantheline, also have ganglion-blocking activity due to antagonism of acetylcholine released from preganglionic nerves. In contrast, papaverine, which has only a weak relaxant effect and is rarely used clinically, is thought to act by inhibiting phosphodiesterase and so causing tissue levels of cyclic AMP to increase (Triner, Vulliemoz, Schwartz, and Nahas, 1970). Mebeverine is also a non-anticholinergic spasmolytic which is substantially more potent than papaverine in experimental animals (Lindner, Selzer, Classen, Gans, Offring, and Zwagemakers, 1963).

In ileus, the activity of all parts of the gut can be stimulated by drugs acting through cholinergic pathways. Stable choline esters such as bethanechol stimulate motility, presumably because they act like the acetylcholine released in the gut wall. Alternatively, the effect of normally released acetylcholine can be enhanced with anticholinesterases such as neostigmine which prevent degradation of the transmitter; this drug also stimulates the muscle itself. Ileus is now known to be due to sympathetic (inhibitory) overactivity rather than to cholinergic nerve dysfunction. The condition is therefore often treated with drugs which block adrenergic neurones or α-receptors, eg, guanethidine or phentolamine respectively, together with an anticholinesterase or stable choline ester (Neeley and Catchpole, 1971). Other stimulants of gut muscle, such as the polypeptide caerulein, have also been used in ileus (Agosti, Bertaccini, Paulucci, and Zarella, 1971).

LAXATIVES

The modes of action of laxatives and antidiarrhoeal agents are less clear than for the other drugs discussed. The numerous laxatives which exist can be

divided into a few classes. The anthraquinone group contains senna, cascara etc; the diphenylmethanes contain phenolphthalein and bisacodyl; the resins, which are irritant and have no place in modern medicine, contain podophyllum, colocynth, etc; and there are other substances such as castor oil (which is thought to act on the small intestine) and lactulose. The anthraquinone laxatives are glycosides which are broken down in the gut mainly to oxymethylanthraquinones. These are thought to stimultate Auerbach's plexus in the colon, and to increase the bulk and softness of the stool by inhibiting water absorption. The diphenylmethane derivatives have been described as 'contact' laxatives since they stimulate motility by acting on sensory nerves in the colon wall (Hardcastle and Mann, 1968). In addition, water absorption might be inhibited as has been shown in animals (Phillips, Love, Mitchell, and Neptune, 1965), and oxyphenisatin can inhibit glucose absorption in human small intestine (Hart and McColl, 1968). Lactulose acts by a different mechanism which again has not been fully elucidated. It is a synthetic disaccharide which reaches the colon intact and is then split by bacterial action mainly into lactic acid. Several effects may be produced. The osmolarity of colonic contents may increase (Pertsiounis, 1970) and, as shown in animal studies, the fall in pH may reduce water absorption (Rousseau and Sladen, 1970) and stimulate propulsion (unpublished data).

ANTIDIARRHOEAL AGENTS

Lastly, the antidiarrhoeal agents. Except where there is a specific cause, such as 5-HT in the carcinoid syndrome which can be antagonized with methysergide, antidiarrhoeal drugs are used empirically. Included in this group are morphine, its relative codeine, and diphenoxylate which resembles pethidine chemically. Morphine affects the whole of the gastrointestinal tract and causes constipation by decreasing propulsion in the small and large intestine. The muscle tone and intraluminal pressure are raised and non-propulsive circular muscle activity is increased (Vaughan-Williams, 1954; Painter and Truelove, 1964a). Morphine has no action on isolated gut muscle, and Daniel *et al* (1959) concluded that it acts on intramural nerves. In the terminal small intestine (Daniel, Sutherland, and Bogoch, 1959) and sigmoid colon (Painter and Truelove, 1964b) a cholinergic mechanism may be involved because atropine or propantheline reduced or prevented the effect of morphine (Daniel *et al*, 1959). However, the possibility remains that the antagonism of acetylcholine merely damped down motility in general. Codeine is presumed to act similarly to morphine. Diphenoxylate also increases segmenting pressure waves in the small intestine (Bárány and Jacobson, 1964) but no studies seem to have been done with this substance on the colon *in vivo* or *in vitro*. This absence of data illustrates the great need for more work on how drugs affect colonic activity, and this in turn requires a greater understanding of colonic physiology.

References

Agosti, A., Bertaccini, G., Paulucci, R., and Zanella, E. (1971). Caerulein treatment for paralytic ileus. *Lancet*, **1**, 395.

Bárány, F., and Jacobson, B. (1964). Endoradiosonde study of propulsion and pressure activity, induced by test meals, prostigmine, and diphenoxylate in the small intestine. *Gut*, **5**, 90-95.

Baumgarten, H. G. (1967). Uber die Verteilung von Catecholaminen im Darm des Menschen. *Z. Zellforsch.*, **83**, 133-146.

Bennett, A. (1965). A pharmacological investigation of human isolated ileum. *Nature (Lond.)*, **208**, 1289-1291.

Bennett, A. (1968). The biological importance of gastrin. *J. roy. Coll. Phycns.*, **2**, 269-273.

Bennett, A., Eley, K. G., and Scholes G. B. (1968) Effects of prostaglandins E_1 and E_2 on human, guinea-pig and rat isolated small intestine. *Br. Jr. Pharmac.* **34**, 630-638.

Bennett, A., and Fleshler, B. (1970). Prostaglandins and the gastrointestinal tract. *Gastroenterology*, **59**, 790-800.

Bennett, A., Fox, C. F., and Stamford, I. F. (1973). Inhibition of prostaglandin synthesis by benorylate. *Rheumatol. and Rehabil.*, **12**, Suppl., 101-105.

Bennett, A., Garrett, J. R., and Howard, E. R. (1968a). Adrenergic myenteric nerves in Hirschsprung's disease. *Brit. med. J.*, **1**, 487-489.

Bennett, A., and Misiewicz, J. J. (1973). Drugs used in treating disordered motility of the alimentary tract. In *International Encyclopedia of Pharmacology and Therapeutics*, Sect. 39A, edited by P. Holton, vol. 2, 433-455. Pergamon Press, Oxford.

Bennett, A., Misiewicz, J. J., and Waller, S. L. (1967). Analysis of the motor effects of gastrin and pentagastrin on the human alimentary tract *in vitro*. *Gut*, **8**, 470-474.

Bennett, A., and Posner, J. (1971). Studies on prostaglandins antagonists. *Brit. J. Pharmacol.*, **42**, 584-594.

Bennett, A., and Stockley, H. L. (1973). A study of the intrinsic innervation of human isolated gastrointestinal muscle using electrical stimulation. *J. Physiol. (Lond.)*, **233**, 34P-34P.

Bennett, A., and Whitney, B. (1966). A pharmacological study of the motility of the human gastrointestinal tract. *Gut*, **7**, 307-316.

Berson, S. A., and Yalow, R. S. (1971). Nature of immunoreactive gastrin extracted from tissues of gastrointestinal tract. *Gastroenterology*, **60**, 215-222.

Brown, J. C. (1971). The purification, amino acid composition and sequence, and physiological activity of motilin, a gastric motor activity stimulating polypeptide from the mucosa of the small intestine of hogs. *Rendic. R. Gastroent.*, **3**, 119.

Bucknell, A. (1966). Ph.D. thesis (*Lond.*).

Bucknell, A., and Whitney, B. (1964). A preliminary investigation of the pharmacology of the human isolated taenia coli preparation. *Brit. J. Pharmacol.*, **23**, 164-175.

Burnstock, G. (1972). Purinergic nerves. *Pharmacol. Rev.*, **24**, 509-581.

Capurso, L., Friedmann, C. A., and Parks, A. G. (1968). Adrenergic fibres in the human intestine, *Gut*, **9**, 678-682.

Connell, A. M. (1962). The motility of the pelvic colon. II. Paradoxical motility in diarrhoea and constipation. *Gut*, **3**, 342-348.

Crema, A., Del Tacca, M., Frigo, G. M., and Lecchini, S. (1968). Presence of a non-adrenergic inhibitory system in the human colon. *Gut*, **9**, 633-637.

Daniel, E. E., Sutherland, W. H., and Bogoch, A. (1959). Effects of morphine and other drugs on motility of the terminal ileum. *Gastroenterology*, **36**, 510-523.

Del Tacca, M., Soldani, G., Selli, M., and Crema, A. (1970). Action of catecholamines on release of acetylcholine from human taenia coli. *Europ. J. Pharmacol.*, **9**, 80-84.

Ehrenpreis, T., and Pernow, B. (1953). On the occurrence of substance P in the rectosigmoid in Hirschsprung's disease. *Acta physiol. scand.*, **27**, 380-388.

Fishlock, D. J., and Gunn, A. (1970). The action of angiotensin on the human colon *in vitro*. *Brit. J. Pharmacol.*, **39**, 34-39.

Fishlock, D. J., and Parks, A. G. (1963). A study of human colonic muscle *in vitro*. *Brit. med. J.*, **2**, 666-667.
Fishlock, D. J., Parks, A. G., and Dewell, J. V. (1965). Action of 5-hydroxytryptamine on the human stomach, duodenum and jejunum *in vitro*. *Gut*, **6**, 338-342.
Fishlock, D. J. (1966). Effect of bradykinin on the human isolated small and large intestine. *Nature (Lond.)*, **212**, 1533-1535.
Fleshler, B., and Bennett, A. (1969). Responses of human, guinea-pig, and rat colonic circular muscle to prostaglandins. (Abstr.) *J. Lab. clin. Med.*, **75**, 872-873.
Furness, J. B., and Costa, M. (1973). The nervous release and the action of substances which affect intestinal muscle through neither adrenoceptors nor cholinoreceptors. *Phil. Trans. roy. Soc. Lond. B.*, **265**, 123-133.
Gagnon, D. J., Devroede, G., and Belisle, S. (1972). Excitatory effects of adrenaline upon isolated preparations of human colon. *Gut*, **13**, 654-657.
Garrett, J. R., Howard, E. R., and Nixon, H. H. (1969). Autonomic nerves in rectum and colon in Hirschsprung's disease. *Arch. Dis. Child.*, **44**, 406-417.
Hardcastle, J. D., and Mann, C. V. (1968). Study of large bowel peristalsis. *Gut*, **9**, 512-520.
Hart, S. L., and McColl, I. (1968). The effect of the laxative oxyphenisatin on the intestinal absorption of glucose in rat and man. *Brit. J. Pharmacol.*, **32**, 683-686.
Harvey, R. F., and Read, A. E. (1973). Effect of cholecystokinin on colonic motility and symptoms in patients with the irritable-bowel syndrome. *Lancet*, **1**, 1-3.
Lindner, A., Selzer, H., Claassen, V., Gans, P., Offringa, O. R., and Zwagemakers, J. M. A. (1963). Pharmacological properties of mebeverine, a smooth-muscle relaxant. *Arch. intern. Pharmacodyn.*, **145**, 378-395.
Misiewicz, J. J., Holdstock, D. J., and Waller, S. L. (1967). Motor responses of the human alimentary tract to near-maximal infusions of pentagastrin. *Gut*, **8**, 463-469.
Misiewicz, J. J., Waller, S. L., and Eisner, M. (1966). Motor responses of the human gastrointestinal tract to 5-hydroxytryptamine *in vivo* and *in vitro*. *Gut*, **7**, 208-216.
Neely, J., and Catchpole, B. (1971). Ileus: the restoration of alimentary-tract motility by pharmacological means. *Brit. J. Surg.*, **58**, 21-28.
Painter, N. S., and Truelove, S. C. (1964a). The intraluminal pressure patterns in diverticulosis of the colon. Parts I and II. *Gut*, **5**, 201-213.
Painter, N. S., and Truelove, S. C. (1964b). The intraluminal pressure patterns in diverticulosis of the colon. Parts III and IV. *Gut*, **5**, 365-373.
Pertsiounis, S. (1970). In: Lactulose in the treatment of portal systemic encephalopathy. *Gastroenterology*, **58**, 595-597.
Phillips, R. A., Love, A. H. G., Mitchell, T. G., and Neptune, E. M., Jr. (1965). Cathartics and the sodium pump. *Nature (Lond.)*, **206**, 1367-1368.
Rousseau, B., and Sladen, G. E. (1970). Effect of luminal pH on intestinal absorption of water and electrolytes. *Gut*, **11**, 1056.
Sandler, M., Karim, S. M. M., and Williams, E. D. (1968). Prostaglandins in amine-peptide-secreting tumours. *Lancet*, **2**, 1053-1054.
Stockley, H. L., and Bennett, A. (1974). The intrinsic innervation of human sigmoid colonic muscle. In *Proceedings of the fourth International Symposium on Gastrointestinal Motility*, edited by E. E. Daniel, Mitchell, Vancouver. pp. 163-176.
Triner, L., Vulliemoz, Y., Schwartz, I., and Nahas, G. G. (1970). Cyclic phosphodietserase activity and the action of papaverine. *Biochem. Biophys. Res. Commun.*, **40**, 64-69.
Vane, J. R. (1971). Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. *Nature [new Biol.]*, **231**, 232-235.
Vaughan-Williams, E. M. (1954). The mode of action of drugs upon intestinal motility. *Pharmacol. Rev.*, **6**, 159-190.

Colonic motility

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Colonic motor activity may be divided into two modes: propulsive contractions or mass movements and non-propulsive contractions or segmental activity. Although it seems that the two modes of activity appear to have different functions, are effected by different types of muscle contraction, and may be mediated through separate pathways, the division should be regarded as convenient for descriptive purposes, rather than resting on sound experimental foundations. Despite considerable progress in electrophysiology and pharmacology of the colon (see reviews by Daniel and Bennett, this symposium), the regulation of human colonic motor function in health and disease is still not well understood. It is not known precisely how either mode of colonic contraction is initiated, although both mass movements and segmental contractions can be experimentally stimulated or inhibited by many pharmacological or physiological stimuli. Nor is it certain how either type of activity is altered in disease. The interplay of the effects of the various biogenic substances and the relationship between absorptive (see Cummings, this symposium) and the motor functions of the large bowel, remain to be worked out.

Mass Movements

Colonic mass movements are difficult to record, and have not been extensively studied. They were initially observed radiologically, but the now known hazards of ionizing radiation limit radiological observation, even with sophisticated time-lapse cinefluorography (Ritchie, Ardran, and Truelove, 1962). Some information on the distribution of faeces before and after a mass movement can be collected by using radioopaque markers (Hinton,