

# Colon physiology

## *A review*

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Considering the size of the organ and the number of symptoms which are rightly or wrongly attributed to it, too little attention is given to understanding how the colon functions. Although many studies concerning the anatomy, nervous intervention, electrical properties and transport properties are available, they are often poorly understood by those treating patients with colonic diseases. This paper focuses on the physiologic properties of the normally functioning colon and will touch briefly on some derangements in physiology which accompany some of the commoner diseases affecting the colon.

### **Structure and function**

The length of the colon varies considerably in the normal population. There is a rough correlation between a person's height and the length of the colon. Although accurate estimation of the length in vivo may be difficult, and postmortem studies may similarly distort the actual length, studies indicate that the colon is approximately 1500 cm in length.<sup>1</sup> The rectal mucosa is a flat surface lacking villi and is lined by columnar epithelial cells. Invaginations from the flat absorptive surface called crypts occur. Below

this lies the muscularis mucosa and the submucosa which lack distinguishing characteristics. The muscle layers are two in number. Surrounding the submucosa is an inner-circular muscular layer, and external to this is a longitudinal muscle layer. Unlike other portions of the tubular gut, the outer muscular layer does not completely surround the tube but, instead, is gathered into three distinct longitudinal bundles called taeniae coli. External to the outer muscular layer is the serosa.

The function of the colon is to allow for the orderly elimination from the body of nonabsorbed food products, desquamated cells from the gut lumen, and detoxified and metabolic end products excreted by the biliary tree. The colon carries out this task with remarkable conservation of fluid and electrolytes such that the quantity eliminated per 24 hours (with the usual diets consumed in industrialized Western nations) is about 10% of that presented to the colon in the same time frame. In addition to conserving volume, the colon shares with the kidney and few other organs (sweat glands, salivary glands) the remarkable capacity to absorb certain electrolytes in a nonisotonic fashion. small volume of stool, thus contributing to sodium conservation in the organism.

Due in large measure to the motility pattern of the colon but also due to the remarkably effective sphincter mechanisms of the anus/rectum, man is able to control elimination of contents from the colon in ways which relatively few species can.

### **Innervation of the human gut**

The innervation of the human gut is complex. Moreover, it is not en-

tirely clear how this innervation is integrated to produce muscular electrical activity and muscular contraction. In general the nervous innervation is of two types: excitatory and inhibitory. It is an oversimplification to state that cholinergic nerves are excitatory and adrenergic nerves are inhibitory. For although it is true in general that the cholinergic system is predominately stimulatory and the adrenergic system is inhibitory, there also exist noncholinergic excitatory nerves and nonadrenergic inhibitory nerves.<sup>2</sup> The presence of cholinergic excitatory nerves has been demonstrated by showing that cholinergic antagonists such as atropine will often reduce or eliminate contractions in an *in vitro* preparation of colonic muscle. Additionally, contractions of *in vitro* preparations are potentiated by anticholinesterases. It has also been shown that when contractions in colonic muscle preparations occur there is a simultaneous release of acetylcholine. One would expect that ganglionic stimulating drugs would also cause muscle contractions in this experimental model. However, there has been considerable difficulty in demonstrating this expected physiologic event.

The presence of noncholinergic excitatory fibers is evidenced by the fact that in the circular muscle layer of the sigmoid colon, contractions have been demonstrated especially at low rates of electrical stimulation, even in the presence of anticholinergic drugs. The mediator for this response is unknown. Five-hydroxytryptamine (serotonin) has been shown to be a mediator in guinea pigs, but this seems to be an unlikely mediator in man since 5-hydroxytryptamine usually causes relaxation

in the human colon muscle.

Adrenergic nerves have been well demonstrated in the human colon. Stimulation of the adrenergic nervous system predominantly causes relaxation of smooth muscles. It has been suggested that the alpha adrenergic receptors may have an excitatory component since noradrenaline given after beta adrenergic blocking results in contraction of the colonic musculature. In any event, in the absence of beta adrenergic blockade, the predominant effect of noradrenaline is relaxation of colonic smooth muscle. There is also some evidence that noradrenaline may act, in part, by blocking the release of acetylcholine from the cholinergic (excitatory) nerves.

To complete the symmetry, there is evidence for nonadrenergic inhibitory nerves. The candidate mediator for this response is adenosine triphosphate (ATP) and thus would be considered part of the purinergic nervous system. The existence of these pathways is shown by the relaxation of smooth muscle which occurs with electrical stimulation even in the presence of adrenergic antagonist.

As noted, the way in which these four nerve types are integrated is poorly understood. However, the anticipated response of the human colon to drugs which are given either to control intestinal symptoms or for other reasons altogether may be predicted when the above mentioned factors are understood. For example, acetylcholine, or drugs which mimic acetylcholine such as bethanechol chloride (Urecholine) would be expected to result in increased muscular activity of the human colon and thus could result in abdominal

cramps. In contrast, anticholinergics such as atropine or synthetic analogs contained in a variety of commonly prescribed medicines intended to reduce abdominal pain and cramping, and so-called functional bowel disease may be expected to reduce muscular contraction by inhibiting the cholinergic nervous system. Interruption of nervous innervation to the colon as in spinal cord injuries increases motor activity and is associated with severe constipation.<sup>3</sup>

### Electrical events in the colon

Unlike other organs which have a repetitive pattern of electrical activity such as the stomach, small bowel, and heart, the colon often has relatively long periods of electrical silence interspersed with "pacemaker" activity. Although the possibility of experimental error such as short-circuiting or inconstant contact of electrodes to the mucosa has been raised<sup>4</sup> as a possible explanation for these observations, this seems unlikely. Most observers have shown that in the distal colon slow electrical waves (between 3 and 12 cycles/min) are present from about 5% to 20% of the time of the recording. In the rectum itself, electrical activity is demonstrable three quarters of the time or more. There is a general tendency for electrical activity to be present a lesser percentage of the time the further cephalad one gets from the anus. Recently, Duthie<sup>5</sup> reported results from studies in more than 150 subjects who were studied with a variety of electrodes including suctional electrodes, implanted electrodes, and cutaneous electrodes. These studies involved portions of the colon more proximal

than those usually reported. He, as others, found that the percentage of time that electrical activity was present decreased as the electrodes were moved cephalad from the anus to a distance of approximately 25 cm. However, when he sampled from electrodes placed in the descending and transverse colon, he found that the percentage of time electrical activity was present increased again.

Duthie<sup>5</sup> also found that slow waves are present throughout the colon. More interestingly, he has been able to distinguish two kinds of slow waves: one has a frequency of 2.5 to 4 cycles/min, and the other 6 to 12 cycles/min. That these are separate physiologic events is evidenced by the fact that pentagastrin given intravenously affects only the slower rhythm and neostigmine affects only the faster rhythm. The 6- to 12-cycle slow rhythm is predominant in the ascending, transverse, and proximal descending colon; whereas the 2.5- to 4-cycle slow waves predominate in the anus and rectum to a distance of approximately 20 to 30 cm. Thus there is a gradient of activity based on the faster frequency of the slow waves in the proximal colon compared to the distal colon.

In addition to slow waves there are also identifiable in the normal colon bursts of high frequency electrical events. These have been called action potentials and are thought to represent contraction of smooth muscle.

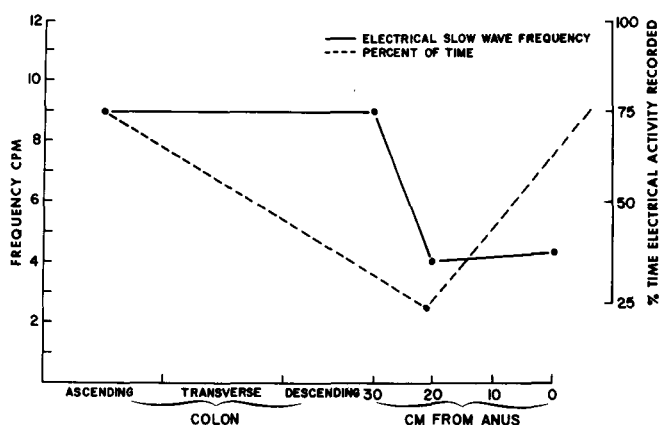
The exact effect of these electrical events on colonic motility is somewhat speculative. The number of electrical waves associated with motor activity in the colon is small; usually less than 15% of slow waves are correlated with motor waves, at least in the

rectosigmoid area. On the other hand, motor contractions during isoelectric periods occur less than 10% of the time. The physiologic correlates that allow some waves to elicit motor contractions while most do not need to be elucidated.

In summary, the faster frequency of slow wave seems to predominate in the proximal colon, whereas the slower form of slow wave predominates in the rectosigmoid. The percent time that electrical activity is present similarly is higher in the proximal colon but decreases until a distance of about 25 cm from the anus is reached, at which point the percent time occupied by electrical activity increases once again, and is present most of the time in the area of the rectal sphincter. Motor waves are usually associated with electrical waves, but only a fraction of electrical waves result in motor contraction (*Figure*).

### Motor activity in the colon

The study of pressure waves in the colon by the use of balloons, open tip catheters, telemetric devices and many isotope studies have resulted in the recognition of a variety of motor wave forms that vary in duration, pressure generated, and frequency of observance. At least three types have been described in normal colons.<sup>6-9</sup> These motor waves seem to have more to do with mixing of colonic contents than they do with propulsion. The predominant type of motor form has often been termed a "segmenting wave" or a "segmental contraction". The purpose of these waves seems to be more to impede the flow of colonic contents. It has been shown that patients with diar-



**Figure.** Slow wave frequency increases as transducer is placed cephalad from anus. The amount of time that electrical activity is recorded decreases with cephalad placement to a distance of approximately 20 cm then increases. (Adapted with permission of Duthie HL: Colonic motility in man. *Mayo Clin Proc* 50: 519-522, 1975.)

rhea have fewer segmenting waves and those with constipation have more segmenting waves.<sup>10</sup>

True peristalsis is seen rarely in the normal colon. Propulsive movement of material over relatively long distances of the colon occur infrequently and often in response to a meal. These movements are called mass movements. When initiated by a meal, the mass movement is referred to as the gastrocolic reflex. The integrity of this reflex remains intact after total gastrectomy<sup>11</sup> and after vagotomy, and does not seem to be related to the hormone gastrin or to identified vagal neuropathways. The genesis for the gastrocolic reflex probably relates to entry of food into the proximal small bowel, initiating movement of contents from the distal ileum across the ileocecal valve into the cecum where distention of the cecum initiates the mass movement. If the mediator of this reflex is neither the vagus nerve nor gastrin, neither is it likely to be serotonin (which has no recognized role in normal gut

motility in humans) or prostaglandins. Different prostaglandins have been shown to have different effects on colonic circular and longitudinal muscle fibers.<sup>2</sup> Additionally, it seems unlikely that prostaglandins have any profound net effect on colonic motility since inhibitors of prostaglandins, such as aspirin, have no marked effect on large bowel function. In medullary thyroid carcinoma associated with increased release of prostaglandins diarrhea may occur, but motility has not been shown to be altered. It seems more likely that the diarrheagenic effect of prostaglandins relates to increased small bowel fluid, causing increased ileal flow.<sup>12</sup> CCK-pancreozymin is another candidate mediator based on its demonstrated ability to stimulate colonic contraction.<sup>13</sup> However, direct evidence for its involvement in colonic mass movements is lacking.

### Clinical considerations

Emotional factors are felt by most to have substantial effects on colonic

activity. Thus, stress interviews in normal volunteers result in increased motility in the human sigmoid colon.<sup>14</sup> These effects are likely mediated by cholinergic nerve traffic.

Using an isotope capsule to study transit times in a group of patients with simple irritable colon, functional constipation, or diverticular disease, Kirwan and Smith<sup>15</sup> were able to show a substantial delay in transit time at the rectosigmoid, splenic flexure, transverse colon, and right colon in this mixed group of patients. Moreover, they were able to show improvement (a reduction by approximately one third) in the transit time following institution of a diet high in bran. These observations are consistent with the notion that increased colonic motor activity (which is regularly observed in such patients during symptomatic periods) serves to impede the flow of contents within the colon.<sup>8</sup>

Snape et al<sup>16</sup> have recently shown that patients with irritable bowel syndrome have increased slow waves in the basal state. Additionally, they have more segmenting motor contractions than normals in response to cholecystokinin and to pentagastrin.

Waller<sup>17</sup> using air-filled balloons at 5-cm intervals from the anal verge studied eight patients with simple functional diarrhea and nine patients with functional constipation. She showed that those with simple diarrhea had reduced levels of colonic motility (fewer and smaller magnitude segmental contractions) and that those with constipation had increased patterns of segmenting contractions. When codeine was administered for several days to the patients with diarrhea, the effect on segmenting contractions was dramatic: co-

deine converted the motor pattern to those seen in constipated people. Conversely, in patients with constipation who started out with increased levels of segmenting contractions, the administration of senna resulted in decreased segmenting pressures so that the constipated patients developed a pattern seen in those with diarrhea.

In patients with diverticular disease, the amount of pressure generated in the sigmoid colon with each motor wave is higher. The well-known effect of morphine in increasing the intensity of pressure waves in normal people and to an even greater extent in patients with diverticular disease makes many gastroenterologists reluctant to use this analgesic for the relief of pain associated with diverticulitis. Indeed, meperidine does *not* cause increased segmental pressure waves in the human colon. Pentazocine (Talwin) decreases colonic intraluminal pressure and may be the preferred drug for this use.<sup>18</sup> Anticholinergics and diphenoxylate also *decrease* segmenting activity in the human colon; this explains their widespread use for diseases of the colon characterized by increased colonic pressures (*Table*).

### Fluids and electrolytes

The volume delivered to the right colon from the ileum amounts to approximately 1500 cc/day.<sup>19, 20</sup> Most of this water is reabsorbed so that stool water amounts to between 100 to 150 cc/day. The capacity of the colon to absorb water is graded. The right colon has a greater ability than the left for water absorption and the rectosigmoid plays practically no role in water absorption. Fluid in the terminal ileum is isotonic with respect to

Table. Drugs and the colon

Drug/agent	Effect	Comment
Codeine	Constipation	Increases segmenting activity
Diphenoxylate	Constipation	Increases segmenting activity
Loperamide	Constipation	Increases segmenting activity
Morphine	Constipation	Increases segmenting activity and intensity
CCK-PZ	? mediates gastrocolic reflex	Stimulates colonic smooth muscle
Bile acids	Diarrhea	Cause colonic secretion of water, electrolytes
Senna and other cathartics	Diarrhea	Decreases segmenting activity; uncouples electrical activity
Bradykinin	? diarrhea in dumping syndrome, carcinoid	Variable effects on smooth muscle—dose dependent
Atropine-like drugs	Antispasmodic	Moderates heightened colonic pressure waves in diverticulosis, irritable bowel
Bran	Bulk agent	Increases stool weight; “normalizes” delayed transit of irritable bowel, diverticulosis
Others		
Prostaglandins	Variable or unproven	
Gastrin	effect in normal	
Secretin	colon	
Glucagon	Antispasmodic	Dramatic inhibition of muscular activity; transient

serum. Thus, the sodium concentration is about 130 mEq/liter, the potassium concentration 10 mEq/liter, the chloride concentration 80 mEq/liter, and the bicarbonate concentration 60 mEq/liter. The colonic mucosa has been shown to absorb avidly sodium and chloride. When the serum sodium concentration is 140 mEq/liter, the fecal water sodium concentration is often in the range of 1 or 2 mEq/liter. This represents a concentration gradient of greater than 100 to 1, demonstrating the enormous ability of colonic mucosa to absorb sodium. The fecal water is not hypotonic despite the low sodium and potassium concentrations, however. The major ionic species in fecal water have been shown to be organic acids.<sup>21, 22</sup> Just as in the kidney, mineralocorticoids further enhance the reabsorption of sodium by the colonic mucosa.<sup>23</sup> Aldosterone blocking agents such as spi-

ronolactone tend to inhibit absorption of sodium against such steep gradients. Although, these gradients are impressive as physiologic events, the importance of the colon in sodium conservation in normal persons should not be overstated. For example, if sodium could not be absorbed by the colon against a concentration gradient then, presumably, the fecal water sodium concentration would be roughly 140 mEq/liter. But since the stool water is only 100 to 150 cc/day this would only represent between 14 and 21 mEq of sodium lost in the stool per day.

Fecal water has a higher concentration of potassium than either plasma or terminal ileal contents. This also is true of bicarbonate, indicating a net secretion of potassium and bicarbonate by the colon.

The reserve capacity of the colon for reabsorption of water and elec-



trolytes has not been established with certainty. In an interesting recent experiment<sup>24</sup> it was shown that instillation into the cecum via a long nasogastric tube of up to 4 *additional* liters of isotonic solution only increased the fecal weight to 268 g. Since the basal input to the cecum is estimated to be 1500 cc/day, this experiment represents 5500 cc of isotonic fluid presented to the colon. Of this amount a mean of 4% was eliminated as fecal water; the remainder appeared as excess urine volume. This clearly indicates an enormous reserve capacity for water and electrolyte reabsorption by the normal intact colon. The limits of the human colon for water and electrolyte reabsorption have not been firmly established.

### **Derangements of water and electrolyte absorption**

There are a number of pathological states characterized by decreased water and electrolyte absorption by the human colon. Many of these disease states convert the colon from a net absorptive organ to a secretory one. Choleric enteropathy results from increased delivery of bile salts to the human colon.<sup>25</sup> Bile salts are normally essentially totally reabsorbed in the distal ileum. They may reach the colon in increased amounts when the terminal ileum has been either resected or is diseased. The bile acids are deconjugated by the bacterial flow of the colon and the deconjugated bile acids inhibit sodium and water reabsorption and stimulate their secretion, resulting in a watery diarrhea. The effect of these agents is mediated through stimulation of the cyclic AMP system,<sup>26, 27</sup> and it has recently been shown in

vitro that propranolol, a blocker of adenylcyclase activity will antagonize the effect of bile acids on colonic mucosa.<sup>28</sup> Of course, if this is borne out in vivo then an exciting new therapeutic modality for choleric enteropathy might materialize.

### **Summary**

The foregoing outline of physiologic events in the normal human colon leaves many unanswered questions. The precise interrelationships of nervous innervation one to the other, and the ways in which the nervous innervation results in neuroelectric wave activity of the colon are unknown. The intermittent nature of the electrical activity in the colon is quite unlike other organs with "pacemakers". Whether this difference represents measuring artifact or a functional difference in the electrical properties of the colon can only be surmised. The coupling mechanism, whereby only a small percentage of electrical events in the colon have a corresponding motor event, remains to be elucidated. The biochemical mediator for mass movements in the colon has yet to be identified.

What is known about colonic physiology serves as a useful framework for understanding such common disease states as diverticulosis, irritable bowel syndrome, and many diarrheal states. The effect on the colon of some commonly used drugs has also been noted.

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