

# 55 Diarrhea and Constipation

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Diarrhea and constipation are exceedingly common and, together, exact an enormous toll in terms of mortality, morbidity, social inconvenience, loss of work productivity, and consumption of medical resources. Worldwide, >1 billion individuals suffer one or more episodes of acute diarrhea each year. Among the 100 million persons affected annually by acute diarrhea in the United States, nearly half must restrict activities, 10% consult physicians, ~250,000 require hospitalization, and ~5000 die (primarily the elderly). The annual economic burden to society may exceed \$20 billion. Acute infectious diarrhea remains one of the most common causes of mortality in developing countries, particularly among impoverished infants, accounting for 1.8 million deaths per year. Recurrent, acute diarrhea in children in tropical countries results in environmental enteropathy with long-term impacts on physical and intellectual development.

Constipation, by contrast, is rarely associated with mortality and is exceedingly common in developed countries, leading to frequent self-medication and, in a third of those, to medical consultation. Population statistics on chronic diarrhea and constipation are more uncertain, perhaps due to variable definitions and reporting, but the frequency of these conditions is also high. United States population surveys put prevalence rates for chronic diarrhea at 2–7% and for chronic constipation at 12–19%, with women being affected twice as often as men. Diarrhea and constipation are among the most common patient complaints presenting to internists and primary care physicians, and they account for nearly 50% of referrals to gastroenterologists.

Although diarrhea and constipation may present as mere nuisance symptoms at one extreme, they can be severe or life-threatening at the other. Even mild symptoms may signal a serious underlying gastrointestinal lesion, such as colorectal cancer, or systemic disorder, such as thyroid disease. Given the heterogeneous causes and potential severity of these common complaints, it is imperative for clinicians to appreciate the pathophysiology, etiologic classification, diagnostic strategies, and principles of management of diarrhea and constipation, so that rational and cost-effective care can be delivered.

## NORMAL PHYSIOLOGY

While the primary function of the small intestine is the digestion and assimilation of nutrients from food, the small intestine and colon together perform important functions that regulate the secretion and absorption of water and electrolytes, the storage and subsequent transport of intraluminal contents aborally, and the salvage of some nutrients that are not absorbed in the small intestine after bacterial metabolism of carbohydrate allows salvage of short-chain fatty acids. The main motor functions are summarized in [Table 55-1](#). Alterations in fluid and electrolyte handling contribute significantly to diarrhea. Alterations in motor and sensory functions of the colon result in

**TABLE 55-1** NORMAL GASTROINTESTINAL MOTILITY: FUNCTIONS AT DIFFERENT ANATOMIC LEVELS

### Stomach and Small Bowel

- Synchronized MMC in fasting
- Accommodation, trituration, mixing, transit
  - Stomach ~3 h
  - Small bowel ~3 h
- Ileal reservoir empties boluses

### Colon: Irregular Mixing, Fermentation, Absorption, Transit

- Ascending, transverse: reservoirs
- Descending: conduit
- Sigmoid/rectum: volitional reservoir

**Abbreviation:** MMC, migrating motor complex.

highly prevalent syndromes such as irritable bowel syndrome (IBS), chronic diarrhea, and chronic constipation.

## NEURAL CONTROL

The small intestine and colon have intrinsic and extrinsic innervation. The *intrinsic innervation*, also called the enteric nervous system, comprises myenteric, submucosal, and mucosal neuronal layers. The function of these layers is modulated by interneurons through the actions of neurotransmitter amines or peptides, including acetylcholine, vasoactive intestinal peptide (VIP), opioids, norepinephrine, serotonin, adenosine triphosphate (ATP), and nitric oxide (NO). The myenteric plexus regulates smooth-muscle function through intermediary pacemaker-like cells called the interstitial cells of Cajal, and the submucosal plexus affects secretion, absorption, and mucosal blood flow. The enteric nervous system receives input from the extrinsic nerves, but it is capable of independent control of these functions.

The *extrinsic innervations* of the small intestine and colon are part of the autonomic nervous system and also modulate motor and secretory functions. The parasympathetic nerves convey visceral sensory pathways from and excitatory pathways to the small intestine and colon. Parasympathetic fibers via the vagus nerve reach the small intestine and proximal colon along the branches of the superior mesenteric artery. The distal colon is supplied by sacral parasympathetic nerves (S<sub>2-4</sub>) via the pelvic plexus; these fibers course through the wall of the colon as ascending intracolonic fibers as far as, and in some instances including, the proximal colon. The chief excitatory neurotransmitters controlling motor function are acetylcholine and the tachykinins, such as substance P. The sympathetic nerve supply modulates motor functions and reaches the small intestine and colon alongside their arterial vessels. Sympathetic input to the gut is generally excitatory to sphincters and inhibitory to non-sphincteric muscle. Visceral afferents convey sensation from the gut to the central nervous system (CNS); initially, they course along sympathetic fibers, but as they approach the spinal cord they separate, have cell bodies in the dorsal root ganglion, and enter the dorsal horn of the spinal cord. Afferent signals are conveyed to the brain along the lateral spinothalamic tract and the nociceptive dorsal column pathway and are then projected beyond the thalamus and brainstem to the insula and cerebral cortex to be perceived. Other afferent fibers synapse in the prevertebral ganglia and reflexly modulate intestinal motility, blood flow, and secretion.

## INTESTINAL FLUID ABSORPTION AND SECRETION

On an average day, 9 L of fluid enter the gastrointestinal (GI) tract, ~1 L of residual fluid reaches the colon, and the stool excretion of fluid constitutes about 0.2 L/d. The colon has a large capacitance and functional reserve and may recover up to four times its usual volume of 0.8 L/d, provided the rate of flow permits reabsorption to occur. Thus, the colon can partially compensate for excess fluid delivery to the colon that may result from intestinal absorptive or secretory disorders.

In the small intestine and colon, sodium absorption is predominantly electrogenic (i.e., it can be measured as an ionic current across the membrane because there is not an equivalent loss of a cation from the cell), and uptake takes place at the apical membrane; it is compensated for by the export functions of the basolateral sodium pump. There are several active transport proteins at the apical membrane, especially in the small intestine, whereby sodium ion entry is coupled to monosaccharides (e.g., glucose through the transporter SGLT1, or fructose through GLUT-5). Glucose then exits the basal membrane through a specific transport protein, GLUT-5, creating a glucose concentration gradient between the lumen and the intercellular space, drawing water and electrolytes passively from the lumen. A variety of neural and nonneural mediators regulate colonic fluid and electrolyte balance, including cholinergic, adrenergic, and serotonergic mediators. Angiotensin and aldosterone also influence colonic absorption, reflecting the common embryologic development of the distal colonic epithelium and the renal tubules.

## SMALL-INTESTINAL MOTILITY

During the fasting period, the motility of the small intestine is characterized by a cyclical event called the migrating motor complex (MMC),