Diarrhoea and constipation in geriatric practice

Edited by
Ranjit N. Ratnaike
MD, FRACP, FAFPHM
Department of Medicine, The University of Adelaide,
The Queen Elizabeth Hospital,
Woodville, South Australia

Foreword by
Gary R. Andrews

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1 Nonimmune defences of the aging gut

Ranjit N. Ratnaike

In the elderly the nonimmunological defences of the gastrointestinal tract are an essential defence mechanism to protect the host against enteric infections. These defences, with aging, are compromised by a variety of external influences.

The nonimmunological defences are the first line of protection against enteric pathogens. The stomach, small intestine and colon are involved. Toxins are expelled by vomiting; pathogens are destroyed by gastric acid. The contact of toxins and bacteria with the small intestinal mucosa is minimized by the motility of the intestine. Pathogens which reach the colon are faced with a hostile population of commensal organisms, unwilling to relinquish their mutually beneficial relationship with their host.

Gastric defences

Vomiting

Vomiting ejects gastric contents and is the most primitive defence mechanism of the gastrointestinal tract. This powerful mechanism for 'clearing' and 'cleansing' gastric contents occurs through vigorous retrograde propulsion and is the most prominent feature of food poisoning due to ingested toxins.

The vomiting centre in the medulla is stimulated via afferent nerve impulses from chemoreceptors in the first part of the duodenum, which are sensitive to emetic substances. The ablation of this area eliminates vomiting despite the ingestion of these substances. Recent work points to an area separate from the vomiting centre in the medulla, called the area postrema or chemoreceptor trigger zone (CTZ), that is sensitive to substances circulating in the blood that cause vomiting.

Gastric acid

The gastric acid barrier is an important defence mechanism against enteric pathogens. Most organisms that cause diarrhoea are acquired orally and are susceptible to gastric acid. Rarely, infections occur due to anal intercourse, instrumentation and unsterile enemas for 'colonic irrigation'.

Gastric juice consists of water, hydrochloric acid, bicarbonate, inorganic ions (mainly sodium and potassium) and mucus, diluted with swallowed salivary juice. The pH of gastric acid and bacterial counts in the stomach show a close correlation. In normal subjects the gastric pH is usually below pH 4, a critical level for protection against enteric pathogens, and the stomach is virtually sterile. At pH 4–5 bacteria in the saliva are present in the stomach. A pH greater than 5 allows bacterial, viral and protozoan pathogens to survive.

The important relationship between gastric acidity and bacterial survival is demonstrated by experiments on human volunteers. A 10 000-fold increase in susceptibility to *Vibrio cholerae* occurs when 2 g of sodium bicarbonate is administered with the bacterial dose. The minimal infectious dose of 10^3–10^4 *Salmonella typhi* is significantly reduced by the simultaneous ingestion of sodium bicarbonate. The risk of diarrhoea due to enteric pathogens increases as the pH of gastric acid rises.

Decreased acid production may be part of the aging process and achlorhydria occurs in up to 20 per cent of subjects over the age of 60 years. A recent study challenges the view that decreased acid production is a primary feature of the aging process. Hurwitz et al. (1997) found in their elderly subjects that decreased acid secretion reflected atopic gastritis. Factors which decrease gastric acidity are pernicious anaemia, atrophic gastritis, malnutrition, gastric carcinoma and the WDHA syndrome (watery diarrhoea, hypokalaemia and achlorhydria). *Helicobacter pylori* infection may result in atrophic gastritis which could decrease the parietal cell mass to cause reduced acid output.

In the elderly the protective effect of the gastric acid barrier is further decreased by drugs used to decrease acid production or neutralize acid already secreted in the treatment of peptic ulceration, severe gastro-oesophageal reflux and the Zollinger–Ellison syndrome (H_2 receptor antagonists, proton pump inhibitors and antacids). The elevation of gastric pH with cimetidine correlates with increased numbers of gastric microflora, and ceasing treatment restores normal gastric pH and sterility within six hours. Diarrhoea has been associated with cimetidine therapy in 3 to 12 per cent of patients. Omeprazole therapy results in bacterial overgrowth in 53 per cent of patients. In the elderly, the use of H_2 blockers is reported to be a significant risk factor for carriage of *Clostridium difficile.*

Other drugs which decrease acid production are anticholinergic drugs and tricyclic antidepressant drugs.

Surgical procedures, such as gastrectomy and vagotomy to decrease gastric acidity before the era of effective oral therapy, are associated with diarrhoea. As soon as seven days after a surgical procedure for acid reduction, significant bacterial colonization occurs and persists up to six months. Gastric stasis and disordered small bowel motility are contributory. The association between partial gastrectomy

and bacterial overgrowth of pathogens in the stomach and upper small intestine and diarrhoea is well documented (see Chapter 15).

Small intestinal defences

The small intestine is a complex multifunctional organ involved in host defence. It receives gastric juice, secretes enzymes, bile and pancreatic juice and is responsible for food digestion and absorption and for the movement of luminal contents to the colon. In addition, by the strategies discussed below the small intestine protects itself from agents that adversely affect its delicate lining, the mucosa, and ultimately the host.

Motility

Motility of the gastrointestinal tract is an important defence mechanism against enteric pathogens and substances harmful to the host.

The environment of the small intestine is continuously changing and presents a hostile milieu to pathogens. Enzymes and secretions to aid digestion that are harmful to pathogens are continuously produced; enterocytes on which bacteria may adhere are constantly shed and replaced; the mucus barrier is swept away and replenished. The motility of the small intestine assists in all these activities to protect the host.

There is no evidence of significantly altered small intestinal motility associated with the aging process. Intestinal motility is associated with migrating myoelectric complexes (MMC). The MMC consists of three phases of activity:

- *Phase 1*. The quiescent phase. There is no spiking activity.
- *Phase 2*. Irregular contractive activity is initiated and increases in intensity.
- *Phase 3*. The dominant phase. Bursts of constant, intense intestinal contractions occur at the maximal frequency. Peristalsis of consecutive intestinal segments takes place. Propulsion of intestinal contents is at a peak and they are swept away in an aboral direction. This phase of the MMC has been aptly described as the 'gastrointestinal housekeeper'. These activity fronts migrate over a 90–120 min period from the antrum of the stomach to the terminal ileum in continuous succession.

The MMC, besides transporting digested food products, removes the mucus layer that is continuously replenished and prevents prolonged contact between enteric pathogens, toxins, and the mucosa of the intestine. Laboratory studies on rats have demonstrated that if the MMC is abolished with drugs (morphine and phenylephrine) for more than 6–15 hours, bacterial overgrowth develops. On cessation of the drugs and the return of the MMC, bacterial overgrowth is abolished. When motility decreases stasis occurs. The products of digestion are an ideal milieu for bacteria to multiply and cause diarrhoea.

The propulsive functions of the intestine are exaggerated when diarrhoea occurs. Increased fluid within the lumen increases motility and the rapid evacuation of intestinal contents prevents or minimizes contact between the mucosal surface of the intestine and the pathogens themselves or their toxins. This raises the question of the role of antimotility agents in the treatment of infective diarrhoea.

The systemic diseases and local conditions listed below involve the small intestine and decrease motility, leading to bacterial overgrowth and diarrhoea (see Chapter 9).

Causes of decreased small intestinal motility

- Diabetic autonomic neuropathy
- Hypothyroidism
- Amyloidosis
- Scleroderma
- Myotonia dystrophica (a hereditary condition characterized by myotonia, muscular wasting, cataracts, testicular atrophy and frontal baldness)
- Lymphoma
- Intestinal pseudo-obstruction
- Radiation enteritis

Drug therapy is also an important cause of decreased intestinal motility and is discussed in Chapter 7.

Mucus

A thick layer of mucus covers the epithelial surface of the intestine to protect the mucosa and lubricate the movement of digested food and faeces (in the colon). Mucus is synthesized and secreted by cells in the gastrointestinal tract. Mucus consists of 95 per cent water, interlinked glycoprotein molecules with a high carbohydrate content, small amounts of proteins and lipids, enmeshed micro-organisms, cells, cell debris, products of digestion and protein from gastrointestinal secretions.

The mucus layer protects the mucosa from enteric pathogens and bacterial toxins, antigens, dietary chemicals and injurious components of bile, pancreatic juice and intestinal secretions. The role of the mucus layer as a major physical impediment to enteric pathogens may be overstated. Mucus provides a barrier to those pathogens that adhere to the mucosa, and is a lubricant which coats pathogens to ease their removal from the gut by peristalsis. A more sophisticated form of protection by the mucus is directed against bacteria. The carbohydrate composition of the glycoprotein mimics the surface of the epithelial cell. Bacteria (which damage the cell by adherence) are thus misinformed, misled and entrapped by the mucus.

For bacteria that secrete a toxin, other preventive strategies are employed. Cholera toxin increases mucus production that binds the toxin and decreases

diffusion to the intestinal mucosal cells. Another protective mechanism attributed to the mucus layer is effected by lysozyme, a protein within the mucus layer that kills bacteria.

The small intestine also prevents or minimizes injury to itself and the host by the antibacterial action of bile and pancreatic secretions. Proteolytic enzymes cause bacterial lysis and in vitro some viruses are susceptible to the action of trypsin. Further protection against injury to the mucosa by bacterial adherence occurs by the constant shedding and renewal of the enterocytes.

The ileocaecal valve

The ileocaecal valve (ICV) is another possible defence mechanism of the gastrointestinal tract. The ICV at the boundary between the small intestine and the colon regulates the passage of digested food and prevents reflux of contaminated large bowel contents to the relatively sterile small intestine. This prevents bacterial colonization of the small intestine, subsequent deconjugation of bile salts, fat malabsorption and diarrhoea. This preventive role is attributed to the ICV because bacterial colony counts in the ileal region adjacent to the ICV are significantly low compared with counts in the caecum. The functions of the ICV are still in question as ileocaecal resection does not lead to altered motility of the bowel and derangement of luminal contents, nor bacterial colonization of the small intestine.

Colonic defences

Normal bacterial flora

Although intestinal infection is minimized by the mechanisms discussed, in the elderly, due to the variety of factors mentioned, many pathogens may survive and reach the colon.

The normal bacterial flora in the colon provide a further 'line' of defence. The bacterial composition of the colon is unique to each individual and is determined early in life by interactions between the host and the bacteria, and between bacteria themselves. The number and types of colonic bacteria are relatively constant throughout life. Even a major change from a nonvegetarian to a vegetarian diet does not significantly alter the species nor the number of colonic flora.

The normal colonic bacteria resist eviction to the exterior with faeces by attaching to the colonic mucosa. 'New' pathogens cannot gain occupancy in the colon as the adhesion sites are already occupied by the commensal bacteria.

These commensal bacteria in the colon form a complex well balanced ecological system to protect the host against infection by a variety of mechanisms: modification of bile acids; stimulation of peristalsis; induction of immunological responses; depletion of essential substrates from the environment; competition for

adhesion sites; creation of restrictive metabolic environments and elaboration of antibiotic-like substances. Therapy with antibiotics (see Chapter 7) affects both the pathogens for which they were intended and, unfortunately, the normal flora. In the 'ecological vacuum' that results, organisms injurious to the host, such as *Clostridium difficile,* proliferate with adverse consequences to the host (see Chapter 8).

Motility

In the colon, motility occurs through two types of waves: segmenting and propulsive. The role of colonic motility as a defence mechanism is not well established.

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