



DAVID ANDERSON

My stomach hurts!

Helping patients deal with GI issues takes detective work and flexible thinking BY MARTIN ROWLAND

Upset or sore stomachs often send patients to the frontshop aisles of their local community pharmacy for relief. Whether or not they go home with the right treatment or advice often depends on a pharmacist's counsel. In this report, we'll revisit the most common causes of gastrointestinal upset and the current recognized responses to those ailments.

DYSPEPSIA

A patient with dyspepsia will complain of abdominal pain or discomfort that is either persistent or episodic, and can

be associated with heartburn, nausea or vomiting, belching or bloating. Although up to 30% of the population can be affected by gastrointestinal (GI) upset of some kind, most sufferers do not initially seek medical advice; they will attempt to self-medicate. For approximately 60% of patients with GI upset, no functional cause for the condition will be found. Of the remainder, 15% to 25% can trace their pain to peptic ulcer disease, 5% to 15% to gastroesophageal reflux disease (GERD) and 2% are affected by a myriad of other causes ranging from pancreatitis to cancer, or by medications, alcohol or smoking.

Common medications that can cause or exacerbate dyspepsia are shown in Table 1. In many cases, when the offending agent is removed, symptoms resolve. Particular attention should be paid to the use of nonsteroidal anti-inflammatory drugs (NSAIDs), including ASA and COX-2 inhibitors. It has been estimated that up to 60% of patients on chronic NSAID therapy will experience dyspepsia, with the rate of heartburn doubled for these patients.

The annual rate of clinically significant upper GI events for patients on chronic NSAID therapy is estimated at 2.5% to 4.5%, with serious complications such as bleeding occurring at a rate of 1% to 1.5% per year. Upper GI symptoms such as heartburn or dyspepsia are very poor predictors of serious events, and the pharmacist should always be alert for signs of GI bleeding, such as melena, hematemesis or epigastric pain, and refer to a physician immediately.

Once other causes such as peptic ulcer disease or gastroesophageal reflux disease have been ruled out, proton pump inhibitors (PPIs) have been shown to be the most effective agents for dyspepsia. H2-receptor antagonists such as ranitidine or famotidine are also effective and can

Table 2

Warning signs and symptoms indicating referral to a physician

- Age >45 years
- Dysphagia (difficulty swallowing)
- Unexplained weight loss
- Palpable mass
- Melena (black, tarry stools)
- Vomiting
- Anemia
- History of previous peptic ulcer or other serious gastric disease



be recommended for short-term symptomatic relief. There is little evidence for the effectiveness of antacids, although some patients may report relief.

Other modalities that have shown benefit include the use of prokinetic agents such as metoclopramide, while also addressing any underlying anxiety. A meta-analysis showed that tricyclic antidepressants significantly helped symptoms, though it failed to differentiate between idiopathic dyspepsia and irritable bowel syndrome. Evidence for the effectiveness of selective serotonin reuptake inhibitors (SSRIs) in this context is lacking however. Although trials have suggested that turmeric or a fixed combination of peppermint and caraway may have some role in the control of dyspeptic symptoms, there is little evidence for other alternative therapies.

FLATULENCE

Excess gas can also cause bloating and discomfort. Among

Table 1

Medications and herbals commonly associated with dyspepsia

- Acarbose
- Alendronate
- Codeine
- Antibiotics (particularly erythromycin)
- Non-steroidal anti-inflammatory drugs
- Orlistat
- Potassium supplements
- Corticosteroids
- Iron supplements
- Metformin
- Theophylline
- Garlic
- Ginkgo biloba
- Feverfew
- Saw palmetto



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Table 3

Non-pharmacological measures for motion sickness

- Eat a light meal within three hours of trip
- Avoid alcohol, strong smells, dairy products and smoking
- Maximize ventilation or exposure to fresh air
- Focus on a stable, distant object and avoid other visual stimuli (e.g. reading)
- Travel in the central part of a ship or aircraft
- Drive the vehicle or travel in the front seat
- Limit head movement



be more effective. Since gas is caused by dietary factors, reducing carbonated drinks, including beer, as well as limiting sorbitol- and mannitol-containing products such as chewing gums and “dietetic” foods may be helpful. Sodium bicarbonate tends to produce gas and should not be used; other antacids have little role in relieving symptoms.

Some foods, such as beans, may produce gas due to incomplete carbohydrate digestion and alpha-galactosidase products such as Beano may be of use. This product is made from *aspergillus niger* and should not be used by patients with mould allergy. Lactose intolerance can be managed by a trial of eliminating dairy products and/or the use of a lactase-containing preparation such

the most common causes of excess gas and its consequent flatulence are excessive swallowing of air (aerophagy), intestinal fermentation of certain foods and lactase deficiency. Some gas-related conditions require physician referral.

Flatulent dyspepsia—when a patient belches repeatedly, is unable to eat a normal-sized meal and complains of abdominal dis-

tension or symptoms suggestive of GERD—is often caused by gallbladder disease. Bloating without excessive gas may be indicative of irritable bowel syndrome or other conditions such as cervical cancer, and warrants medical referral.

While simethicone is often used to treat gas, the evidence for its effectiveness is largely anecdotal and preventive strategies may

Table 4

Signs and symptoms of *c. difficile* infection

- Watery diarrhea (sometimes bloody)
- Green/mucousy stool
- Fever
- Loss of appetite
- Nausea
- Abdominal pain/tenderness
- Pseudomembranous colitis (PMC)
- Toxic megacolon



as Lactaid. If these measures are ineffective, referral to a physician should be made.

Any patient suspected of having a more serious condition should be referred to a physician. The most common of these conditions are peptic ulcer disease, GERD and cancer. See Table 2 for warning signs and symptoms that require immediate referral.

MOTION SICKNESS

Motion sickness is a common condition. It has been recognized since antiquity (the term nausea is derived from the Greek word *naus*—ship) and has been demonstrated in all forms of transportation as well as in other settings such as watching certain films or while on amusement park rides.

Motion sickness can present as the familiar nausea and vomiting group of symptoms. Sufferers may also experience hypersalivation, pallor or cold sweats. The mental-psychic group of symptoms is less common overall, but may predominate in patients with anxiety-related conditions. These symptoms may include malaise, headache, drowsiness and generally feeling miserable.

It is no longer believed that the cause of motion sickness is overstimulation of the vestibular system. Instead, the neural mismatch theory proposes that the syndrome is caused by the discordance of visual, vestibular and proprioceptive cues (i.e. motion detected by the middle ear, but not by the eyes, or vice versa).

Women are more prone to symptoms than men and incidence is increased during menses, pregnancy or when taking oral contraceptives. Overall, incidence declines with age.

Treatment remains centered on antidopaminergic agents such as promethazine or metoclopramide, antihistamines such as dimenhydrinate and meclizine, or anticholinergic agents such as scopolamine.

In Canada, dimenhydrinate is the most popular agent used for this indication and the precautions associated with this drug are well known. Dimenhydrinate is relatively short acting so may not last for a longer trip such as a transcontinental flight. In this situation, meclizine or a long-acting formulation of dimenhydrinate may be a better choice. Much of the action of the drugs may derive from antimuscarinic properties. Since these properties are largely absent from the second generation or “non-drowsy” antihistamines, such as loratadine or cetirizine, these agents are much less effective for motion sickness.

Scopolamine patches are effective but may require up to eight hours to take effect. While causing somewhat less drowsiness

than antihistamines, scopolamine may have other anticholinergic effects (particularly ocular). If eye pain occurs, the patch should be removed and medical attention sought. Occasionally, a discontinuation syndrome has been encountered after long-term use.

Alternative therapies for motion sickness include ginger or bilateral acupressure bands. Evidence for their effectiveness is anecdotal only and has not been adequately demonstrated in clinical trials. Symptoms can, however, often be ameliorated by non-pharmacological measures; these are shown in Table 3.

C. DIFFICILE DIARRHEA

The rise of antibiotic-associated diarrhea has been an increasing concern within the Canadian healthcare system. Approximately 25% of cases of antibiotic-associated diarrhea are found to be caused by *Clostridium difficile* (*c. difficile*) overgrowth in the bowel. This anaerobic gram-positive bacillus is found as a colonizing agent in around 2% of the general population but can reach up to 50% in patients hospitalized for four weeks or longer. These individuals will often remain asymptomatic until exposed to an antimicrobial agent. Symptoms may appear after an incubation period of approximately one week, but incubation periods ranging from one day to six weeks have been noted. Mortality has been estimated to be between 1% to 2%. Signs and symptoms of *c. difficile* infection are shown in Table 4 and risk factors in Table 5.

The pharmacist may be ideally placed to recognize and refer these patients for immediate medical attention, realizing that the most important factor may be a thorough history of exposure to the healthcare system and consumption of antimicrobial agents. Although certain antibiotics such as clindamycin, amoxicillin and third generation cephalosporins (such as ceftriaxone or cefotaxime) have most commonly been implicated, every currently marketed agent has been suspected as responsible for some cases. Recurrence of disease has been estimated from 5% to 40%, and a previous history of *c. difficile*-associated diarrhea is reason for suspicion of recurrence.

If *c. difficile*-associated diarrhea is suspected, ensure that no antimotility agents, such as loperamide, diphenoxylate or codeine are administered to the patient. Since the effects of the disease are caused by two toxins, A and B, produced by the microorganism, retaining these within the bowel by decreasing GI motility will prolong the course of the disease. These agents may also

cause a risk of precipitating toxic megacolon.

First-line treatment is usually metronidazole or oral vancomycin as an alternative. Since vancomycin is too large a molecule to pass through the gut mucosa, intravenous vancomycin will not reach its intended site of action and hence has no role in this disease. Fluid and electrolyte replacement solution may be safely administered ad libitum.

The use of probiotics is controversial due to the uncertain nature of some commercial preparations.

Table 5

Risk factors for *c. difficile* associated diarrhea

- Exposure to antimicrobial agents
- GI surgery/manipulation
- Extended hospital or other residential healthcare admission
- Serious underlying illness
- Immunocompromised
- Elderly
- History of previous *c. difficile* infection or colonization
- Proton pump inhibitor use (controversial)

It is thought that some preparations such as lactobacillus may help restore the normal gut flora. It seems the most effective prepa-

rations contain *Saccharomyces boulardii*, a yeast that releases a protein that interferes with the binding of toxin A to its receptor

site. Cholestyramine is a resin that is thought to bind to the toxins and is sometimes prescribed to reduce symptoms. Since it will also bind to many oral medications, the pharmacist should review the timing of the patient's entire regimen and ensure that cholestyramine is given at least one hour after or four hours before any other oral drugs. ✱

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