Gastroesophageal Reflux Disease: Approaching the Burning Issues

Mary Anne Cooper MSc, MD, FRCPC, Department of Medicine, University of Toronto; Lecturer, Sunnybrook and Women's Health Sciences Centre, Toronto, ON.

Introduction

Gastroesophageal reflux disease (GERD), the abnormal reflux of gastric and duodenal contents into the esophagus, is common. Almost 50% of the North American population experience symptoms once a month and 10% have symptoms daily.[1] Patients most commonly complain of pyrosis and regurgitation, but other symptoms such as dysphagia, chest pain and nausea are not rare.[1] As well, respiratory tract symptoms such as cough, hoarseness and asthma may be attributable to GERD (Table 1).[1,2]

Acid reflux into the esophagus is a normal physiologic event. It occurs after meals when the lower esophageal sphincter (LES) tone is reduced. The LES opens, creating a common cavity with the stomach. Because stomach pressures are higher than esophageal pressures, gastric contents reflux into the esophagus. Formal measurement with 24-hour pH monitoring indicates that the pH of the esophagus should be < 4 for < 4% of the time. Factors that increase acid contact time with the esophagus promote GERD.

GERD in the Elderly

There are reasons to suspect that GERD may be more common in older than younger people, although there are only minor intrinsic changes in the functional nature of esophageal tissue that are due to aging.[1,3] As well, age-related changes have not been documented in 24-hour pH esophageal recordings.[1] However, older people do have decreased saliva production that reduces flushing of the esophageal surface.[1,2] The elderly also are more likely to be on medication that can interfere with esophageal motility and reduce LES tone. Furthermore, older people tend to have more medical illnesses that affect esophageal motility and tone, such as stroke and neuromuscular disease.[3]

Most data indicate that the percentage of older patients (defined by the literature as ≥ 60–62 years) who complain of GERD is equivalent to that of younger patients, and that they complain of similar symptoms.[1,4] Other data, however, indicate that GERD is more common in the elderly.[5] Regardless, diagnosis of GERD on the basis of symptoms alone likely underestimates the prevalence of this condition in older patients. Older patients tend to complain less than younger patients with the same degree of injury, and esophageogastroduodenoscopy and esophageal pH monitoring indicate that older patients have more severe disease with reduced symptoms.[2,5-8] These findings may be due to altered visceral sensitivity to pain and / or distension.[2,7]

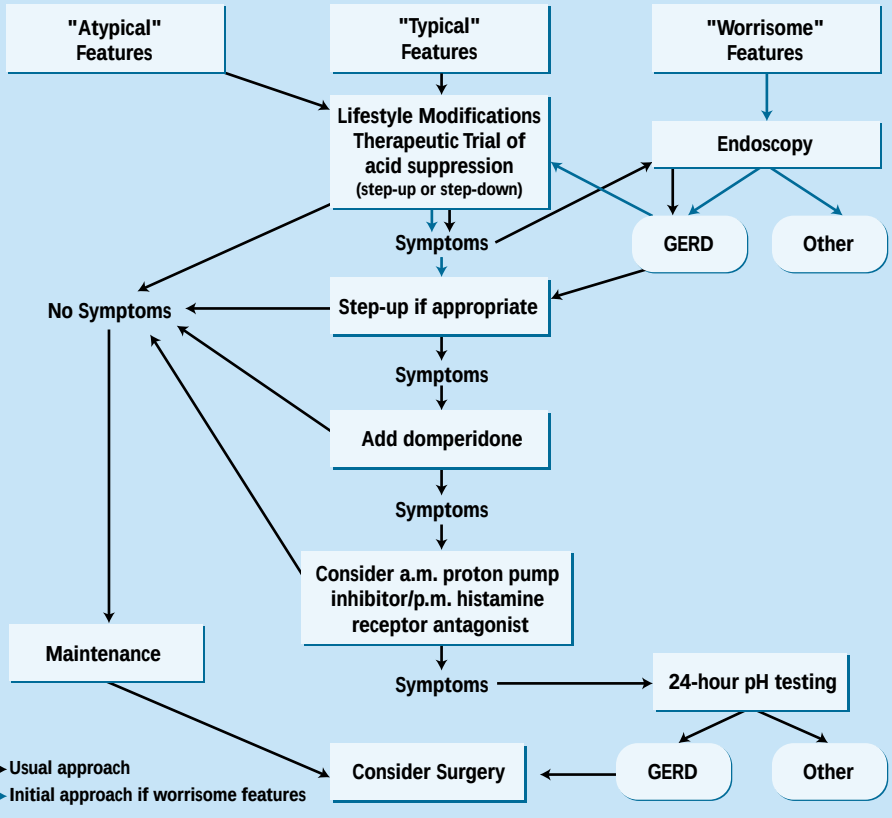
Treatment Approaches

The diagnosis and treatment of GERD are based on the patient's presentation (Figure 1). When complaints are typical, such as pyrosis or regurgitation, a trial of therapy is reasonable.[9] In fact, a successful thera-

Table 1
Symptoms of GERD

Typical	Atypical	Worrisome
Heartburn	Chest pain	Dysphagia
Regurgitation	Cough	Weight loss
	Hoarseness	
	Asthma	

Figure 1: An Approach to the Management of Gastroesophageal Reflux Disease (GERD)



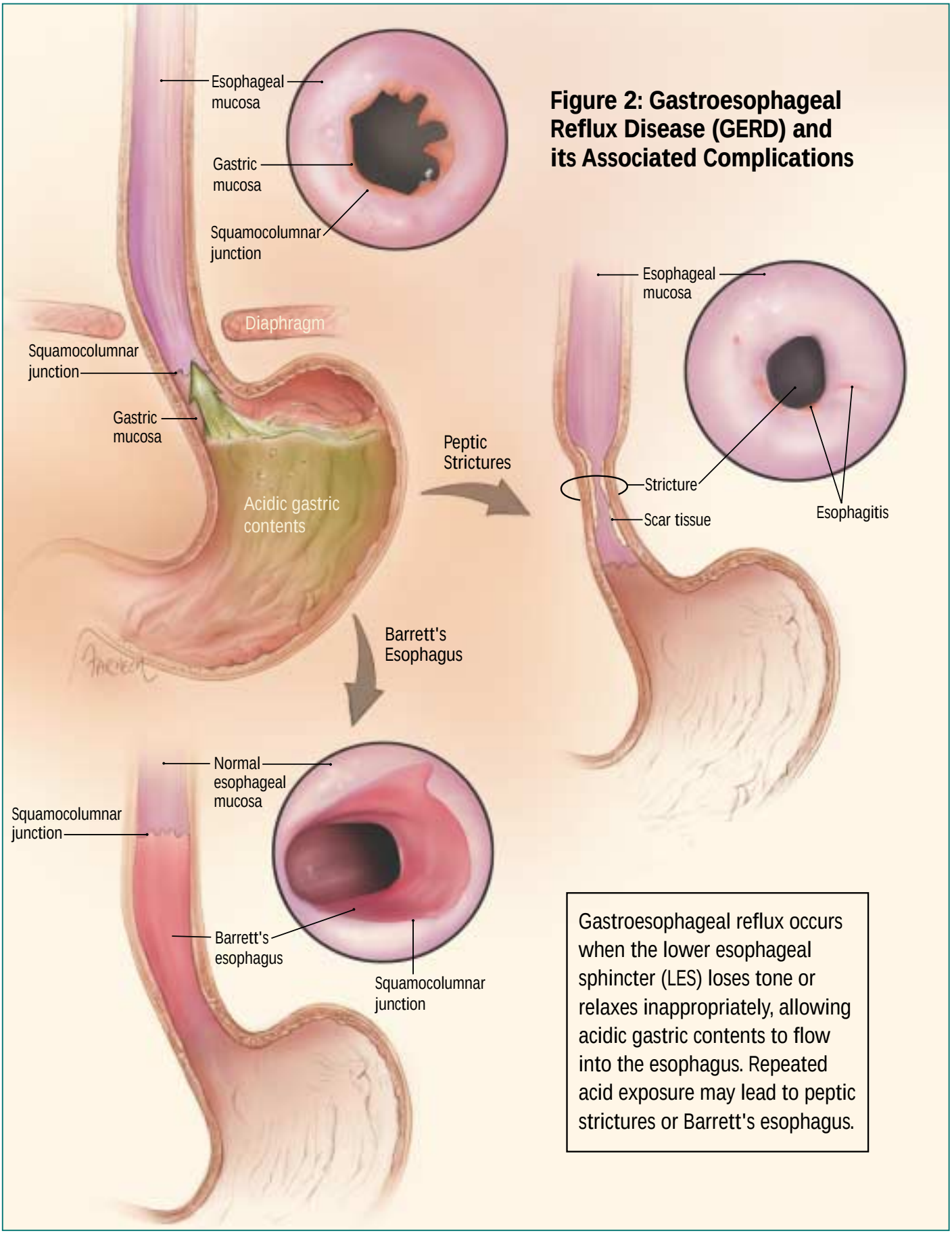


Figure 2: Gastroesophageal Reflux Disease (GERD) and its Associated Complications

Gastroesophageal reflux occurs when the lower esophageal sphincter (LES) loses tone or relaxes inappropriately, allowing acidic gastric contents to flow into the esophagus. Repeated acid exposure may lead to peptic strictures or Barrett's esophagus.

peutic trial helps confirm the diagnosis. For patients with worrisome features or who have failed a trial of therapy, further investigation is warranted. Upper gastrointestinal tract barium studies are insensitive to clinically important reflux and have limited value for GERD. Esophageogastroduodenoscopy is the procedure of choice. Although GERD does not always produce visible esophageal changes, subtle changes can be seen and features of Barrett's esophagus can be identified. Furthermore, esophageogastroduodenoscopy enables the examiner to perform therapeutic intervention (e.g., dilation of strictures), and other diseases, such as tumour or peptic ulcer disease, can be excluded.[9]

Lifestyle Modification

Treatment of GERD is directed at reducing acid contact with the esophageal mucosa. The goal of therapy is to eliminate symptoms, heal mucosal damage and prevent recurrence of symptoms and complications. This is accomplished with both lifestyle modifications and pharmacotherapy. While lifestyle changes on their own are not always sufficient, they should not be overlooked. Recommendations include:[1,9]

- elevation of the head of the bed (usually 10–15cm) to reduce nocturnal reflux events;
- avoidance of postprandial recumbency (two to three hours);
- cessation of smoking and alcohol, which reduce LES tone;
- avoidance of foods such as tea, coffee, colas and peppermints, which reduce LES tone;
- weight loss may be beneficial.

Antacids

Pharmacotherapy centres on acid reduction. It is reasonable for patients with mild symptoms to use over-the-counter (OTC) antacids such as alginic acid or OTC histamine receptor antagonists (H_2RAs). These medications may be particularly beneficial if used before known provocative activities (e.g., meals and exercise). Up to 20% of patients respond to such treatments.[9]

Acid Suppression

GERD usually requires stronger acid suppression than is provided by OTC therapies. The esophageal mucosa lacks the features that protect gastric mucosa from acid damage, such as bicarbonate secretion, mucous production and epithelial cell migration to cover areas of denudation.[5,10] Therefore, greater and longer-term acid suppression is required in patients with GERD than in those with peptic ulcer disease.

Four H_2RAs are currently available for the treatment of GERD (Table 2). They are effective in healing 50% of patients with esophagitis and provide symptomatic relief in 60%.[9] High doses of H_2RAs are usually required, however, to achieve this efficacy.[9]

It is clear from the literature that proton pump inhibitors (PPIs) provide the best acid suppression and are often required for treatment of GERD. There are now five PPIs available (Table 2), and all are equally effective. They have been shown to result in complete symptom resolution and mucosal healing in 95% of patients,[1] and are capable of doing so faster than H_2RAs.[9]

Maintenance therapy—possibly life-long—is usually needed for continued symptomatic relief, as approximately 89% of patients relapse within six months of reduction or discontinuation of their therapy.[11] Full-dose PPIs, therefore, are often required for maintenance to keep symptoms in abeyance and reduce complications.[9,11]

Side effects of PPIs appear to be mild and uncommon. There was concern with the introduction of PPIs that long-term use might give rise to carcinoid tumours because of constant antral G-cell stimulation by the profound acid suppression. While hypergastrinemia does occur (levels two to four times normal), no cases of gastrinoma attributable to PPIs have been reported within the 10 years of their use throughout North America, Europe and Australia.[9,12] Similarly, gastric acid contributes to production of a relatively sterile proximal gastrointestinal tract, yet bacterial overgrowth does not seem to occur either.[9]

While acid suppression with PPIs is profound, some people still experience breakthrough in their symptoms. This may occur if GERD is not the underlying problem or, as suggested by recent data, there may be unsuppressed nocturnal acid secretion. Such patients may require a morning PPI and a bedtime H_2RA.[11]

Prokinetic Therapy

Acid suppression is the mainstay of therapy but there may be a role for a prokinetic agent in some patients. Cisapride, a serotonin agonist, and the H_2RA ranitidine in combination have been shown to be more effective than ranitidine alone, and the combination of the PPI omeprazole and cisapride was the best of five treatment protocols for both healing and maintenance of esophagitis.[13] Cisapride is no longer available in Canada (or the United States), however, leaving us with the choice of metoclo-

Table 2
Acid Suppression Medications Used in the Treatment and Maintenance of GERD

Drug	Doses
Histamine receptor antagonists (H_2RA)	
cimetidine (Tagamet®)	800mg q.h.s. to 600mg b.i.d.
famotidine (Pepcid®)	20mg b.i.d.
ranitidine (Zantac®)	150mg b.i.d.
nizatidine (Axid®)	150mg b.i.d.
Proton pump inhibitors (PPIs)	
esomeprazole (Nexium®)	20mg o.d. to 40mg o.d.
lansoprazole (Prevacid®)	30mg o.d.
omeprazole (Losec®)	20mg o.d. to 20mg b.i.d.
pantoprazole (Pantoloc®)	40mg o.d.
rabeprazole (Pariet®)	20mg o.d.

pramide or domperidone. Both are dopamine antagonists and increase LES tone and improve gastric emptying. Metoclopramide, however, crosses the blood-brain barrier and is associated with neurological side effects that include extrapyramidal symptoms. As such, domperidone is the treatment of choice: domperidone does not cross the blood-brain barrier and so lacks the neurological side effects of metoclopramide; diarrhea is experienced in 2% of patients. Domperidone is unlikely to be beneficial as therapy alone, but may be useful when added to an H_2RA or a PPI. A typical dose of domperidone is 10mg t.i.d. or q.i.d. There is some evidence that doses of 20mg q.i.d. may be required.[14]

The Step-up or the Step-down Approach

There are two approaches to the pharmacotherapy of GERD: the "step-up" and the "step-down" approach. In the step-up approach, one uses the least amount of acid suppression and then titrates the dose to what is required for symptom control. In the step-down approach, one starts with a strong dose of acid suppression and then slowly reduces the amount to the minimum necessary. There is no evidence to suggest that one approach is of greater benefit or more economical than the other.[9,11,15] The choice of treatment approach is based on patient presentation, physician preferences and prescribing patterns and cost / medical insurance issues. From a patient's perspective, PPIs are frequently preferred as they are often effective with once-daily dosing.

Complications of GERD

Complications of GERD include peptic stricture of the esophagus and Barrett's esophagus (Figure 2). Peptic strictures can be dilated but will recur without maintenance therapy, and long-term acid suppression with PPI therapy is indicated in this situation. The time between symptomatic recurrence and the need for repeat dilation is lengthened by the use of PPIs.[3,9]

Barrett's esophagus is a condition in which the squamous epithelium of the esophagus is replaced by intestinal columnar epithelium. It is thought to be an adaptive mechanism to repeated acid exposure. Structural change does not occur and so endoscopy is required for diagnosis. This is a premalignant condition with a risk of esophageal cancer 30 times greater than baseline.[4] Although they will not reverse metaplasia, PPIs are indicated in this condition as well.

What if Patients Don't Respond to Standard Therapy?

Occasionally, patients do not respond to medical management. PPIs are so effective in managing GERD that a lack of therapeutic response should lead one to question the diagnosis. If the patient was given a trial of therapy, an esophageogastroduodenoscopy is indicated to rule out other problems, particularly an esophageal neoplasm. If this has already been done and medications are ineffective, then 24-hour esophageal pH monitoring is required to quantify acid reflux and correlate reflux events with clinical symptoms.

If the diagnosis of GERD is verified and maximal medical therapy is insufficient, antireflux surgery (fundoplication) should be considered. Surgery also may be an option in patients who can be successfully treated pharmacologically, but in whom lifelong medication is impractical or unappealing. Recently, a reversible endoscopic procedure has been developed that tightens the LES. Its reversibility and minimally invasive nature make it appealing, but long-term results remain to be seen.[1,11]

Summary

GERD is common in the general population, and may be even more prevalent in the elderly than in younger people. Most patients will respond to acid suppression, but full-dose PPIs are often required for both treatment and maintenance therapy. For patients with worrisome features or who do not respond to acid suppression, investigation with esophageogastroduodenoscopy is warranted. For patients in whom medical therapy is unsuccessful or in whom long-term medication is unacceptable, surgical therapy should be considered. ◆

No competing financial interests declared.

References

1. Linder JD, Wilcox CM. Acid peptic disease in the elderly. Gastroenterol Clinics North Amer 2001;30:363-76.
2. Fass R, Pulliam G, Johnson C, et al. Symptom severity and oesophageal chemosensitivity to acid in older and young patients with gastro-oesophageal reflux. Age Ageing 2000;28:125-30.
3. Sallout H, Mayoral W, Benjamin S. The aging esophagus. Clinics Geriatric Med 1999;15:439-55.
4. Triadafilopoulos G, Sharma R. Features of symptomatic gastroesophageal reflux disease in elderly patients. Am J Gastroenterol 1997;92:2007-11.
5. Collen MH, Abdulian JD, Chen YK. Gastroesophageal reflux disease in the elderly: more severe disease that requires aggressive therapy. Am J Gastroenterol 1995;90:1053-7.
6. Mold JW, Reed LE, Davis AB, et al. Prevalence of gastroesophageal reflux in elderly patients in a primary care setting. Am J Gastroenterol 1991;86:965-70.
7. Patel RS, Rao SSC. Biochemical and sensory parameters of the human esophagus vary with age (abstract). Am J Gastroenterol 1995;90:1567.
8. Grade A, Pullium G, Johnson C, et al. Reduced chemoreceptor sensitivity in patients with Barrett's esophagus may be related to age and not to the presence of Barrett's epithelium. Am J Gastroenterol 1997;92:2040-3.
9. DeVault KR, Castell DO. Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. Am J Gastroenterol 1999;94:1434-42.
10. Orlando RC. Why is the high grade inhibition of gastric acid secretion afforded by proton pump inhibitors often required for healing of reflux esophagitis? An epithelial perspective. Am J Gastroenterol 1996;91:1692-6.
11. Castell DO. Medical, surgical, and endoscopic treatment of gastroesophageal reflux disease and Barrett's esophagus. J Clin Gastroenterol 2001;33:262-6.
12. Klinkenberg-Knol EC, Nelis F, Dent J, et al. Long-term omeprazole treatment in resistant gastroesophageal reflux disease: efficacy, safety, and influence on gastric mucosa. Gastroenterol 2000;118:661-9.
13. Vigneri A, Termini R, Leandro G, et al. A comparison of five maintenance therapies for reflux esophagitis. N Engl J Med 1995;333:1106-10.
14. Boivin M. Role of prokinetic agents in the treatment of gastroesophageal reflux disease. Can J Gastroenterol 1993;7:414-6.
15. Goeree R, O'Brien B, Hunt R, et al. Economic evaluation of long term management strategies of erosive oesophagitis. Pharmacoeconomics 1999;16:679-97.