LEARNING OBJECTIVES
After completing this lesson, the reader will be able to:

1. Define and discuss the epidemiology of dyspepsia and symptomatic and asymptomatic peptic ulcer disease.
2. Identify the risk factors associated with peptic ulcer disease.
3. Provide evidence-based advice to patients presenting to the pharmacy with dyspeptic symptoms.
4. Provide evidence-based advice to practitioners on current management and prevention of peptic ulcer disease in high-risk patients.

To successfully complete the post-test for this lesson, you may need access to a recent edition (e.g., 2008, 2009) of the Compendium of Pharmaceuticals and Specialties (CPS) for additional information.

INSTRUCTIONS
1. After carefully reading this lesson, study each question in the post-test and select the one option you believe is the best answer. Although more than one option may be considered acceptable, only one option is the best answer.
2. To pass this lesson, a grade of at least 70% (14 out of 20) is required. If you pass, your CEU(s) will be recorded with the relevant provincial authority(ies). (Note: some provinces require individual pharmacists to notify them.)

ANSWERING OPTIONS
A. For immediate results, answer online at www.canadianhealthcarenetwork.ca.
B. Mail or fax the printed answer card to (416) 764-3937. Your reply card will be marked and you will be advised of your results within six to eight weeks in a letter from Pharmacy Practice.

NOTE: All faxed or mailed reply cards must be submitted one month before lesson expiry date.

Introduction
Upper gastrointestinal (GI) symptoms are common complaints that can lead to self-medication, visits to pharmacies and physicians, time lost from work and a reduced quality of life. Peptic ulcer disease (PUD), although decreasing in incidence, will result in any of the above scenarios, plus definitive therapy, and may result in complications requiring hospitalization. This lesson will review current management principles of dyspepsia, peptic ulcer disease, and prevention strategies in high-risk patients.
Definitions and epidemiology

Dyspepsia is a symptom complex rather than a specific disease. Patients usually present to their physician or pharmacist describing symptoms or saying, “I think I have an ulcer or indigestion.” These symptoms are subjective and may be language- and culture-dependent.1

The Canadian Dyspepsia Working Group (CanDys) agreed on the following working definition of dyspepsia: “Dyspepsia is a symptom complex of epigastric pain or discomfort thought to originate in the upper gastrointestinal tract, and it may include any of the following symptoms: heartburn, acid regurgitation, excessive burping/belching, increased abdominal bloating, nausea, feeling of abnormal fullness or slow digestion, or early satiety.”2

The term “functional dyspepsia” refers to dyspeptic symptoms lasting 12 weeks or more, within the last 12 months, in the absence of any definitive pathology found on investigation, usually meaning upper endoscopy oesophagogastroduodenoscopy (OGD) has been performed.

Dyspepsia is common. A 1994 survey of over 1,000 Canadians found that close to 40% of the population have experienced either heartburn or other symptoms of hyperacidity, in other words, dyspepsia, at least once in their lifetime. At least a third of these either self-medicating or visited a physician for the problem.3 In the United States, the point prevalence (occurring at any one time) is approximately 25%; patients having symptoms typical of reflux being excluded. For many people dyspepsia is a chronic condition.

A recent systematic review of the incidence of PUD shows that it remains a relatively common problem worldwide, with the annual incidence ranging from 0.1–0.19% for physician-diagnosed PUD, and from 0.03–0.17% for PUD diagnosed during hospitalization. This review also showed that, although declining overall, the incidence varies among countries.4 However, in terms of patients with dyspeptic symptoms, only about 5% of patients in a Canadian study who underwent OGD had an ulcer although most (43%) had evidence of esophagitis.5 Conversely, many patients found to have an ulcer will give a history of dyspeptic symptoms leading up to the diagnosis.

PATHOPHYSIOLOGY

The pathophysiology of dyspepsia and peptic ulceration encompasses a wide range of factors. Ultimately, peptic ulceration results when aggressive factors overwhelm the defensive factors of the upper GI mucosa. Classically, duodenal ulcers have been thought to be often accompanied by hypersecretion of gastric acid while gastric ulcers often occur despite normal acid secretion. In patients presenting with dyspepsia, OGD will show mainly esophagitis (43%) and peptic ulceration in considerably fewer patients (5.8%).5 The pathophysiology of this functional dyspepsia remains obscure, but the proposed mechanisms include disorder motility, altered visceral sensation, altered intestinogastric reflexes, gastric acid sensitivity and psychological distress, including abuse.6

Acetylsalicylic acid (ASA), nonsteroidal anti-inflammatory drugs (NSAIDs) and COX-2 inhibitors are the drug classes most commonly linked to dyspepsia and ulceration. Few other commonly used drugs, with the possible exception of calcium channel blockers (CCBs), have been studied in such a way as to provide a reasonable causative link to dyspepsia. In one study, patients taking PPIs were much more likely to have started taking CCBs in the previous month than other drugs. CCBs are known to cause reflux, however, and the PPI may have been started specifically for heartburn.7 Corticosteroids and bisphosphonates are often mentioned as causes of peptic ulceration, bleeding, and perforation but the evidence suggests the risk is low or non-existent for both drug classes.8,9

Prostaglandins (PGs) are known to be essential in maintaining the integrity of the upper GI mucosa. They have been shown to increase mucus secretion, increase minute amounts of bicarbonate that remains under the mucus and allow normal endothelial cell turnover.10 ASA, NSAIDs and, to a much lesser extent, COX-2 inhibitors decrease the production of the PGs. A “topical” or “irritant” effect of these drugs on the gastric mucosa is often mentioned but the proof such an effect exists has not yet been proven.

NSAID-specific risk factors for GI complications include dosage, duration, the specific NSAID compound and possibly 2C9 cytochrome polymorphisms, which can result in slower metabolism of many NSAIDs.11 The World Health Organization (WHO) has conducted a meta-analysis12 of studies to ascertain the risk of GI complications with specific NSAIDs

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**Table 1**

Relative risk of developing a GI complication from a specific NSAID according to a meta-analysis by the WHO11

<table>
<thead>
<tr>
<th>DRUG</th>
<th>RELATIVE RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td>indomethacin</td>
<td>2.25</td>
</tr>
<tr>
<td>naproxen</td>
<td>1.83</td>
</tr>
<tr>
<td>diclofenac</td>
<td>1.73</td>
</tr>
<tr>
<td>piroxicam</td>
<td>1.66</td>
</tr>
<tr>
<td>ibuprofen</td>
<td>1.43</td>
</tr>
<tr>
<td>meloxicam</td>
<td>1.24</td>
</tr>
</tbody>
</table>

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**Table 2**

Factors increasing the risk of GI complications from NSAIDs/ASA11

- Age > 65 years
- Prior peptic ulcer
- High NSAID dosage
- Concurrent anticoagulants
- Concurrent corticosteroids

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Dyspepsia and peptic ulcer disease: clinical pathophysiology and current management

(1). However, not all patients who receive these drugs develop ulcers and additional risk factors have been identified, mainly through case-control studies (Table 2). The more risk factors the patient has, the greater likelihood of ulceration and complications such as bleeding. The single most common risk factor is age over 65 years.

Helicobacter pylori, a gram-negative bacterium, (Table 1) can cause gastritis, peptic ulcers and dyspeptic symptoms. This organism is uniquely adapted for survival in the acidic environment of the stomach, producing alkaline ammonia from urea found in most body fluids. It has been estimated that half of the world’s population is infected with H. pylori, commonly found in the elderly and people from developing countries. Interestingly, it can produce acid hypersecretion and duodenal ulceration in some patients, chronic gastritis leading to gastric ulcers or gastric cancer in others. The percentage of ulcers diagnosed in North America as H.pylori-positive is decreasing but is still greater than 50%.

The prevalence of ulcer disease appears to be increased in patients with certain chronic diseases including COPD, renal disease and alcoholic cirrhosis, but no such association has been established for drinkers without cirrhosis. No study has established a convincing link between diet and PUD. Heavy cigarette smoking is a risk factor for PUD and its complications. The mechanism could be decreased prostaglandin production found in the gastric mucosa of smokers. There is conflicting data on whether emotional stress plays a role in causing or exacerbating PUD.

Zollinger-Ellison syndrome is a rare condition in which pancreatic endocrine tumours secrete gastrin, a hormone that causes the production of high levels of gastric acid. The excess gastric acid leads to the development of multiple peptic ulcers.

Assessment of patients

Many patients with dyspepsia consult a pharmacist or a general practitioner about their symptoms not only because they want relief but also because they may fear some serious disease. Thus, it is important for the pharmacist to know what information to obtain from the patient in order to make the most appropriate recommendation.

The CanDys working group developed an easy five-step inquiry to determine the most suitable management option for the patient (Table 3). These questions focus on: 1) the source of the symptoms (GI or non-GI causes) 2) the presence of alarm features, 3) recent and regular intake of ASA/NSAID/COX-2 inhibitor, 4) dominant symptoms (heartburn and/or regurgitation), and 5) the possibility of H. pylori infection.

The patient’s responses will determine if a trial of a medication is suitable, if discontinuation of a potential offending agent is warranted, or if further investigation and the urgency of follow-up, is more appropriate. Many patients have ulcer-like pain but subsequently are not found to have an ulcer on definitive investigation with endoscopy or imaging studies. However, abdominal pain is the cardinal symptom of peptic ulcer disease.

The pain of duodenal ulceration is described as “burning” or “gnawing” in

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Adjusted OR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>nsNSAID users alone</td>
<td>1.00</td>
</tr>
<tr>
<td>High-intensity NSAID use (&gt;1 standard dose/day)</td>
<td>1.48</td>
</tr>
<tr>
<td>nsNSAID + PPI</td>
<td>0.50</td>
</tr>
<tr>
<td>Celecoxib alone</td>
<td>0.34</td>
</tr>
<tr>
<td>nsNSAID + low-dose misoprostol**</td>
<td>0.61</td>
</tr>
<tr>
<td>nsNSAID + high-dose misoprostol</td>
<td>0.42</td>
</tr>
<tr>
<td>COX-2 inhibitor + PPI</td>
<td>0.23</td>
</tr>
<tr>
<td>H2-antagonists</td>
<td>1.34</td>
</tr>
</tbody>
</table>

ns = non-selective, OR=odds ratio
* mainly as Arthrotec®
95% Confidence intervals omitted

Relative risk for admission to hospital for upper GI complications due to peptic ulcer (736 patients)
**table 6**

<table>
<thead>
<tr>
<th>Cardiovascular and GI risk groups and recommended anti-inflammatory drug and cytoprotection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low GI risk*</td>
</tr>
<tr>
<td>Low CV risk (no ASA)</td>
</tr>
<tr>
<td>High CV risk (on ASA)</td>
</tr>
</tbody>
</table>

* GI risk is arbitrarily classified as low, high and very high if the annualized ulcer complication rates are <1% (e.g., 20–64 years), 1–5% (e.g., older ages), and >5% (e.g., multiple risk factors, prior ulcer bleeding), respectively.

**table 7**

**Causes of “H. pylori, NSAID, ASA-negative” ulcers**

- Missed *H. pylori* infection
- Unrecognized NSAID/ASA usage
- Other medications
- Crohn’s disease
- Neoplasm/lymphoma
- Severe systemic disease
- Zollinger-Ellison syndrome

**table 8**

**Changes in absorption of some drugs in association with the concomitant administration of PPIs or H2-antagonists**

<table>
<thead>
<tr>
<th>Decreased Absorption</th>
<th>Removed H. pylori-positive patient successfull will lessen the likelihood of recurrence of the ulcer should the inflammatory drug or ASA be re-instituted.</th>
</tr>
</thead>
<tbody>
<tr>
<td>itraconazole</td>
<td>acetaminophen</td>
</tr>
<tr>
<td>atazanavir</td>
<td>dipyriramole</td>
</tr>
<tr>
<td>Increased Absorption</td>
<td>naproxen+ PPI/miso</td>
</tr>
<tr>
<td>nifedipine</td>
<td>digoxin</td>
</tr>
<tr>
<td>alendronate</td>
<td>dopamine</td>
</tr>
</tbody>
</table>

*Studies carried out in normal volunteers and/or clinical outcomes not assessed

- Patients with gastric ulcers also describe “burning” or “gnawing” pain in the epigastrium. This pain occurs sooner after meals than duodenal ulcer pain, and may actually be worsened by food. Vomiting may bring relief from the pain.

- The presence of peptic ulcers can be confirmed only by endoscopy or barium swallow imaging. Many patients may be told by their physicians that, based on their symptoms, they have an ulcer and treat it as such; however, that diagnosis is uncertain unless one of the above-mentioned investigations is carried out. Most older patients who are found to have an ulcer should be tested for *H. pylori* as the presence of the organism is higher in older patients. Even if the older patient found to have ulcer has been taking an NSAID or ASA, treating an *H. pylori*-positive patient successfully will lessen the likelihood of recurrence of the ulcer should the inflammatory drug or ASA be re-instituted.

- Some patients who present to hospital with upper GI bleeding have no previous symptoms of ulcer disease; this seems to be especially true in the elderly taking ASA, NSAIDs or COX-2 inhibitors. Pharmacists should appropriately inform older patients who are starting these drugs about the possibility of dyspeptic symptoms, but, more importantly, advise them to stop taking the drug at the first sign of black stools (melena) or vomiting blood and seek emergency care.

**Management of the patient with un-investigated dyspepsia**

This patient presents to their pharmacist or general practitioner seeking an explanation for their symptoms and an appropriate treatment, if necessary.

An antacid or OTC H2 blocker can be suggested initially when there are no alarm features mentioned by the patient, if the dyspeptic symptoms are infrequent or if there might be a delay in seeing their physician, that should be the recommendation. For the patient who gives a history of being on ASA, an NSAID, COX-2 inhibitor, and possibly a calcium channel blocker, the healthcare professional must determine if the offending agent can be discontinued. In the case of ASA, the exact indication for the drug must be known because this will determine if the drug can be stopped, even temporarily. A discussion with the patient’s cardiologist or neurologist may be required. Often, NSAIDs and COX-2 inhibitors can be discontinued temporarily to determine if they are the cause of the dyspepsia.

Studies of the prevention of NSAID-related ulcers have shown that adequate acid suppression lowers the frequency of ulcer development and reduces dyspepsia. Regardless of whether the dyspepsia disappears on the discontinuation of the anti-inflammatory agent or ASA, patients require treatment or prevention of further dyspeptic symptoms if the offending agent has to be restarted.

Strategies for the primary prevention of GI adverse events in NSAID/ASA users include co-therapy with PPIs or prostaglandin analogues and eliminating other risk factors, such as *H. pylori*. Several other approaches, including the use of clopidogrel instead of ASA for primary or secondary prevention of coronary artery disease, the use of H-2 antagonists or sulcrate, and the preferential use of enteric-coated or buffered ASA, have been shown to be ineffective.
for the prevention of PUD or its complications (Table 4).15

Both co-administration of high-dose (600–800 micrograms/day) misoprostol and the use of COX-2 inhibitors have been shown to reduce the risk of upper GI complications among long-term users of NSAIDs.13,16 While the use of PPIs or low-dose misoprostol can reduce the incidence of asymptomatic ulcers and erosions, there are no randomized controlled trials to show that these agents reduce the risk of NSAID-related upper GI complications. Nonetheless, the data from these studies are often extrapolated by practitioners to the use of any of these strategies to reduce the incidence of dyspepsia in patients taking NSAIDs or ASA, with the assumption that there will be a reduction of ulcers also. A recent study using the Manitoba Population Health Research Data Repository17 has shown that most of these gastroprotective strategies are also effective in protecting patients from symptomatic ulcers and upper GI bleeding in a "real life" setting (Table 5).

Physicians and pharmacists, however, must do a better job of providing high-risk NSAID/ASA users with gastroprotective therapy; several studies have shown under-utilization of these beneficial drugs in high-risk patients.18 Given the current concern about the cardiovascular toxicity of NSAIDs and COX-2 inhibitors, it is now suggested that both the patient’s cardiovascular risk factors and ulcer risk be considered when choosing an anti-inflammatory.19 (Table 6)

The patient with dyspepsia whose dominant symptom is heartburn or acid regurgitation most likely has gastroesophageal reflex disease (GERD). This paper will not discuss these patients. Readers may access other current reviews or guidelines to guide their management of these patients.20,21

Patients with dyspepsia who are either from a high-prevalence population, such as those from a developing nation, or who are under 50 years of age and without any other alarm features, can undergo a test-and-treat strategy for H. pylori. If the test is positive, the patient should be treated with either an approved regimen or one that has at least been tested in a randomized controlled trial.

In accordance with the recommendations of the Canadian Helicobacter pylori Consensus Conference,2 first-line eradication therapies are three-drug combination treatments consisting of a PPI in a standard dose with either clarithromycin plus amoxicillin or clarithromycin plus metronidazole, all taken twice daily for one week. These regimens usually result in an 80% eradication rate.2 Factors that have been identified as contributing to treatment failure are non-adherence to the regimen, antibiotic resistance and accelerated metabolism of the PPI. Other guidelines recommend 10–14 days of therapy but there is no overall universal recommendation, yet.

Sequential therapy is a new concept in eradication therapy. The most tested sequence consists of a PPI and amoxicillin 1 g (both twice daily) administered for the first five days followed by triple therapy consisting of the PPI, clarithromycin 500 mg and tinidazole 500 mg (all twice daily) for the remaining five days. One trial of this regimen versus a standard regimen was significantly more effective in patients with a clarithromycin-resistant strain of H. pylori. A recent meta-analysis of 10 trials found an eradication rate of 93.4% (95% CI:91.3–95.5) compared to an eradication rate of 76.9% (95% CI:71–82.8) with standard triple therapy.22 Presumably, metronidazole could be substituted for the tinidazole, which is not available in North America, should one of these regimens be prescribed by a gastroenterologist.

Salvage therapies after failure of initial treatment regimens can include use of any of the following: antibiotics such as levofloxacin or rifabutin, increasing the number of days of therapy to 10–14, doubling the dose of the PPI, or instituting quadruple therapy with a PPI, bismuth, tetracycline and metronidazole, if the latter regimen was not used as initial therapy. Several of these strategies, such as increasing both the PPI dose and the length of therapy may be used concurrently but there is currently no consensus which of these strategies should be tried first.

The use of combination therapy for the treatment of H. pylori, especially in the form of single, convenient dispensing formats may lead to a lack of attention of possible drug interactions with all drugs involved, so pharmacists must ensure the patient’s present drug regimen will not be affected by any of the agents in the H. pylori eradication regimens.

Most clinical trials of drug therapy for dyspepsia have assessed patients with functional dyspepsia, which means they have been found to have a normal gastric and duodenal mucosa on endoscopy. Whether the data from these trials can be extrapolated to patients with uninvestigated dyspepsia who present to the pharmacist or general practitioner for the first time is unknown. In summary, these trials show that antacids are no more effective than placebo, H-2 antagonists or a prokinetic agent (cisapride was used in the studies), provide modest benefit over placebo, and PPIs (mainly omeprazole) were more effective than an alginate product (i.e., Gaviscon) or H-2 antagonists.2

A Dutch group recently attempted to determine the most cost-effective empirical strategy for initial management of dyspepsia in the primary care setting. They compared a step-up regimen of antacids, ranitidine 150 mg twice daily and pantoprazole 40 mg daily to a step-down (reverse order) approach. Patients used the next ‘step’ therapy when there was insufficient response to the previous one. Over six months, both approaches were equally effective in patients with new-onset dyspepsia. Although the costs of the step-up approach were lower, the earlier response of patients to treatment in the step-down group may influence...
decisions on treatment choice in everyday practice.23,24

**Peptic ulcer disease**

Acid suppression remains the cornerstone for the treatment of PUD, whether as part of an *H. pylori* eradication regimen, NSAID/ASA-induced ulcers, or other less common causes of the ulcers.25 Ulcers not caused by NSAID/ASA/Cox-2 inhibitors may demand the involvement of a gastroenterologist (Table 7).

An approved or evidence-based *H. pylori* regimen, as outlined above, should be used when the test is positive. Eradication should be documented with the urea-breath test (UBT) when an ulcer has been diagnosed; any acid-suppressing drugs, especially PPIs, should be discontinued at least two weeks before the UBT, as they can lead to a false-negative test, and a possible recurrence of the ulcer if the organism has not actually been eradicated.

An NSAID/ASA-induced ulcer should be treated with the most effective acid suppressing drugs available, a PPI. Ulcer healing may be accelerated by discontinuing the NSAID, even temporarily.

NSAID/ASA peptic ulcers and other, less common non-*H. pylori* ulcers should be treated for four to eight weeks. Generally speaking, duodenal ulcers should be treated for four to six weeks and gastric ulcers for six to eight weeks and PPIs give superior healing rates compared to H-2 antagonists.

Patients who present with a bleeding ulcer will benefit from endoscopic therapy, such as epinephrine injection of the ulcer, and concurrent intravenous pantoprazole or high-dose oral PPI for 72 hours before stepping down to standard oral PPI dosing.26,27

**Selected adverse effects and drug interactions of acid suppression due to PPIs**

Generally, PPIs as a class of drugs have been thought to be relatively free of major adverse effects and drug interactions. Recent information suggests that the prescribing and subsequent monitoring of these drugs requires more attention.

The use of PPIs is associated with community-acquired pneumonia (CAP), *C. difficile* diarrhea, and hip fractures.26-30 All of these associations can be explained by profound acid suppression which can lead both to the colonization of the upper GI tract with pathogens and a decreased absorption of calcium. The types of studies carried out to make these associations can be criticized for the usual biases inherent in observational and case-control studies. However, they do have biologic plausibility and thus should at least cause practitioners to consider both, the initial prescription, and re-evaluation of their continued use in all patients who are candidates for the potential benefits of this class of drugs. Nonetheless, patients can be assured that the risk of the above adverse outcomes is low.

Alteration of gastric acid secretion and the resulting change in intra-gastric pH has been shown to affect the rate and extent of absorption of several drugs. A recent systematic review of the literature has found that the efficacy and toxicity of several important drugs (Table 8) could be changed by the addition of acid-suppression therapy.31 Because the magnitude of the interaction in any given patient is unpredictable, an assessment of the need for the acid suppression therapy must occur in every patient. A decrease in acid secretion can also reduce the absorption of some micronutrients, such as vitamin B12, iron and calcium; in certain patients, this could lead to clinical manifestations of deficiency.

Several recent studies have documented a harmful interaction between clopidogrel (Plavix) and certain PPIs. Clopidogrel reduces the risk of atherothrombotic events in patients with acute coronary syndrome and those undergoing percutaneous coronary intervention. Some of these patients may also require ASA as part of their therapy and PPIs may be indicated for ulcer prevention. Clopidogrel is a pro-drug that must be activated by several cytochrome P450 enzymes, including 2C19, the enzyme required for the metabolism of several PPIs. Increased hospitalization for recurrent MI has been found in patients receiving the antiplatelet drug and either omeprazole, lansoprazole, and rabeprazole but not with pantoprazole.22,23 Again, the types of studies carried out to show this interaction may have the usual biases found in observational and case-control studies. However, until further definitive studies are carried out to determine the validity and extent of this interaction, patients receiving clopidogrel should not receive omeprazole. Patients already receiving this combination should be switched to pantoprazole or, if appropriate, an H-2 antagonist, as no members of this latter class of acid suppressor is metabolized by 2C19. The delayed recognition of this interaction (clopidogrel has been on the market for approximately eight years) should encourage regulatory bodies and the pharmaceutical industry to more rigorously investigate the possibility of drug (activation) interactions with pro-drugs during preclinical trials.

**Summary**

Dyspepsia is a common complaint among adults and they will frequently present to a pharmacy or their general practitioner seeking answers and relief. Each patient must be asked a set of important questions in order to determine the correct management strategy. A recent Belgian study34 showed that pharmacists can direct a majority of patients with dyspepsia to appropriate care using a similarly structured
approach. Patients starting NSAIDs/ASA must be assessed for both their cardiovascular and GI risks with these drugs. *H. pylori*, although decreasing in prevalence, still presents a challenge in eradication and some new, but more complex, regimens show promise in increasing eradication rates. PUD is less common today but appropriate therapy must be based on the etiology. PPIs remain the most useful agent in many cases of dyspepsia and ulcers but recent information about new risks of adverse effects and interactions must be considered before prescribing and dispensing them, and mandates an intermittent re-evaluation of their value in any given patient.

Questions

To answer online, go to www.canadianhealthcarenetwork.ca, CE section, CE Online, Pharmacy Practice

**1.** What is the incidence of dyspepsia in Canada?
   a. 10–15%  
   b. 20–25%  
   c. 35–40%  
   d. 60–75%

**2.** Which of the following symptoms is NOT considered in the definition of dyspepsia?
   a. heartburn  
   b. nausea  
   c. abdominal bloating  
   d. hiccups

**3.** If 100 patients complaining of abdominal pain for the first time are sent to a gastroenterologist for endoscopy, approximately how many will actually be found to have a peptic ulcer?
   a. 5  
   b. 20  
   c. 40  
   d. >50

**4.** Besides NSAIDs and ASA, prescribing of which class of drugs was found to be disproportionately followed by a prescription for a PPI, suggesting drug-induced dyspepsia?
   a. ACE inhibitors  
   b. calcium channel blockers  
   c. vitamin K antagonists  
   d. corticosteroids

**5.** Several studies have looked at the rate of GI complications after ingestion of specific NSAIDs. Which of the following was usually shown to have the highest rate of upper GI complications?
   a. ibuprofen  
   b. meloxicam  
   c. diclofenac  
   d. indomethacin

**6.** Which of the following patients would most likely develop an ulcer from taking 325 mg ASA daily after their coronary bypass surgery?
   a. a 70-year-old man  
   b. a 48-year-old man with a history of dyspepsia  
   c. a 55-year-old woman with a history of ASA intolerance  
   d. a 60-year-old woman taking alendronate

**7.** Which of the following clinical conditions has NOT been linked to *H. pylori* infection?
   a. gastroesophageal reflux disease  
   b. chronic gastritis  
   c. peptic ulcer  
   d. gastric cancer

**8.** Based on evidence, patients should be told to avoid/stop which of the following to lessen their risk of getting a peptic ulcer?
   a. alcohol  
   b. caffeine  
   c. smoking  
   d. spicy food

**9.** Which of the following symptoms would prompt you to refer a patient who is complaining of some dyspeptic symptoms to their general practitioner?
   a. excessive belching  
   b. nighttime heartburn  
   c. difficulty swallowing  
   d. sour taste in mouth

**10.** Which of the following would be the most important to tell a 61-year-old woman who is starting to take naproxen 500 mg bid?
   a. take each pill with food  
   b. go to the ER if you develop black stools  
   c. take each pill with some antacid  
   d. do not crush the pills before ingesting

**11.** MS is a 66-year-old man who is about to be discharged from the hospital after an episode of acute coronary syndrome with a prescription for ASA 325 mg daily. Which of the following would be the most effective strategy to prevent a future peptic ulcer in MS?
   a. take the ASA with food  
   b. make sure it is an enteric-coated product  
   c. MS should also have a prescription for an H2-antagonist  
   d. MS should also have a prescription for a PPI

**12.** A 67-year-old patient who already takes ASA 81 mg daily for unstable angina requires an anti-inflammatory agent. Which of the following would be the most appropriate for this patient?
   a. naproxen  
   b. naproxen plus a PPI  
   c. celecoxib  
   d. celecoxib plus a PPI

**13.** Which of the following patients would most likely benefit from a test for *H. pylori* and subsequent treatment if the test result is positive?
   a. a 35-year-old man with predominant symptoms of heartburn  
   b. a 55-year-old woman complaining of dysphagia  
   c. a 41-year-old woman with first time symptoms of dyspepsia  
   d. a 46-year-old woman on an NSAID for a month with dyspeptic symptoms

**14.** All of the following statements are true about step-up/step-down therapy for the treatment of uninvestigated dyspepsia EXCEPT:
   a. Step-up therapy is slightly more cost-effective than step-down therapy.  
   b. Step-down therapy gives better initial symptom control.  
   c. The first agent in the step-up program is an antacid.  
   d. The step-down regimen involves using a PPI and an H2-blocker at the same time.

**15.** A 68-year-old man is found to have a bleeding gastric ulcer; he has taken ASA 325 mg daily since his coronary bypass operation about three months ago. The ASA is stopped and he is placed on a PPI for six weeks; endoscopy at six weeks shows the ulcer has healed. Which of the following is the most appropriate management strategy now?
   a. start ASA 325 mg plus a PPI  
   b. start ASA 81 mg daily  
   c. start clopidogrel 75 mg daily  
   d. start ASA 81 mg daily plus an H2-blocker

**16.** A 58-year-old woman is re-started on a PPI because her dyspeptic symptoms have returned. She says she saw on the Internet that PPIs are not proven as causative. Which of the following would be the most appropriate response to her concerns about using the PPI long-term?
   a. Suggest she take extra calcium tablets and avoid individuals who appear to be “sick.”  
   b. Suggest she get “flu” and “pneumonia” shots and take extra calcium tablets.  
   c. Suggest she not take the PPI and just use antacids.  
   d. Tell her the risk of these complications is low and PPIs are not proven as causative.
1. A 48-year-old man has had a coronary stent placed after an abnormal cardiac catheter examination. He has a history of gastric ulcers and takes a PPI. He presents to your pharmacy with a prescription for clopidogrel. Based on current evidence, his PPI should be changed, if necessary, to:
   a. omeprazole
   b. pantoprazole
   c. lansoprazole
d. esomeprazole

2. Which stroke prevention drug may be less effective when taken with a PPI?
   a. ASA
   b. ASA/extended-release dipyriramole (Aggrenox®)
c. ticlopidine
d. warfarin

3. A 69-year-old man is being treated with an approved anti-H. pylori regimen for an H. pylori-positive duodenal ulcer. Four weeks after the initial prescription was given, he still has some symptoms and a urea breath test shows ongoing H. pylori infection. All of the following have been associated with reduced effectiveness of the approved anti-H. pylori regimens EXCEPT:
   a. poor adherence to regimen
   b. antibiotic resistance
c. rapid metabolism of the PPI
d. taking concurrent probiotics

4. Which of the following is NOT a documented or proposed useful strategy for re-treatment of H. pylori?
   a. double the dose of the PPI
   b. change the antibiotic combination
c. give the antibiotics intravenously
d. change to a bismuth-containing regimen

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**References**


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**This lesson is valid until November 10, 2012.** Information about dyspepsia and peptic ulcer disease, clinical pathophysiology and current management, may change over the course of this time. Readers are responsible for determining the most current aspects of this topic.

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