Gastrointestinal Disorders

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Learning Objectives

1. Review and apply national guideline treatment strategies to the following gastrointestinal (GI) disorders: gastroesophageal reflux disease (GERD), peptic ulcer disease (PUD), ulcerative colitis (UC), Crohn disease (CD), viral hepatitis, chronic liver disease, constipation, diarrhea, irritable bowel syndrome (IBS), nausea, vomiting, pancreatitis, and upper GI bleeding, including prevention of stress-related mucosal disease (SRMD).

2. Recommend appropriate pharmacologic and nonpharmacologic interventions for the management of GERD.

3. Differentiate between clinical signs, symptoms, risk factors, and treatment of PUD associated with both *Helicobacter pylori* and nonsteroidal anti-inflammatory drugs.

4. Discuss the role of pharmacologic intervention in the treatment of nonvariceal upper GI bleeding and the prevention of SRMD.

5. Review the clinical differences in signs, symptoms, and treatment of CD and UC.

6. Identify the common manifestations of chronic liver disease and their treatment.

7. Review the treatment and prevention of both acute and chronic viral hepatitis.

8. Recognize pertinent information for educating patients and prescribers about the appropriate use of pharmacologic agents for various GI disorders.

9. Recommend appropriate pharmacologic and nonpharmacologic interventions for diarrhea and constipation.

10. Review recommendations for the treatment and prevention of nausea and vomiting.

11. Discuss the clinical and treatment differences between acute and chronic pancreatitis.

12. Discuss the role of pharmacologic intervention in the treatment of IBS.

13. Discuss commonly encountered statistical tests and concepts, using GI disorders as examples.

Self-Assessment Questions

*Answers and explanations to these questions can be found at the end of the chapter.*

1. A 58-year-old African American man presents with a 2-month history of burning epigastric pain and intermittent difficulty swallowing. The pain is unrelieved by positional changes or by eating, and he has tried over-the-counter (OTC) antacids with minimal relief. He takes amlodipine 5 mg/day for hypertension and ibuprofen 5 mg/day for ibuprofen for occasional back pain. Which is best for this patient?

   A. Initiate famotidine 20 mg/day.
   B. Refer for possible endoscopic evaluation.
   C. Initiate omeprazole 20 mg twice daily.
   D. Change amlodipine to hydrochlorothiazide.

2. A 50-year-old woman is seen today in the clinic for severe pain related to the swelling of three of her metacarpophalangeal joints on each hand and swelling of her right wrist. She is unable to write or perform her usual household activities. Radiograms of these joints reveal bony decalcifications and erosions. A serum rheumatoid factor is obtained, which is elevated. Her medical history includes type 2 diabetes mellitus, hypertension, and dyslipidemia. Her medications include metformin 1000 mg twice daily, glyburide 10 mg/day, metoprolol 100 mg twice daily, aspirin 81 mg/day, and rosuvastatin 5 mg/day. The primary care provider would like to initiate systemic anti-inflammatory therapy for this patient’s rheumatoid arthritis with high-dose nonsteroidal anti-inflammatory drug (NSAID) therapy; however, the primary care provider is worried about potential gastrointestinal (GI) toxicity. Which regimen is best for treating this patient’s pain while minimizing the risk of GI toxicity?

   A. Celecoxib 400 mg twice daily.
   B. Indomethacin 75 mg/day plus ranitidine 150 mg/day.
   C. Naproxen 500 mg twice daily plus omeprazole 20 mg/day.
   D. Piroxicam 20 mg/day plus misoprostol 600 mcg three times/day.
3. A 68-year-old Hispanic man is assessed in the emergency department for a 36-hour history of black, tarry stools; dizziness; confusion; and vomiting a substance resembling coffee grounds. He has a medical history of osteoarthritis, hypertension, myocardial infarction (MI) in 1996 and 1998, and seasonal allergies. He has been taking naproxen 500 mg twice daily for 4 years, metoprolol 100 mg twice daily, aspirin 325 mg/day, and loratadine 10 mg/day. Nasogastric (NG) aspiration is positive for blood, and subsequent endoscopy reveals a 3-cm antral ulcer with a visible vessel. The vessel is obliterated using an epinephrine solution, and a rapid urease test is negative for *Helicobacter pylori*. Which recommendation is best for this patient?

- A. Intravenous ranitidine 50 mg/hour for 5 days.
- B. Sucralfate 1 g four times/day by NG tube.
- C. Oral lansoprazole 15 mg/day by NG tube.
- D. Pantoprazole 80 mg intravenous bolus, followed by an 8-mg/hour infusion.

4. A 38-year-old white woman presents with an 8-week history of new-onset cramping abdominal pain together with two to four bloody stools per day. She has a medical history of urinary tract infection and reports an allergy to “sulfa”-containing medications (shortness of breath). Colonoscopy reveals diffuse superficial colonic inflammation consistent with ulcerative colitis (UC). The inflammation is continuous and extends to the hepatic flexure. Which drug therapy is best?

- A. Sulfasalazine 4 g/day.
- B. Hydrocortisone enema 100 mg every night.
- C. 6-mercaptopurine (6-MP) 75 mg/day.
- D. Mesalamine (Delzicol) 1.6 g orally three times/day.

5. A 45-year-old African American man with a history of alcoholic cirrhosis (Child-Pugh class B) was seen in the clinic today for a follow-up. He was recently referred for screening endoscopy, which revealed several large esophageal varices. He has no history of bleeding; 1 month ago, propranolol 10 mg orally three times/day was initiated. At that time, his vital signs included temperature 98.7°F, heart rate (HR) 85 beats/minute, respiratory rate (RR) 15 breaths/minute, and blood pressure (BP) 130/80 mm Hg. At his evaluation today, he seems to be tolerating the propranolol dose and has no new concerns. His vital signs now include temperature 98.6°F, HR 79 beats/minute, RR 14 breaths/minute, and BP 128/78 mm Hg. Which is the best course of action?

- A. Continue current therapy, with a close follow-up in 4 weeks.
- B. Increase propranolol to 20 mg orally three times/day.
- C. Add isosorbide dinitrate 10 mg orally three times/day.
- D. Change propranolol to atenolol 25 mg orally once daily.

6. A new stool antigen test to detect *H. pylori* was tested in 1000 patients with suspected peptic ulcer disease (PUD), and 865 had a positive result. All patients had also undergone a concomitant endoscopy with biopsy and culture as the gold standard comparative test, and 900 had a positive result. Of these 900 patients with confirmed disease, only 850 also had a positive result with the new stool antigen test. From these results, which best represents the sensitivity and specificity of the new stool antigen test?

- A. Sensitivity 82%, specificity 86%.
- B. Sensitivity 85%, specificity 97%.
- C. Sensitivity 94%, specificity 85%.
- D. Sensitivity 96%, specificity 90%.

7. A 50-year-old Asian woman is seeking advice about a recent possible exposure to hepatitis A virus (HAV). She saw on the local news report that a chef at a local restaurant where she had eaten about 3 weeks earlier had active HAV. Having heard that HAV could be transmitted through food, she would like to know her options. She has not previously received the HAV vaccine. Which is the best recommendation for this patient?

- A. Initiate HAV vaccine.
- B. Administer HAV immune globulin.
- C. Continue to observe the patient for symptoms.
- D. Initiate HAV vaccine and immune globulin.
8. A 48-year-old woman is admitted to the general medicine floor with abdominal pain, severe nausea and vomiting, and abdominal distension secondary to alcoholic hepatitis. She has a history of alcohol abuse for 20 years and takes no current medications. Her serum creatinine (SCr) is 0.5 mg/dL, aspartate aminotransferase (AST) 250 IU/L, alanine aminotransferase (ALT) 60 IU/L, total bilirubin 10.3 mg/dL, prothrombin time 19 seconds (control 12 seconds), and albumin 2.1 g/L. An abdominal paracentesis shows no evidence of spontaneous bacterial peritonitis. She reports no known drug allergies. What treatment is best for this patient’s alcoholic hepatitis?
   A. Naproxen 220 mg orally twice daily.
   B. Octreotide 50 mcg/hour intravenously.
   C. Prednisolone 40 mg/day.
   D. Midodrine 7.5 mg three times daily.

9. A 50-year-old, 80-kg man with a history of intravenous drug abuse and chronic hepatitis C virus (HCV) (genotype 2) was initiated on pegylated interferon (PEG-IFN) 180 mcg subcutaneously and ribavirin 400 mg orally twice daily 2 weeks ago. He returns to the clinic today with fatigue, scleral icterus, and pallor. There is no clinical evidence of bleeding. Laboratory values reveal the following: hematocrit 31% (baseline 39%), total bilirubin 3.2 mg/dL (indirect 2.7 mg/dL, direct 0.5 mg/dL), AST 150 IU/mL (baseline 300 IU/mL), ALT 180 IU/mL (baseline 400 IU/mL), SCr 0.7 mg/dL, HCV RNA 1 x 10^6 copies/mL, white blood cell count (WBC) 7.8 x 10^3 cells/mm^3, and platelet count 160,000/mm^3. Which is the most likely cause of this patient’s current symptoms?
   A. Worsening of his liver disease secondary to inadequate treatment.
   B. An adverse effect secondary to treatment with PEG-IFN.
   C. Systemic manifestations of chronic HCV disease.
   D. An adverse effect secondary to treatment with ribavirin.

10. A 35-year-old man with a history of Crohn disease (CD) is in the clinic today with a chief concern of mucopurulent drainage from an erythematous region on his abdomen. Examination reveals a moderate-size enterocutaneous fistula in the left upper abdominal area. He takes mesalamine (Pentasa) 250 mg 4 capsules three times/day and azathioprine 150 mg/day. His physician wants to prescribe infliximab. Which recommendation is best when initiating infliximab therapy?
   A. Rule out tuberculosis by purified protein derivative or QuantiFERON-TB test.
   B. Administer a test dose before the initial infusion.
   C. Admit to the hospital for the administration of all doses.
   D. Obtain an echocardiogram to assess cardiac function.

11. A 41-year-old woman with a history of bipolar disorder and recurrent urinary tract infections is admitted to the general medicine service with severe nausea, vomiting, fever, and back pain. On examination, she has fever, dry mucous membranes, and right-sided costovertebral tenderness. A urinalysis, which reveals many bacteria, is positive for leukocyte esterase. Her SCr is 1.3 mg/dL and blood urea nitrogen (BUN) is 29 mg/dL, and she is 65 inches tall and weighs 70 kg. She takes risperidone 6 mg twice daily and sertraline 150 mg/day. She reports an allergy to trimethoprim/sulfamethoxazole that causes a rash. Which drug would be best for treating this patient’s nausea?
   A. Prochlorperazine 10-mg tablet orally twice daily.
   B. Metoclopramide orally disintegrating tablets (ODTs) 5 mg three times/day.
   C. Ondansetron 4 mg intravenously three or four times/day.
   D. Diphenhydramine 50 mg intravenously three or four times/day.
12. A 75-year-old man with a history of hypertension, type 2 diabetes mellitus, and chronic low back pain is admitted to the hospital for abdominal pain lasting 2 days. He denies fever, chills, or sick contacts. His last bowel movement was 3–4 days ago. On examination, he is afebrile and has moderate left upper and lower quadrant tenderness. An abdominal radiograph reveals large amounts of stool in the colon with no signs of obstruction. He currently takes lisinopril 20 mg/day, verapamil 240 mg once daily, acetaminophen 500 mg four times/day, oxycodone sustained release 20 mg twice daily, and oxycodone/acetaminophen 5/325 mg as needed for pain. His SCr is 1.8 mg/dL (baseline 1.7 mg/dL); he is 58 inches tall and weighs 68 kg. Which therapy would be best to manage this patient’s constipation?
   A. Sodium phosphate oral solution.
   B. Bisacodyl suppository.
   C. Methylcellulose tablets.
   D. Methylnaltrexone injection.

13. A 65-year-old man with a history of hypothyroidism, heart failure, and MI is admitted to the intensive care unit with severe community-acquired pneumonia. Six hours after admission, he develops acute respiratory failure, hypotension, and acute kidney injury from presumed sepsis; he is placed on mechanical ventilation. An NG tube is placed. He currently takes ramipril 10 mg/day, metoprolol 100 mg twice daily, levothyroxine 125 mcg/day, and aspirin 81 mg/day. His WBC is $25 \times 10^3$ cells/mm$^3$, platelet count 170,000/mm$^3$, SCr 3.8 mg/dL (baseline 1.1 mg/dL), potassium 4.9 mEq/L, BUN 65 mg/dL, international normalized ratio (INR) 1.1, AST 30 IU/mL, and ALT 45 IU/mL. He is 68 inches tall and weighs 79 kg. Which approach is most appropriate for preventing stress-related mucosal disease (SRMD) in this patient?
   A. Sucralfate 1 g four times/day by NG tube.
   B. Magnesium hydroxide 30 mL four times/day by NG tube.
   C. Cimetidine 8-mg/hour intravenous infusion.
   D. Pantoprazole 40 mg intravenously once daily.

14. A newly available NSAID was designed to reduce the incidence of adverse GI events compared with traditional NSAIDs. A large retrospective cohort study compares the incidence of ulceration and bleeding associated with the use of this new NSAID with that of ibuprofen and naproxen. The results indicate that the new agent is associated with no statistically or clinically significant reduction in ulceration or bleeding with long-term use compared with ibuprofen and naproxen. The investigators of the study argue that the lack of difference in safety is because the drug is being promoted as safer; therefore, most patients receiving it are at a much higher baseline risk of NSAID-induced ulceration and bleeding. If this phenomenon did indeed affect the study results, which potential source of bias would probably be present?
   A. Recall bias.
   B. Misclassification bias.
   C. Interviewer bias.
   D. Channeling bias.

15. A new enzyme immunoassay for HCV RNA has a reported sensitivity of 95% and a specificity of 92%. If the prevalence of HCV in a cohort of 500 patients is 40%, which best represents the positive predictive value of this new test?
   A. 75%.
   B. 89%.
   C. 92%.
   D. 96%.
I. GASTROESOPHAGEAL REFUX DISEASE (GERD)

A. Definition

1. “GERD is defined by consensus and as such is a disease comprising symptoms, end-organ effects and complications related to the reflux of gastric contents into the esophagus, oral cavity, and/or the lung”

Strength of guideline evidence is rated by the GRADE system (Level of Evidence and Strength).

Table 1. Level of Evidence and Strength

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Definition</th>
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<tbody>
<tr>
<td>High</td>
<td>Further research was unlikely to change the authors’ confidence in the estimate of the effect</td>
</tr>
<tr>
<td>Moderate</td>
<td>Further research would probably affect confidence in the estimate of effect</td>
</tr>
<tr>
<td>Low</td>
<td>Further research would be expected to have an important impact on the confidence in the estimate of the effect and would be likely to change the estimate</td>
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<table>
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<tr>
<th>Strength of Evidence</th>
<th>Definition</th>
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<tr>
<td>Strong</td>
<td>The desirable effects of an intervention clearly outweigh the undesirable effects</td>
</tr>
<tr>
<td>Conditional</td>
<td>There is uncertainty about the trade-offs</td>
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2. Definition subdivides GERD into the following categories:
   a. Symptoms without erosions on endoscopy (nonerosive reflux disease)
   b. Symptoms with erosions on endoscopy (erosive reflux disease)

3. Symptoms
   a. Typical symptoms: heartburn (pyrosis), regurgitation, acidic taste in the mouth
   b. Extraesophageal or atypical symptoms: Chronic cough, asthma-like symptoms, recurrent sore throat, laryngitis or hoarseness, dental enamel loss, and noncardiac chest pain; sinusitis, pneumonia, bronchitis, and otitis media are less common atypical symptoms.
   c. Alarm symptoms: dysphagia, odynophagia, bleeding, weight loss, choking, chest pain, and epigastric mass. These symptoms warrant immediate referral for more invasive testing.
   d. Aggravating factors: recumbency (gravity), elevated intra-abdominal pressure, reduced gastric motility, decreased lower esophageal sphincter (LES) tone, and direct mucosal irritation
   e. Long-term complications: esophageal erosion, strictures or obstruction, Barrett esophagus, and reduction in patient’s quality of life

B. Diagnosis

1. Symptoms
   a. A presumptive diagnosis of GERD can be established in the setting of typical symptoms of heartburn and regurgitation. Empiric therapy with a proton pump inhibitor (PPI) is recommended if patient has typical symptoms of heartburn or regurgitation. (Strong recommendation/Moderate level of evidence)
   b. Screening for H. pylori is not recommended. (Strong/Low)
   c. Patients with noncardiac chest pain that is suspected of having been caused by GERD should have a diagnostic evaluation before institution of therapy. (Strong/Low)

2. Endoscopy: Upper endoscopy is not necessary in the presence of typical GERD symptoms. Endoscopy is recommended in the presence of alarm symptoms and in the screening of patients at high risk of complications. Repeat endoscopy is not indicated in patients without Barrett esophagus in the absence of new symptoms. (Strong/Moderate)
3. Manometry: Recommended for preoperative evaluation but has no role in the diagnosis of GERD (Strong/Low)

4. Ambulatory pH testing
   a. Ambulatory esophageal reflux monitoring is indicated before considering endoscopic or surgical therapy in patients with nonerosive reflux disease as part of the evaluation of patients who are refractory to PPI therapy and in situations when the diagnosis of GERD is in question. (Strong/Low)
   b. Ambulatory reflux monitoring is the only test that can assess reflux symptom association. (Strong/Low)
   c. Ambulatory reflux monitoring is not necessary in the presence of short- or long-segment Barrett esophagus to establish a diagnosis of GERD. (Strong/Moderate)

C. Treatment Strategies for GERD
   1. Nonpharmacologic interventions and lifestyle modifications are unlikely to control symptoms in most patients. The American Gastroenterological Association (AGA) guidelines cite insufficient evidence to advocate lifestyle modifications for all patients; rather, they advocate use in targeted populations. Thus, the following lifestyle modifications should be implemented only in the patient populations specified.
      a. Dietary modifications in patients whose symptoms are associated with certain foods or drinks. Routine global elimination of food triggers not recommended according to the 2013 guidelines. (Conditional/Low)
         i. Avoid aggravating foods and beverages; some may reduce LES pressure (alcohol, caffeine, chocolate, citrus juices, garlic, onions, peppermint or spearmint) or cause direct irritation (spicy foods, tomato juice, coffee).
         ii. Reduce fat intake (high-fat meals slow gastric emptying) and portion size.
         iii. Avoid eating 2–3 hours before bedtime.
         iv. Remain upright after meals.
      b. Weight loss if overweight or recent weight gain (Conditional/Mod)
      c. Reduce or discontinue nicotine use in patients who use tobacco products (affects LES).
      d. Elevate head of bed and avoid meals 2–3 hours before bedtime if nocturnal symptoms. (Conditional/Low)
      e. Avoid tight-fitting clothing (decreases intra-abdominal pressure).
      f. Avoid medications that may reduce LES pressure, delay gastric emptying, or cause direct irritation: α-adrenergic antagonists, anticholinergics, benzodiazepines, calcium channel blockers, estrogen, nitrates, opiates, tricyclic antidepressants, theophylline, NSAIDs, and aspirin.

   2. Pharmacologic therapies
      a. Initial treatment depends on the severity, frequency, and duration of symptoms.
         i. “Step-down” treatment: Starting with maximal therapy, such as therapeutic doses of PPIs, is always appropriate as a first-line strategy in patients with documented esophageal erosion. Advantages: Rapid symptom relief, avoidance of overinvestigation. Disadvantages: Potential overtreatment, higher drug cost, increased potential for adverse effects
         ii. “Step-up” treatment: Start with lower-dose over-the-counter (OTC) products. Advantages: Avoids overtreatment, has lower initial drug cost. Disadvantages: Potential undertreatment (partial symptom relief; may take longer for symptom control; may lead to overinvestigation)
      b. The AGA treatment guideline recommendation summary follows.
### Table 2. AGA Treatment Guideline Recommendation

<table>
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<th>Area</th>
<th>Recommendation (Level/Strength)</th>
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| Treatment  | • Erosive esophagitis should be treated with an 8-week course of PPIs; no major differences in products (Strong/High)  
• Use maintenance PPIs if return of symptoms or complications (Strong/Moderate)  
• Bedtime histamine-2 receptor antagonists can be used if a.m. PPI and nighttime symptoms, but tachyphylaxis develops (Conditional/Low)  
• Further testing needed before use of metoclopramide or baclofen (Conditional/Mod) |
| Dosing     | • Traditional PPIs should be given 30–60 minutes before meals (Strong/Moderate)  
• Newer PPIs offer dosing flexibility in relation to meals (Conditional/Moderate)  
• Initiate PPIs once daily before a.m. meal (Strong/Moderate)  
• Twice-daily PPIs if partial response to once-daily PPIs or nighttime symptoms (Strong/Low)  
• Twice daily if partial response to once daily or can switch to another PPI (Conditional/Low) |

PPI = proton pump inhibitor.

c. Pharmacologic agents

i. Antacids

(a) Calcium-, aluminum-, and magnesium-based products are available OTC in a wide variety of formulations (capsules, tablets, chewable tablets, and suspensions).

(b) Neutralizing acid and raising intragastric pH results in decreased activation of pepsinogen and increased LES pressure; rapid onset of action but short duration, necessitating frequent dosing

(c) Some products (Gaviscon) contain the antirefluxant alginic acid, which forms a viscous layer on top of gastric contents to act as a barrier to reflux (variable added efficacy).

(d) Used as first-line therapy for intermittent (less than twice weekly) symptoms or as breakthrough therapy for those on PPI/histamine-2 receptor antagonist (H2RA) therapy; not appropriate for healing established esophageal erosions

(e) Adverse reactions: Constipation (aluminum), diarrhea (magnesium), accumulation of aluminum and magnesium in renal disease with repeated dosing

(f) Drug interactions: Chelation (fluoroquinolones, tetracyclines); reduced absorption because of increases in pH (ketoconazole, itraconazole, iron, atazanavir, delavirdine, indinavir, nelfinavir) or increases in absorption, leading to potential toxicity (raltegravir, saquinavir)

ii. Histamine-2 receptor antagonists

(a) Reversibly inhibit histamine-2 receptors on the parietal cell

(b) All agents available as prescription and OTC products; a variety of formulations available; generics exist for all prescription products