CHAPTER 12

GASTROENTEROLOGY

1. **Define gastroesophageal reflux disease (GERD). What causes it?**
GERD is stomach acid refluxing into the esophagus. It is due to inappropriate, intermittent relaxation of the lower esophageal sphincter. Patients with a hiatal hernia have a much greater incidence of GERD (see question 4).

2. **Describe the classic symptoms of GERD. How is it treated?**
The main complaint is usually "heartburn," often related to lying supine after eating. GERD may also cause abdominal or chest pain. Initial treatment is to elevate the head of the bed and to avoid coffee, alcohol, tobacco, spicy and fatty foods, chocolate, and medications with anticholinergic properties. If this approach fails, antacids, histamine-2 (H2) blockers, and proton-pump inhibitors (PPIs) may be tried. Many patients have already tried over-the-counter remedies before presentation, and many physicians begin empiric treatment at the first visit, since "lifestyle modifications" usually fail. Surgery (Nissen fundoplication) is reserved for severe or resistant cases.

3. **What are the sequelae of GERD?**
Sequelae of GERD include esophagitis, esophageal stricture (which may mimic esophageal cancer), esophageal ulcer, hemorrhage, Barrett esophagus, and esophageal adenocarcinoma (Fig. 12.1).

4. **What is a hiatal hernia? How is it different from a paraesophageal hernia?**
A hiatal hernia is a sliding hernia, which means that the whole gastroesophageal junction moves above the diaphragm, pulling the stomach with it. This common and benign finding may predispose to GERD. In a paraesophageal hernia, the gastroesophageal junction stays below the diaphragm, but the stomach herniates through the diaphragm into the thorax. This type of hernia is uncommon but serious; it may become strangulated and should be surgically repaired.

5. **How does peptic ulcer disease (PUD) present?**
PUD classically presents with chronic, intermittent, epigastric pain (burning, gnawing, or aching) that is localized and often relieved by antacids or milk. Look for epigastric tenderness. Other signs and symptoms include occult blood in the stool and nausea or vomiting. PUD is more common in men. The two types of PUD are gastric and duodenal ulcers.

6. **Explain the classic differences between duodenal and gastric ulcers.**

	DUODENAL	GASTRIC
% of cases	75	25
Acid secretion	Normal to high	Normal to low
Main cause	*Helicobacter pylori*	Use of nonsteroidal antiinflammatory drugs, including aspirin
Peak age	Forties	Fifties
Blood type	O	A
Eating food	Pain gets better, then worse 2–3 hours later	Pain not relieved or made worse

7. **What is the diagnostic study of choice for PUD?**
Endoscopy is the gold standard (most sensitive test), but an upper gastrointestinal barium study is cheaper and less invasive. Empiric treatment with medications may be tried in the absence of diagnostic studies if the symptoms are typical. If endoscopy is done, a biopsy of any gastric ulcer is mandatory to exclude malignancy. Duodenal ulcers do not have to be biopsied initially, because malignancy is rare.

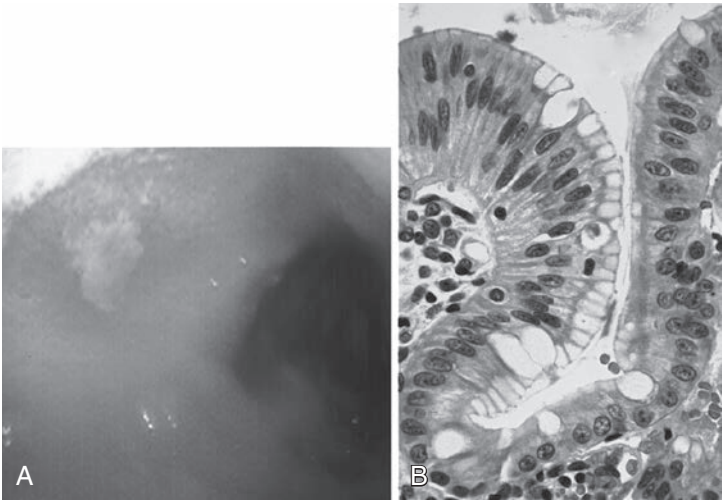

Fig. 12.1. Barrett's esophagus is defined by both endoscopic and histologic components. Endoscopically there must be visible pink columnar epithelium within the tubular esophagus (A) that histologically has intestinalized metaplastic columnar epithelium defined by the presence of true goblet cells (B, *arrows*) on hematoxylin and eosin staining. Barrett esophagus should not be diagnosed without both components. *(From Patterson GA.* Pearson's thoracic and esophageal surgery. *3rd ed. London: Churchill Livingstone, 2008, Fig. 36.2.)*

8. What is the most feared complication of PUD? What should you suspect if an ulcer does not respond to treatment?

Perforation is the most feared complication of PUD. Look for peritoneal signs, history of PUD, and free air on an abdominal radiograph (Fig. 12.2). Treat with antibiotics (such as ceftriaxone and metronidazole) and laparotomy with repair of the perforation. If ulcers are severe, atypical (e.g., located in the jejunum), or nonhealing, think about stomach cancer or Zollinger-Ellison syndrome (gastrinoma; check gastrin level). PUD is also a cause of GI bleeding, which can be severe in some cases.

9. How is PUD treated initially?

First, remember that diet changes are not thought to help heal ulcers, although reduced alcohol and tobacco use may speed healing. Stop all NSAID use. Start treatment proton-pump inhibitors, test for *Helicobacter pylori* infection, and treat with antibiotics if positive. Many regimens exist, but the most commonly used is triple therapy with a proton pump inhibitor, clarithromycin, and amoxicillin.

10. Name the surgical options for ulcer treatment. What complications may occur?

Surgical options are generally considered only if medical treatment has failed or if complications are present (perforation, bleeding). Surgical procedures for PUD include antrectomy, vagotomy, and Billroth I or II procedures. After surgery (especially with Billroth procedures), watch for dumping syndrome (weakness, dizziness, sweating, and nausea or vomiting after eating). Patients may also develop hypoglycemia 2–3 hours after a meal, which causes recurrence of the same symptoms, as well as afferent loop syndrome (bilious vomiting after a meal relieves abdominal pain), bacterial overgrowth, and vitamin deficiencies (vitamin B_{12} and/or iron, causing anemia).

11. Define achlorhydria. What causes it?

Achlorhydria is absence of hydrochloric acid (HCl) secretion. It is due most commonly to **pernicious anemia,** in which antiparietal cell antibodies destroy acid-secreting parietal cells, causing achlorhydria and vitamin B_{12} deficiency. Achlorhydria is often associated with other endocrine autoimmune disorders (e.g., hypothyroidism, vitiligo, diabetes, hypoadrenalism). Achlorhydria may also be caused by surgical gastric resection.

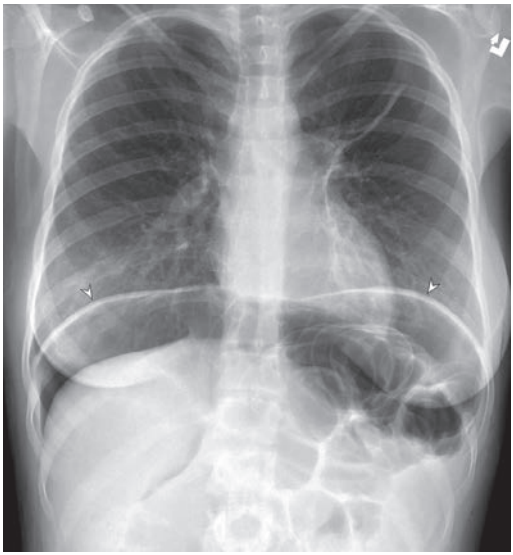

Fig. 12.2. Pneumoperitoneum from bowel perforation on conventional radiographs. Upright radiograph shows the large amount of free intraperitoneal air (lucent area just inferior to the diaphragm). *(From Goldman L.* Goldman's Cecil medicine. *24th ed. Philadelphia: Saunders, 2011, Fig. 135.1.)*

12. What are classic differences between upper and lower gastrointestinal (GI) bleeds?

	UPPER GI BLEED	LOWER GI BLEED
Location	Proximal to ligament of Treitz	Distal to ligament of Treitz
Common causes	Gastritis, ulcers, varices, esophagitis	Vascular ectasia, diverticulosis, colon cancer (Fig. 12.3), colitis, inflammatory bowel disease, hemorrhoids
Stool	Tarry, black stool (melena)	Bright red blood seen in stool (hematochezia)
NGT aspirate	Positive for blood	Negative for blood

NGT, Nasogastric tube

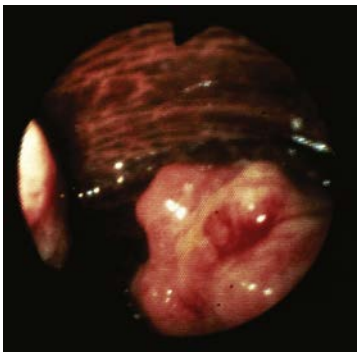

Fig. 12.3. Colonoscopic photograph of a pale colon cancer easily seen against the dark background of pseudomelanosis coli. *(From Feldman M, Friedman L, Brandt L.* Sleisenger and Fordtran's gastrointestinal and liver disease. *9th ed. Philadelphia: Saunders, 2010, Fig. 124.8. Courtesy of Juergen Nord, MD, Tampa, Florida.)*

13. How is a GI bleed treated?

The first step is to *make sure that the patient is stable* by checking the ABCs (airways, breathing, circulation) and giving intravenous fluids and blood, if needed, before searching for a diagnosis. Next, place a nasogastric tube, and test the aspirate for blood to help determine whether the patient has an upper GI bleed (blood present in the aspirate) or lower GI bleed (blood absent in the aspirate). Start a proton pump inhibitor drip. **Endoscopy** is usually the first test performed (upper or lower, depending on symptoms and nasogastric tube aspirate). Endoscopically treatable lesions include ulcers, polyps, vascular ectasias, and varices.

14. What radiologic imaging studies can be done to localize a GI bleed? Does surgery have a role?

Radionuclide (i.e., nuclear medicine) scans can detect slow or intermittent bleeds if a source cannot be found with endoscopy. Angiography can detect more rapid bleeds, and embolization of bleeding vessels can be done during the procedure. Surgery is reserved for severe or resistant bleeds and typically involves resection of the affected bowel (usually colon).

15. Define diverticulosis. What are its complications?

Diverticulosis is characterized by sac-like mucosal projections through the muscular layer of the colon and/or rectum. It is extremely common, and the incidence increases with age. It is thought to be caused in part by a low-fiber, high-fat diet. Complications include GI bleeding (common cause of painless lower GI bleeds) and diverticulitis (inflammation of a diverticulum). Diverticulitis can lead to abscess formation, fistula formation, sepsis, or large bowel obstruction.

16. How do you diagnose and treat diverticulitis? What test should a patient have after a treated episode of diverticulitis?

Signs and symptoms of diverticulitis include left lower quadrant pain or tenderness, fever, diarrhea or constipation, and leukocytosis. The pathophysiology is similar to appendicitis: stool or other debris impacts within the outpouched mucosea (the diverticulum) and causes obstruction, leading to bacterial overgrowth and inflammation. The diagnosis can be confirmed with a CT scan (Fig. 12.4), if needed, which can also help to rule out complications such as perforation or abscess. In the absence of complications, the treatment is antibiotics that cover bowel flora (e.g., a fluoroquinolone plus metronidazole) and bowel rest (i.e., no oral intake). Surgery in the form of a bowel resection may be needed when diverticulitis is complicated by perforation or abscess.

After a treated episode of diverticulitis, all patients need colon cancer screening with colonoscopy (colon carcinoma with perforation can mimic diverticulitis clinically and on CT). These studies should be avoided during active diverticulitis, however, due to an increased risk for perforation. Patients should maintain a high-fiber diet.

17. How is diarrhea categorized?

According to etiology:

- Systemic. Any illness can cause diarrhea as a systemic symptom, especially in children (e.g., infection).
- Osmotic
- Secretory
- Malabsorptive
- Infectious
- Exudative
- Altered intestinal transit

18. Define osmotic diarrhea. How can an easy diagnosis be made?

Osmotic diarrhea is caused by nonabsorbable solutes that remain in the bowel, where they retain water (e.g., lactose or other sugar intolerance). When the patient stops ingesting the offending substance (e.g., avoidance of milk or a trial of not eating), the diarrhea stops—an easy diagnosis.

19. What causes secretory diarrhea?

Secretory diarrhea results when the bowel secretes too much fluid. It is often due to bacterial toxins (cholera, some species of *Escherichia coli*), VIPoma (pancreatic islet cell tumor that secretes vasoactive intestinal peptide), or bile acids (after ileal resection). Secretory diarrhea persists even when the patient stops eating.

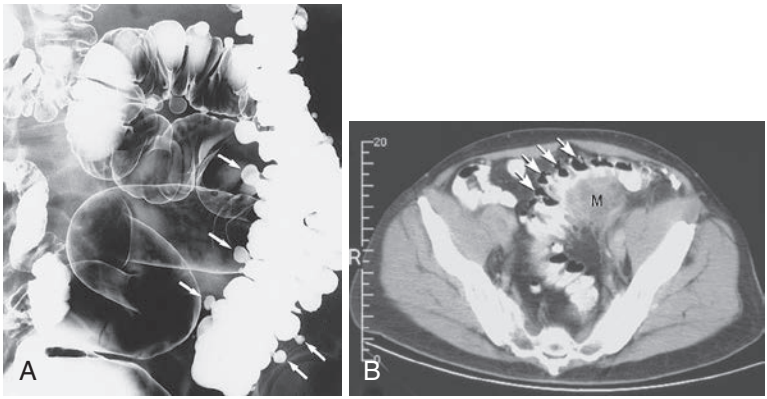

Fig. 12.4. Diverticulosis of the colon is seen on this oblique view of the sigmoid colon (A) during a double-contrast barium enema showing multiple outpouchings (*arrows*) that represent diverticula. Diverticula also can be seen in a computed tomography (CT) scan (B) as outpouchings (*arrows*), but a developing focal inflammatory mass (M) also is compatible with a developing abscess. *(From Mettler F.* Essentials of radiology. *2nd ed. Philadelphia: Saunders, 2004, Fig. 6.73.)*

20. What are the common causes of malabsorptive diarrhea?

Celiac disease (look for dermatitis herpetiformis, and avoid gluten in the diet; Fig. 12.5), Crohn disease, and postgastroenteritis (due to depletion of brush-border enzymes). Malabsorptive diarrhea improves with bowel rest (i.e., when the patient is not eating).

21. What are the common clues to infectious diarrhea? What are the common causes?

Look for fever and white blood cells in the stool (only with invasive bacteria such as *Shigella, Salmonella, Yersinia,* and *Campylobacter* spp.; not found with toxigenic bacteria). Travel history (Montezuma's revenge caused by *E. coli*) is also a tip-off. Hikers and stream-drinkers may have *Giardia* infection, which presents with steatorrhea (fatty, greasy, malodorous stools that float) due to small bowel involvement and unique protozoal cysts in the stool. Treat *Giardia* with metronidazole. Also watch for *Clostridium difficile* diarrhea in patients with a history of antibiotic use. Test the stool for *C. difficile* toxin, and if the result is positive, treat with oral metronidazole (oral vancomycin is a second-line agent if metronidazole is not an option).

22. What causes exudative diarrhea?

Exudative diarrhea results from inflammation in the bowel mucosa that causes seepage of fluid. Mucosal inflammation is usually due to inflammatory bowel disease (Crohn disease or ulcerative colitis; see question 27) or cancer. Patients commonly have fever and white blood cells in the stool, as in infectious diarrhea, but a *lack* of pathogenic organisms, chronicity, and nonbowel symptoms are clues.

23. What are the common causes of diarrhea due to altered intestinal transit?

This type of diarrhea is seen after bowel resections, in patients taking medications that interfere with bowel function, and in patients with hyperthyroidism or neuropathy (e.g., diabetic diarrhea). Watch for factitious diarrhea, which is caused by secret laxative abuse.

24. Define irritable bowel syndrome. How do you recognize it?

Irritable bowel syndrome is a common cause of gastrointestinal complaints. Patients may be anxious or neurotic and have a history of diarrhea aggravated by stress; bloating; abdominal pain relieved by defecation; and/or mucus in the stool. Look for psychosocial stressors in the history and normal physical findings and test results. Irritable bowel syndrome is a diagnosis of exclusion; you must do at least basic lab tests, stool exam, and sigmoidoscopy. Because it is so common, however, it is the most likely diagnosis if the question gives no positive findings, especially in young adults (female-to-male ratio = 3:1).

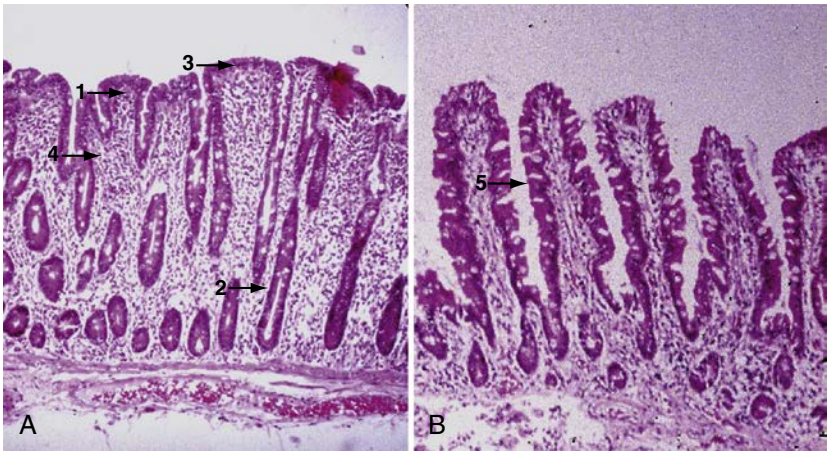

Fig. 12.5. Mucosal pathology in celiac disease. A, Duodenal biopsy specimen of a patient with untreated celiac disease. The histologic features of severe villus atrophy (*arrow 1*), crypt hyperplasia (*arrow 2*), enterocyte disarray (*arrow 3*), and intense inflammation of the lamina propria and epithelial cell layer (*arrow 4*) are evident. B, Repeat duodenal biopsy after 6 months on a strict gluten-free diet. There is marked improvement, with well-formed villi (*arrow 5*) and a return of the mucosal architecture toward normal. *(From Feldman M, Friedman L, Brandt L.* Sleisenger and Fordtran's gastrointestinal and liver disease. *9th ed. Philadelphia: Saunders, 2010, Fig. 104.2.)*

25. What should you do if a patient has diarrhea?

In all patients with diarrhea, watch for and treat dehydration and electrolyte disturbances, especially metabolic acidosis and hypokalemia. Diarrhea is a common and preventable cause of death in underdeveloped countries. Do a rectal exam, look for occult blood in stool, and examine the stool for bacteria (Gram stain and culture), ova and parasites, fat content (steatorrhea), and white blood cells.

26. What should you watch for in children after a bout of diarrhea?

After bacterial (especially *E. coli* or *Shigella* sp.) diarrhea in children, watch for **hemolytic uremic syndrome,** which is characterized by thrombocytopenia, hemolytic anemia (schistocytes, helmet cells, and fragmented red blood cells on peripheral blood smear), and acute renal failure. Treatment is supportive. Patients may need dialysis and/or transfusions.

27. Specify the classic differences between Crohn disease and ulcerative colitis.

	CROHN DISEASE	ULCERATIVE COLITIS
Place of origin	Distal ileum, proximal colon	Rectum
Thickness of pathology	Transmural	Mucosa/submucosa only
Progression	Irregular (skip-lesions)	Proximal, continuous from rectum; no skipped areas
Location	From mouth to anus	Involves only colon, rarely extends to ileum
Bowel habit changes	Obstruction, abdominal pain	Bloody diarrhea
Classic lesions	Fistulas/abscesses, cobblestoning, string sign on barium x-ray (Fig. 12.6)	Pseudopolyps, lead-pipe colon on barium x-ray (Fig. 12.7), toxic megacolon
Colon cancer risk	Slightly increased	Markedly increased
Surgery	No (may make worse)	Yes (proctocolectomy with ileoanal anastomosis)

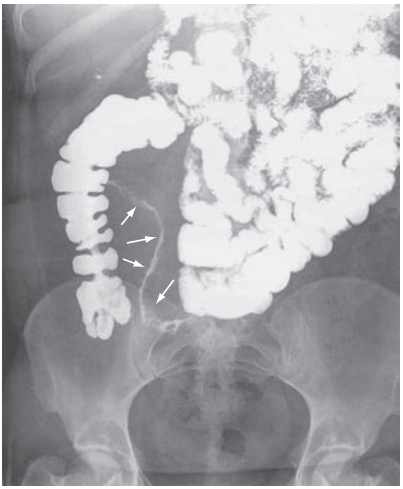

Fig. 12.6. Small bowel follow-through in a patient with Crohn disease that demonstrates a string sign in the right lower quadrant. The classic radiologic string sign (*arrows*) of a markedly narrowed bowel segment amidst widely spaced bowel loops is a result of spasm and edema associated with active inflammation. *(From Feldman M, Friedman L, Brandt L.* Sleisenger and Fordtran's gastrointestinal and liver disease. *9th ed. Saunders, 2010, Fig. 111.4.* Courtesy of Dr. Jack Wittenberg, Boston, Mass.)

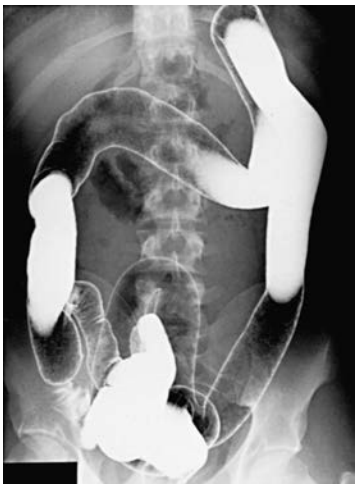

Fig. 12.7. A double-contrast barium enema in a patient with long-standing ulcerative colitis demonstrates a marked loss of haustration. The terminal ileum is normal. *(From Feldman M, Friedman L, Brandt L.* Sleisenger and Fordtran's gastrointestinal and liver disease. *8th ed. Philadelphia: Saunders, 2006, Fig. 109.9.)*

28. Describe the extraintestinal manifestations of inflammatory bowel disease.

Both forms of inflammatory bowel disease can cause uveitis, arthritis, ankylosing spondylitis, erythema nodosum, erythema multiforme, primary sclerosing cholangitis, failure to thrive or grow in children, toxic megacolon, anemia of chronic disease, and fever. Toxic megacolon is more common in ulcerative colitis; look for markedly distended colon on abdominal radiograph.

29. How is inflammatory bowel disease treated?

Patients are treated with 5-aminosalicylic acid, with or without a sulfa drug (e.g., sulfasalazine), when stable. Steroids and other immune modulators (e.g., azathioprine) are used during severe disease flare-ups.

30. What causes toxic megacolon? How is it treated?

Toxic megacolon is classically seen with inflammatory bowel disease (especially ulcerative colitis) and infectious colitis (especially *C. difficile*). It may be precipitated by the use of antidiarrheal medications, which, for this reason, are usually not given for infectious diarrhea. Most patients have a high fever, leukocytosis, abdominal pain, rebound tenderness, and a dilated segment of colon on abdominal radiograph. Toxic megacolon is an emergency! Start treatment by discontinuing all antidiarrheal medications. Do not allow the patient to eat, place a nasogastric tube, and start intravenous fluids. Give antibiotics to cover bowel flora (such as ceftriaxone and metronidazole). Give steroids if the cause is inflammatory bowel disease. Surgery is required if perforation occurs (free air is seen on abdominal radiograph).

31. List the common findings of acute liver disease.

- Elevated liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], bilirubin, alkaline phosphatase, and/or prothrombin time and international normalized ratio [INR])
- Jaundice
- Nausea and vomiting
- Right upper quadrant pain or tenderness
- Hepatomegaly

32. List the common causes of acute liver disease.

- Alcohol
- Medications
- Infection (usually hepatitis)
- Reye syndrome
- Biliary tract disease
- Autoimmune disease

33. What is the classic abnormality on liver function tests in patients with alcoholic hepatitis?

An elevated AST that is more than twice the value of ALT, although both may be elevated.

34. What clues suggest hepatitis A? Describe the diagnostic serology.

Look for outbreaks from a foodborne source. There are no long-term sequelae of infection, although acute liver failure is a remote possibility. IgM antihepatitis A virus (HAV) is positive during jaundice or shortly thereafter. The incubation period for hepatitis A is about 4 weeks, though IgM may be detected by the time symptoms begin.

35. How is hepatitis A acquired? What is the best treatment?

Hepatitis B is acquired through needles, sex, or perinatal transmission. Transfused blood is now screened for hepatitis B, but this risk of transmission is still about 1/200,000 according to the American Red Cross. A history of transfusion years ago is still a risk factor (screening by blood banks began in 1972 in the United States). Prevention is the best treatment (vaccination). Interferon alfa-2b, peginterferon alfa-2a, adefovir, dipivoxil, entecavir, telbivudine, or tenofovir can be tried in patients with chronic hepatitis and elevated liver enzymes.

36. Describe the serology of hepatitis B infection, including the surface, core, and "e" markers.

The hepatitis B surface antigen (HBsAg) is positive with any unresolved infection (acute or chronic). The hepatitis B "e" antigen (HBeAg) is a marker for infectivity; patients positive for the hepatitis B "e" antibody (HBeAb) have a low likelihood of spreading disease. The first antibody to appear is the IgM hepatitis B core antibody (HBcAb), which appears during the "window phase" when both HBsAg and hepatitis B surface antibody (HBsAb) are negative. Positive HBsAb means that the patient is immune (as a result of either recovery from infection or vaccination); HBsAb never appears if the patient has chronic hepatitis.

Make sure you know and understand Table 12.1 and Fig. 12.8. They are high yield.

TABLE 12.1. Serologic Markers at Different Stages of Disease

	HBSAG	HBEAG	HBEAB	HBSAB	HBCAB
Incubation	+	+	-	-	-
Acute stage	+	+	-	-	+
Persistent carrier	+	+/-	-/+	-	+
Recovery (immune)	-	-	+	+	+
Immunization	-	-	-	+	-

The presence of HBeAg and anti-HBe depends on degree of infectivity.
Adapted from Cohen J, Powderly WG, Berkley SF, et al. *Infectious diseases*, 2nd ed. Edinburgh: Mosby, 2004, 2015, with permission.

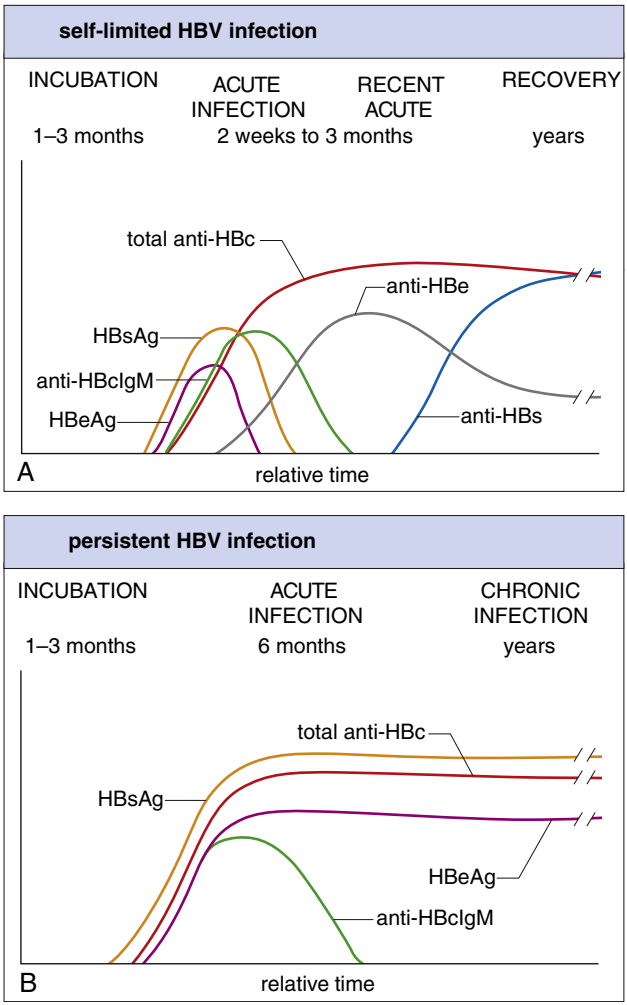

Fig. 12.8. A, Clinical and virologic course of hepatitis B, with recovery. B, Clinical and virologic course in a carrier of hepatitis B. *(From Goering R, Dockrell H, Wakelin D, et al.* Mims' medical microbiology. *4th ed. Philadelphia: Elsevier; 2007. Redrawn from Farrar WE, Wood MJ, Innes JA, et al.* Infectious diseases. *2nd ed. London: Mosby International; 1992.)*

37. What are the possible sequelae of chronic hepatitis B or C?
Cirrhosis and hepatocellular cancer (only with chronic, not acute, infection).

38. What should be given to persons acutely exposed to hepatitis B?
Hepatitis B immunoglobulin and hepatitis B vaccination or hepatitis B vaccination alone have been demonstrated to be effective in preventing transmission after exposure to hepatitis B virus.

39. Which type of viral hepatitis is the new king of chronic hepatitis?
Hepatitis C. The hepatitis C virus is the most likely cause of hepatitis after a blood transfusion. Although blood is now screened for hepatitis B and C, the hepatitis C test was developed later (screening in the United States began in 1972 for hepatitis B and 1992 for hepatitis C). Hepatitis C is also more likely than hepatitis B to progress to chronic hepatitis, cirrhosis, and cancer. Because of the relatively high prevalence in the "Baby Boomer" generation and lack of symptoms, the Centers for Disease Control has recommended that all Americans born between 1945 and 1965 have a one-time screening test for hepatitis C.

40. Describe the serology and treatment for hepatitis C.
A positive hepatitis C antibody means that the patient has had an infection in the past but does not mean the infection has been cleared. Most patients become chronic carriers of the virus. A test for hepatitis C virus RNA is available to detect and quantify the virus. Patients with hepatitis C should also be tested for HIV and hepatitis B. They should be tested for antibodies to hepatitis A and B to determine if vaccination is required.

Treatment of hepatitis C is rapidly evolving since the development of direct-acting antiviral medications. These medications are highly effective and offer the potential to avoid treatment with interferon and sometimes ribavirin. All patients with a detectable hepatitis C viral level over a 6-month period should be considered for treatment. Treatment regimens depend upon the hepatitis C genotype. Genotype 1 is the most common in the United States. Specific treatment regimens are likely beyond the scope of USMLE Step 2 but are included here for thoroughness:

- Ledipasvir-sofosbuvir
- Elbasvir-grazoprevir with or without ribavirin
- Ombitasvir-paritaprevir-ritonavir plus dasabuvir with or without ribavirin
- Simeprevir plus sofosbuvir
- Daclatasvir plus sofosbuvir

A virologic response to treatment is assessed by measuring the viral load at 12 weeks following completion of therapy. A sustained virologic response (SVR) is defined as an undetectable viral level at 24 weeks post treatment.

41. When is hepatitis D seen? Describe the serology.
Hepatitis D is seen only in patients with hepatitis B. It may become chronic (with hepatitis B co-infection) and is acquired in the same ways as hepatitis B. IgM antibodies to the hepatitis D antigen demonstrate resolution of recent infection. Presence of the hepatitis D antigen, hepatitis D virus RNA, and high levels of IgM antibodies to hepatitis D indicates chronicity.

42. How is hepatitis E transmitted? What is special about the infection in pregnant women?
Hepatitis E is transmitted like hepatitis A (via food and water; no chronic state). It is often fatal in pregnant women (for unknown reasons).

43. What are the classic causes of drug-induced hepatitis?
Acetaminophen, isoniazid and other tuberculosis drugs (e.g., rifampin and pyrazinamide), halothane, HMG CoA-reductase inhibitors, and carbon tetrachloride. The first step in treatment is to stop the drug.

44. When should you suspect idiopathic autoimmune hepatitis? What is the serologic marker?
Idiopathic autoimmune hepatitis is classically seen in 20- to 40-year-old women with anti–smooth muscle or antinuclear antibodies and no risk factors or lab markers for other causes of hepatitis. Treat with steroids.

45. What are the usual causes of chronic liver disease?
Alcohol, hepatitis, and metabolic diseases. Watch for the stigmata of chronic liver disease: gynecomastia, testicular atrophy, palmar erythema, spider angiomas on skin, and ascites.

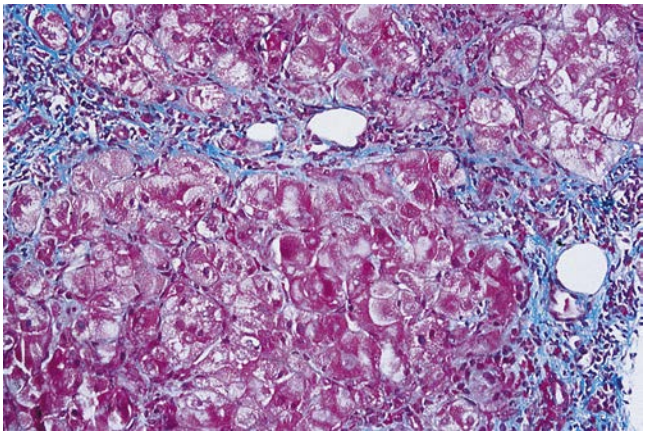

Fig. 12.9. Chronic viral hepatitis. Portal-portal bridging fibrosis is seen in long-standing chronic hepatitis C. *(From Odze RD, Goldblum JR.* Surgical pathology of the GI tract, liver, biliary tract, and pancreas. *2nd ed. Philadelphia: Saunders, 2009, Fig. 38.10.)*

46. Which species of viral hepatitis can lead to chronic liver disease?

Hepatitis B, C, and D. Hepatitis D can cause infection only in the setting of coexisting hepatitis B (Fig. 12.9).

47. Define hemochromatosis. How do you recognize it?

Hemochromatosis, in its primary form, is usually autosomal recessive; look for a family history. Nearly 1 in 250 people in the United States are homozygous for this condition, although penetrance and clinical expression are variable. The pathophysiology is incompletely understood but includes excessive iron absorption by the intestine. Excessive iron is deposited in the liver (potentially causing cirrhosis and/or hepatocellular carcinoma), pancreas (potentially causing diabetes), heart (resulting in dilated cardiomyopathy), skin (causing pigmentation classically known as **bronze diabetes**), and joints (arthritis). Men are symptomatic earlier and more often because women lose iron with menstruation. Treat with phlebotomy. Secondary iron overload can cause secondary hemochromatosis, which is classically due to an anemia that results in ineffective erythropoiesis (e.g., thalassemia) and excessive iron intake.

48. Define Wilson disease. How do you recognize it? How is it treated?

Wilson disease is an autosomal recessive disease caused by the effects of excessive serum copper. Serum **ceruloplasmin** (a copper transport protein) is usually low or absent, and serum copper may be normal. Biopsy shows excessive copper in the liver. Patients classically have liver disease with central nervous system and psychiatric manifestations (due to copper deposits in the basal ganglia; another name for this disease is hepatolenticular degeneration) and **Kayser-Fleischer** rings in the eye. Treat with penicillamine (copper chelator).

49. What are the clues to a diagnosis of alpha$_1$ antitrypsin deficiency?

The classic description is a young adult who develops cirrhosis and/or emphysema without risk factors for either. Alpha$_1$ antitrypsin (AAT) deficiency has an autosomal recessive inheritance pattern; look for a positive family history. Diagnosis requires a serum AAT less than 11 μmol/L as well as a severely deficient genotype.

50. What metabolic derangements accompany liver failure?

Coagulopathy: prolonged prothrombin time (PT). In severe cases, partial thromboplastin time (PTT) also may be prolonged. Vitamin K does not solve the problem because it cannot be utilized by the damaged liver. Symptomatic patients must be treated with fresh frozen plasma.

Jaundice/hyperbilirubinemia: elevated conjugated and unconjugated bilirubin with hepatic damage (vs. biliary tract disease; see below).

Hypoalbuminemia: the liver synthesizes albumin.

Ascites: due to portal hypertension and/or hypoalbuminemia. Ascites can be detected on physical exam by shifting dullness or a positive fluid wave. A possible complication is **spontaneous bacterial peritonitis**

due to infected ascitic fluid that can lead to sepsis. Look for fever and/or change in mental status in a patient with known ascites. Perform a paracentesis, examine the ascitic fluid for elevated white blood cell count (especially neutrophils), and do Gram stain, culture and sensitivity tests, glucose (low with infection), and protein (high with infection). The usual causes are *E. coli, Streptococcus pneumoniae,* and other enteric bugs. Treat with broad-spectrum antibiotics (cefotaxime is a common choice).

Portal hypertension: seen with cirrhosis (chronic liver disease); causes hemorrhoids, varices, and caput medusae (engorged veins on the abdominal wall).

Hyperammonemia: the liver clears ammonia. Treat with decreased protein intake (source of ammonia) and lactulose. The last choice is neomycin (which is no longer used as much as it once was), which kills bowel flora that make ammonia.

Hepatic encephalopathy: mostly due to hyperammonemia; often precipitated by protein intake, GI bleed, or infection. Look for asterixis (the flapping of outstretched hands) and/or mental status changes.

Hepatorenal syndrome: liver failure may cause kidney failure.

Hypoglycemia: the liver stores glycogen.

Disseminated intravascular coagulation: activated clotting factors are cleared by the liver.

51. What signs and symptoms suggest biliary tract obstruction as a cause of jaundice?

- Elevated conjugated bilirubin. Conjugated bilirubin is more elevated than unconjugated bilirubin because the liver still functions and can conjugate bilirubin, but conjugated bilirubin cannot be excreted because of biliary tract disease.
- Markedly elevated alkaline phosphatase
- Pruritus
- Clay-colored stools
- Dark urine, which is strongly positive for conjugated bilirubin. Unconjugated bilirubin is not excreted in the urine because it is tightly bound to albumin.

52. What are the commonly tested types of biliary tract obstructions?

Bile duct obstruction, cholestasis, cholangitis, primary biliary cirrhosis, and primary sclerosing cholangitis.

53. What are the two major causes of common bile duct obstruction? How are they distinguished?

The most common cause is obstruction with a gallstone (choledocholithiasis). Look for a history of gallstones or the four Fs (female, forty, fertile, and fat). Ultrasound often images the stone; if not, use magnetic resonance cholangiopancreatography (MRCP) or endoscopic retrograde cholangiopancreatography (ERCP). Treatment is endoscopic removal of the stone. The second major cause of common bile duct obstruction is cancer. Look for weight loss. Pancreatic cancer is the most common type; look for **Courvoisier sign** (jaundice with a palpably enlarged gallbladder). Sometimes cholangiocarcinoma or bowel cancer blocks the common bile duct.

54. What are the two common causes of cholestasis?

Medications (e.g., birth control pills, trimethoprim-sulfamethoxazole, phenothiazines, androgens) and pregnancy.

55. What clues suggest a diagnosis of primary biliary cirrhosis?

This condition is usually seen in middle-aged women with no risk factors for liver or biliary disease. It causes marked pruritus, jaundice, and positive **antimitochondrial antibodies.** The rest of the work-up is negative. Cholestyramine helps with symptoms, but the only treatment is liver transplantation.

56. Who gets primary sclerosing cholangitis?

Primary sclerosing cholangitis usually occurs in young adults with inflammatory bowel disease (usually ulcerative colitis). It presents similarly to bacterial cholangitis. Fever, chills, pruritis, and right upper quadrant abdominal pain are common.

57. What usually precipitates cholangitis? What is the tip-off to its presence? How is it treated?

Cholangitis is usually precipitated by a gallstone that blocks the common bile duct with subsequent infection of the bile duct system. The tip-off is the presence of **Charcot triad:** fever, right upper quadrant pain, and jaundice. Treat with antibiotics, and remove gallstones surgically or endoscopically after the acute infection has resolved.

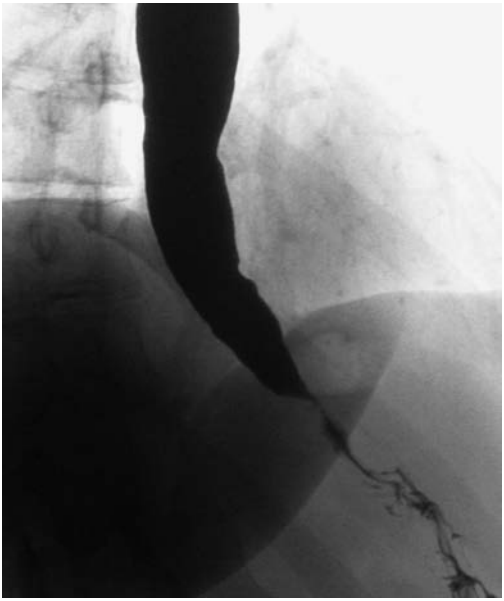

Fig. 12.10. Classic appearances of achalasia. Note the tapered appearance of the gastroesophageal junction with the column of barium above. *(From Adam A.* Grainger & Allison's diagnostic radiology. *5th ed. London: Churchill Livingstone, 2008, Fig. 30.21.)*

58. What are the classic symptoms of esophageal disease?

Dysphagia (difficulty in swallowing) and/or odynophagia (painful swallowing). Patients may also have atypical chest pain.

59. Define achalasia. How is it diagnosed and treated?

Achalasia is caused by incomplete relaxation of a hypertensive lower esophageal sphincter and loss or derangement of peristalsis. It is usually idiopathic but may be secondary to **Chagas disease** (South America). Patients have intermittent dysphagia for solids and liquids but no heartburn because the lower esophageal sphincter stays tightly closed and does not allow acid reflux. Barium swallow reveals a dilated esophagus with distal "bird-beak" narrowing (Fig. 12.10). The diagnosis is often confirmed with esophageal manometry. Treat with calcium channel blockers, pneumatic balloon dilatation, or botulinum toxin injection. Surgery (myotomy) is a last resort. Patients have an increased risk for esophageal carcinoma.

60. What are the signs and symptoms of esophageal spasm? How is it treated?

Both diffuse esophageal spasm (Fig. 12.11) and nutcracker esophagus (best thought of as a special variant of esophageal spasm) are characterized by irregular, forceful, and painful esophageal contractions that cause intermittent chest pain. Diagnose with esophageal manometry. Treat with calcium channel blockers and, if needed, surgery (myotomy).

61. What clues suggest scleroderma as the cause of esophageal complaints?

Scleroderma may cause aperistalsis due to esophageal fibrosis and atrophy of smooth muscle. The lower esophageal sphincter often becomes incompetent, and many patients have heartburn (opposite of achalasia). Look for positive antinuclear antibody and mask-like facies as well as other autoimmune symptoms. Remember also the **CREST** syndrome, which consist of **c**alcinosis, **R**aynaud phenomenon, **e**sophageal dysmotility, **s**clerodactyly, and **t**elangiectasias.

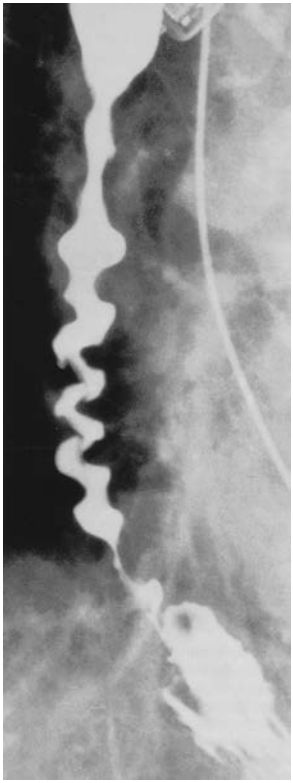

Fig. 12.11. Barium esophagogram showing a "corkscrew" esophagus in a patient with diffuse esophageal spasm. The patient had dysphagia and chest pain. Upper endoscopy was normal. *(From Feldman M, ed.* Gastroenterology and hepatology: the comprehensive visual reference. *New York: Churchill Livingstone, 1997, with permission.)*

62. What do you need to know about the epidemiology of esophageal cancer?

First, the epidemiology has recently changed, as adenocarcinoma is now more common than squamous cell carcinoma. Adenocarcinoma is due to the long-standing effects of gastric acid reflux and thus occurs in the distal esophagus. Squamous cell carcinoma is usually caused by alcohol and tobacco (synergistic effect) and is classically seen in black men over the age of 40 years who smoke and drink alcohol. Patients complain of weight loss and food "sticking" in the chest (solids more than liquids). The tumor is usually in the proximal esophagus.

63. What is the relationship between Barrett esophagus and esophageal cancer?

Barrett esophagus, which is usually caused by long-standing GERD, predisposes to esophageal adenocarcinoma. Barrett esophagus describes a columnar metaplasia of the normally squamous cell esophageal mucosa. Once Barrett esophagus is seen on endoscopy and confirmed with endoscopic biopsy, periodic biopsies must be done to monitor for the development of esophageal cancer.

64. What causes acute pancreatitis?

More than 80% of cases are due to alcohol or gallstones. Remember the mnemonic I GET SMASHED:

I = Idiopathic
G = Gallstones
E = Ethanol
T = Trauma
S = Steroids

M = Mumps (and other infections) or Malignancy
A = Autoimmune
S = Scorpion sting
H = Hypercalcemia or Hypertriglyceridemia
E = ERCP
D = Drugs (e.g., isoniazid, furosemide, simvastatin, steroids, azathioprine)

65. What are the signs and symptoms of acute pancreatitis?

Patients classically have epigastric abdominal pain that radiates to the back, nausea with vomiting that fails to relieve the pain, leukocytosis, and elevated amylase and lipase levels. Watch for **Grey Turner sign** (blue-black flanks) and **Cullen sign** (blue-black umbilicus), both of which are due to a hemorrhagic pancreatic exudate and indicate severe pancreatitis. Remember that perforated ulcers are also associated with elevated amylase and lipase levels and present similarly. However, patients usually have free air on abdominal radiographs and a history of peptic ulcer disease.

66. How is acute pancreatitis treated?

Patients are not allowed to eat, a nasogastric tube is often placed, and intravenous fluids and narcotics are given. For pain control, hydromorphone or fentanyl is often used. Other options include meperidine (which has a risk of seizures) or morphine (which causes sphincter of Oddi spasm, though clinical evidence of this is lacking).

67. What are the complications of acute pancreatitis?

Complications include pseudocyst formation (drain surgically if symptomatic and persistent for several weeks), abscess or infection (treat with antibiotics and drainage if needed), and chronic pancreatitis (calcifications of the pancreas may be seen on CT or plain abdominal films).

68. What causes chronic pancreatitis? How is it treated?

Chronic pancreatitis in the United States is almost always due to alcoholism and usually results from repeated bouts of acute pancreatitis. Gallstones do not cause chronic pancreatitis. Chronic pancreatitis may lead to diabetes, steatorrhea (excessive fat in the stool due to lack of pancreatic enzymes), calcification of the pancreas (which may be seen on a plain abdominal radiograph), and fat-soluble vitamin deficiencies (due to malabsorption). The incidence of pancreatic cancer is slightly increased in patients with pancreatitis, although smoking is a greater risk factor than alcohol for pancreatic cancer.

Treat chronic pancreatitis with alcohol abstinence, oral pancreatic enzyme replacement, and fat-soluble vitamin supplements.

69. Distinguish between Mallory-Weiss and Boerhaave tears in the esophagus. How are they diagnosed?

Mallory-Weiss tears are superficial erosions in the esophageal mucosa, whereas Boerhaave tears are full-thickness esophageal ruptures. Both may cause a GI bleed and are usually seen with vomiting and retching (alcoholics and bulimic patients) if they are not iatrogenic (due to endoscopy). Diagnosis is usually made with endoscopy, during which bleeding vessels should be sclerosed, and/or from contrast radiographs. Mallory-Weiss tears usually stop bleeding on their own or with endoscopic treatment, but Boerhaave tears require immediate surgical repair and drainage.

70. What is the rule about bowel contrast when a GI perforation is suspected?

For all GI studies, barium is preferred because it provides higher quality images. However, with suspected GI perforation, do not use barium because it can cause chemical peritonitis or mediastinitis when a perforation/leak is present. Instead, use water-soluble contrast (e.g., Gastrografin). Things get tricky in patients with a significant risk for aspiration, because the lungs tolerate barium well but develop chemical pneumonitis from water-soluble contrast. When in doubt, give water-soluble contrast, followed by barium once perforation has been excluded.

71. What are the common GI malformations in children? How are they distinguished?

NAME*	PRESENTING AGE	VOMIT DESCRIPTION	FINDINGS/KEY WORDS
Pyloric stenosis	0–3 mo	Nonbilious, projectile	Males >> females; palpable olive-shaped mass in the epigastrium; low Cl/low K metabolic alkalosis
Intestinal atresia	0–1 wk	Bilious	"Double-bubble" sign, Down syndrome

NAME*	PRESENTING AGE	VOMIT DESCRIPTION	FINDINGS/KEY WORDS
TE fistula†	0–2 wk	Food regurgitation	Respiratory compromise with feeding, aspiration pneumonia, inability to pass a nasogastric tube into the stomach, gastric distention (from air)
Hirschsprung disease	0–1 yr	Feculent	Abdominal distention, obstipation, no nerve ganglia seen on rectal biopsy; males >> females
Anal atresia	0–1 wk	Late, feculent	Detected on initial exam in the nursery; males > females
Choanal atresia	0–1 wk	—	Cyanosis with feeding, relieved by crying; inability to pass a nasogastric tube through nose

Cl, Chloride; *K*, potassium; *TE*, tracheoesophageal
*Treat each of these conditions with **surgical repair**.
†The most common variant (85% of cases) has esophageal atresia with a fistula from the bronchus to the distal esophagus. The result is gastric distention, as each breath transmits air to the GI tract. Be able to recognize a sketch of this most common variant (Fig. 12.12).

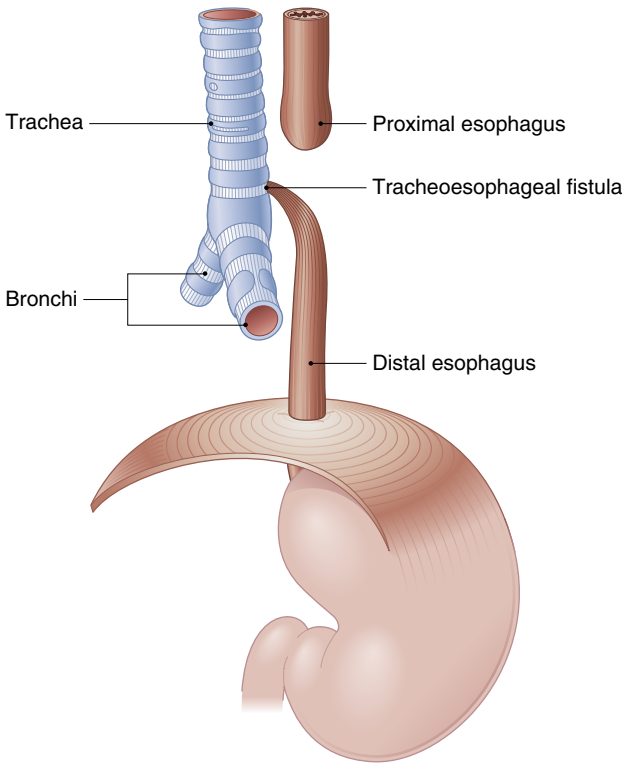

Fig. 12.12. Tracheoesophageal fistula. Diagram of the most common type of esophageal atresia and tracheoesophageal fistula. *(From Gilbert-Barness, E.* Potter's pathology of the fetus, infant and child. *2nd ed. St. Louis: Mosby, 2007, Fig. 25.6.)*

72. What other pediatric GI conditions are commonly found on Step 2? How are they distinguished?

NAME	PRESENTING AGE	VOMIT DESCRIPTION	FINDINGS/KEY WORDS
Intussusception	3 mo–2 yr	Bilious	Currant-jelly stools (blood and mucus), palpable sausage-shaped mass; treat with pneumatic or hydrostatic enema guided by fluoroscopy or ultrasound (diagnostic and therapeutic)
Necrotizing enterocolitis	0–2 mo	Bilious	Premature baby, fever, rectal bleeding, air in bowel wall. Treat with NPO, orogastric tube, IV fluids, and antibiotics
Meconium ileus	0–1 wk	Feculent, late	Cystic fibrosis manifestation (as is rectal prolapse)
Midgut volvulus	0–2 yr	Bilious	Sudden onset of pain, distention, rectal bleeding, peritonitis, "bird's beak" on abdominal radiograph; treat with surgery
Meckel diverticulum	0–2 yr	Varies	Rule of 2s*; GI ulceration/bleeding; use Meckel scan to detect; treat with surgery
Strangulated hernia	Any age	Bilious	Physical exam detects bowel loops in inguinal canal

IV, Intravenous, *NPO*, nothing by mouth (no feedings)
*Rule of 2s for Meckel diverticulum: 2% of population affected (most common GI tract abnormality; remnant of omphalomesenteric duct), 2 inches long, within 2 feet of ileocolic junction, presents in the first 2 years of life. Meckel diverticulum can cause intussusception, obstruction, or volvulus.

73. Which GI malformation primarily causes respiratory problems?

Diaphragmatic hernia, which is more common in males. Ninety percent are on the left side. The main point to know is that bowel herniates into the thorax through the diaphragmatic defect, compressing the lung and impeding lung development (pulmonary hypoplasia develops). Patients present with respiratory distress and have bowel sounds in the chest and bowel loops in the thorax on chest radiographs (Fig. 12.13). Treat with surgical correction of the diaphragm.

74. How are omphalocele and gastroschisis differentiated?

An **omphalocele**, associated with other congenital anomalies, is located in the midline, the sac contains multiple abdominal organs, the umbilical ring is absent, and other anomalies are common. **Gastroschisis** is to the right of the midline, only small bowel is exposed (no true hernia sac), the umbilical ring is present, and other anomalies are rare (Fig. 12.14).

75. What is Henoch-Schönlein purpura? Why is it mentioned in the GI section?

Henoch-Schönlein purpura is a vasculitis that may present with GI bleeding and abdominal pain. Look for a history of upper respiratory infection, characteristic rash on lower extremities and buttocks (Fig. 12.15), swelling in hands and feet, arthritis, and/or hematuria and proteinuria. Treat supportively with hydration, rest, and pain relief.

76. What is the most common cause of diarrhea in children?

As a primary cause, probably viral gastroenteritis (e.g., Norwalk virus, rotavirus). Remember, however, that diarrhea is often a nonspecific sign of any systemic illness (e.g., otitis media, pneumonia, urinary tract infection).

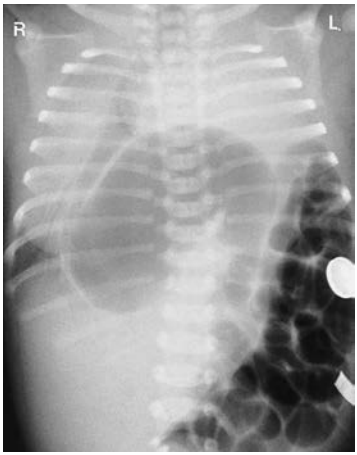

Fig. 12.13. Diaphragmatic hernia shown in a newborn with significant respiratory difficulty. An anteroposterior (AP) view of the chest and abdomen demonstrates opacification of the left hemithorax, with bowel loops pushing up into the opacified left hemithorax. This condition carries a high fatality rate and should be recognized immediately. *(From Mettler F.* Essentials of radiology. *2nd ed. Philadelphia: Saunders, 2004, Fig. 9.13.)*

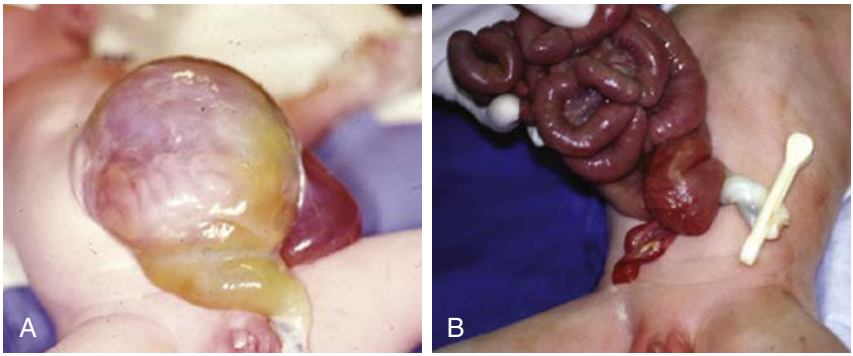

Fig. 12.14. Abdominal wall defects. A, Omphalocele with intact sac. B, Gastroschisis with eviscerated multiple bowel loops to the right of the umbilical cord. *(From Townsend CM.* Sabiston textbook of surgery. *19th ed. Philadelphia: Saunders, 2012, Fig. 67.20.)*

77. True or false: Children may develop inflammatory bowel disease and irritable bowel syndrome.

True. Abdominal pain may be the result of inflammatory bowel disease or irritable bowel syndrome. Diarrhea, fever, bloody stools, anemia, joint pains, and poor growth are more concerning for inflammatory bowel disease. GI complaints may also be due to anxiety or psychiatric problems. Watch for separation anxiety, children who do not want to go to school, depression, and child abuse.

78. What is the first step in evaluating neonatal jaundice? Why is jaundice of concern in a neonate?

The first step is to determine whether the jaundice is physiologic or pathologic. Measure total, direct, and indirect bilirubin. The main concern is bilirubin-induced neurologic dysfunction (BIND), which is due to high levels of unconjugated bilirubin with subsequent deposit in the basal ganglia. Kernicterus is the term for the chronic and permanent sequelae of BIND. Look for poor feeding, seizures, flaccidity, opisthotonos, and apnea in the setting of severe jaundice.

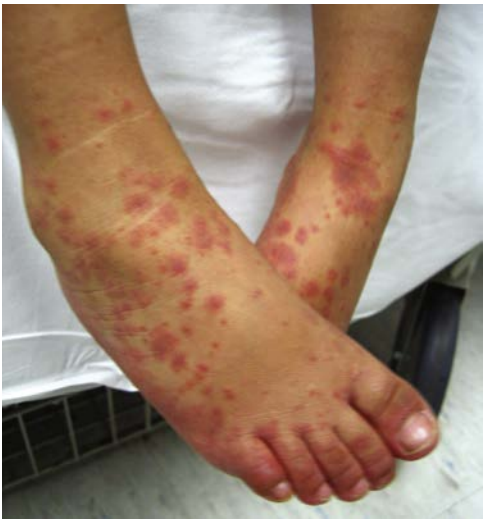

Fig. 12.15. Henoch-Schönlein purpura in a 7-year-old child. Note typical red-purple rash on the lower extremities. *(From Marx J.* Rosen's emergency medicine. *7th ed. St. Louis: Mosby, 2009, Fig. 170.10. Courtesy of Marianne Gausche-Hill, MD.)*

79. What causes physiologic jaundice of the newborn? Who gets it?

Physiologic (nonpathologic) jaundice is caused by normal neonatal changes in bilirubin metabolism, which results in increased bilirubin production, decreased bilirubin clearance, and increased enterohepatic circulation. These changes result in the low-risk unconjugated (indirect) bilirubinemia that occurs in most newborns and is even more prevalent in premature infants. Bilirubin is mostly unconjugated because of incomplete maturation of liver function. In full-term infants, bilirubin is less than 12 mg/dL, peaks at day 2–4, and returns to normal by 2 weeks. In premature infants, bilirubin is less than 15 mg/dL, peaks at 3–5 days, and may be elevated for up to 3 weeks.

80. How is severe hyperbilirubinemia recognized?

Severe hyperbilirubinemia (sometimes called pathologic jaundice) is suggested by jaundice that is recognized in the first 24 hours of life, total bilirubin that is higher than the hour-specific 95th percentile, a rate of rise is greater than 0.2 mg/dL per hour, jaundice in a term newborn after 2 weeks of age, or a direct bilirubin concentration that is more than 20% of the total bilirubin.

81. What are the causes of neonatal jaundice?

Breastfeeding jaundice: occurs in 1 in 10 breastfed infants and is typically seen in the first week of life. This is essentially an exaggerated physiologic jaundice due to insufficient milk intake, which leads to fluid and weight loss and an inadequate number of bowel movements to remove bilirubin from the body.

Breast milk jaundice: typically presents after the first 3 to 5 days of life and has traditionally been defined as the persistence of physiologic jaundice beyond the first week of life. Breast milk jaundice results from a direct effect of breast milk itself as human milk promotes an increase in intestinal absorption of bilirubin. Bilirubin levels peak within 2 weeks after birth and decline to normal levels by 12 weeks of age. Breastfeeding can continue as long as the hyperbilirubinemia remains in the safe zone.

Illness: infection or sepsis, hypothyroidism, liver insult, cystic fibrosis, and other illnesses may prolong neonatal jaundice and lower the threshold for kernicterus. The youngest, sickest infants are at greatest risk for hyperbilirubinemia and kernicterus.

Hemolysis: from Rhesus (Rh) incompatibility or congenital red cell diseases (e.g., hereditary spherocytosis, elliptocytosis, G6PD deficiency) that cause hemolysis in the neonatal period. Look for

anemia, peripheral smear abnormalities, positive family history, and higher levels of unconjugated bilirubin.

Metabolic disorders: Crigler-Najjar syndrome causes severe unconjugated hyperbilirubinemia, whereas Gilbert syndrome causes a mild form. Rotor and Dubin-Johnson syndromes cause conjugated hyperbilirubinemia.

Biliary atresia: full-term infants with clay- or gray-colored stools and high levels of conjugated bilirubin. Treat with surgery.

Medications: avoid sulfa drugs in neonates; they displace bilirubin from albumin and may precipitate kernicterus.

82. How is severe hyperbilirubinemia treated?

Unconjugated hyperbilirubinemia that persists, rises above 15 mg/dL, or rises rapidly is treated with **phototherapy** to convert unconjugated bilirubin to a water-soluble form that can be excreted. A last resort is exchange transfusion, but don't even think about it unless the level of unconjugated bilirubin is greater than 20 mg/dL.

83. What should you do if an infant is born to a mother with active hepatitis B?

An infant born to a mother with active hepatitis B should receive the first immunization shot and hepatitis B immune globulin at birth.