Practice file

Editing file

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Abdominal pain

Q1: You see a 47-year-old man in clinic with a three-month history of epigastric dull abdominal pain. He states that the pain is worse in the mornings and is relieved after meals. On direct questioning, there is no history of weight loss and the patient's bowel habits are normal. On examination, his abdomen is soft and experiences moderate discomfort on palpation of the epigastric region. The most likely diagnosis is:

A. Gastric ulcer
B. Gastro-oesophageal reflux disease (GORD)
C. Duodenal ulcer
D. Gastric carcinoma
E. Gastritis

Explanation: Although all of the answers may present with abdominal pain, the key to the answer is in the history. Duodenal ulcers (C), which are four times more common than gastric ulcers, classically present with abdominal pain which is usually relieved after meals or drinking milk. Gastric ulcers (A) on the other hand present with abdominal pain which tends to worsen after meals. In either duodenal/gastric ulcers, weight loss may be an associated symptom, but this is usually more common in gastric ulcers. Patients who suffer from GORD (B) usually experience retrosternal discomfort ('heartburn') after meals and on lying flat. In addition, abdominal discomfort and pain in patients with gastritis (E) usually occurs after meals. Gastric carcinomas (D) tend to present with abdominal pain and drastic weight loss (e.g. 2–3 stone weight loss in the space of three months).

Q2: Which of the following is the most common cause of duodenal ulcers?

A. NSAIDs
B. Helicobacter pylori
C. Alcohol abuse
D. Chronic corticosteroid therapy
E. Zollinger–Ellison syndrome

Explanation: The most common causative agent that gives rise to approximately 90 percent of duodenal ulcers is infection with H. pylori (B) (a helical-shaped gram-negative microaerophilic bacterium). The bacteria favours low pH environments and, with the help of its flagella, moves to the epithelial lining of the stomach and duodenum. The bacterium produces ammonia and proteases which break down the epithelial linings of the stomach and duodenal mucosa causing ulceration. Non-steroidal anti-inflammatory drugs (NSAIDs) (A), alcohol abuse (C), chronic corticosteroid therapy (D) and Zollinger–Ellison syndrome (E) (increase in gastrin production, from e.g. a gastrinoma, which stimulates the parietal cells of the stomach to produce excess hydrochloric acid leading to peptic ulceration) are all less common causes of peptic ulceration.

Q3: A 55-year-old woman is referred by her GP for upper gastrointestinal (GI) endoscopy following a four-month history of epigastric pain despite treatment with antacids and proton pump inhibitors (PPIs). The results demonstrate a duodenal ulcer coupled with a positive campylobacter-like organism (CLO) test. The patient has no past medical history and has no known drug allergies. The most appropriate treatment is:

A. Seven-day course of twice daily omeprazole 20 mg, 1 g amoxicillin and 500 mg clarithromycin
B. Seven-day course of twice daily omeprazole 20 mg
C. Seven-day course of twice daily omeprazole 20 mg and 1 g amoxicillin
D. Seven-day course of twice daily omeprazole 20 mg and 500 mg clarithromycin
E. Seven-day course of twice daily 1 g amoxicillin and 500 mg clarithromycin

Explanation: This patient has been diagnosed with a duodenal ulcer secondary to H. pylori infection. The CLO test (also known as the rapid urease test) is positive, confirming the presence of the bacterium. A 7-day course of 'triple therapy' (PPI + two antibiotics) is recommended for patients with duodenal ulcers positive for H. pylori. The eradication therapy regimen is based on twice daily dosing and, as well as aiming to clear the H. pylori infection with the antibiotics, the PPI is used to enhance the healing of the ulcer. Therefore in this scenario, (A) is the most appropriate from the list. For patients who are allergic to penicillin, clarithromycin and metronidazole can be used instead.

Answers: Q1: C | Q2: B | Q3: A

Abdominal pain

Q4: A 56-year-old woman becomes the chief financial officer of a large company and, several months thereafter, develops upper abdominal pain that she ascribes to stress. She takes an over-the-counter antacid with temporary benefit. She uses no other medications. One night she awakens with nausea and vomits a large volume of coffee grounds-like material; she becomes weak and diaphoretic. Upon hospitalization, she is found to have an actively bleeding duodenal ulcer. Which of the following statements is true?

A. The most likely etiology is adenocarcinoma of the duodenum.
B. The etiology of duodenal ulcer is different in women than in men.
C. The likelihood that she harbors Helicobacter pylori is greater than 50%.
D. Lifetime residence in the United States makes H pylori unlikely as an etiologic agent.
E. Organisms consistent with H pylori are rarely seen on biopsy in patients with duodenal ulcer.

Explanation: Duodenal ulcer is more common in men than women, but H pylori is present in 70% of patients (men and women) who have a duodenal ulcer not associated with NSAID ingestion. In gastric ulcer disease, the incidence of H pylori is 30% to 60%. Helicobacter pylori is more common in developing countries but is often seen in the United States. It is more common in patients with low socioeconomic status, in particular those with unsanitary living conditions, which suggests that H pylori is transmitted by fecal-oral or oral-oral routes. In patients with duodenal ulcer, organisms consistent with H pylori are frequently seen on biopsy. Before the discovery of H pylori, most duodenal ulcers would reoccur. Adenocarcinoma of the duodenum is a rare cause of upper gastrointestinal bleeding.

Q5: A 36-year-old man presents for a well-patient examination. He gives a history that, over the past 20 years, he has had three episodes of abdominal pain and hematemesis, the most recent of which occurred several years ago. He was told that an ulcer was seen on a barium upper GI radiograph. You obtain a serum assay for H pylori IgG, which is positive. What is the most effective regimen to eradicate this organism?

A. Omeprazole 20 mg orally once daily for 6 weeks
B. Ranitidine 300 mg orally once daily at bedtime for 6 weeks
C. Omeprazole 20 mg twice daily, amoxicillin 1000 mg twice daily, and clarithromycin 500 mg twice daily for 14 days
D. Bismuth subsalicylate and metronidazole twice daily for 7 days
E. Benzathine penicillin, 1.2 million units intramuscularly weekly for three doses

Explanation: Although acid suppression therapy leads to 80% healing rates after 4 weeks of treatment, acid reduction with omeprazole or ranitidine alone does not eradicate H pylori. Three- or four-drug therapy, including bismuth or (most often) proton pump inhibitor, combined with two antibiotics effective against H pylori, will be necessary to eradicate the organism. Longer duration of therapy (ie, 14 days) leads to a greater healing rate. This regimen will eradicate H pylori in more than 90% of patients. Patients whose H pylori has been eradicated have only a 5% chance of ulcer recurrence (compared to 60%-70% of patients not treated for H pylori). Follow-up tests to prove H pylori eradication are not recommended in the usual patient who becomes asymptomatic. If the peptic ulcer should recur (again, this happens infrequently), either direct testing of a biopsy specimen or a test for urease activity in the stomach is necessary, as the serological studies remain positive for many years. Benzathine penicillin is commonly used to treat syphilis but not Helicobacter.

Answers: Q4: C | Q5: C

Abdominal pain

Q6: A 34-year-old man presents with substernal discomfort. The symptoms are worse after meals, particularly a heavy evening meal, and are sometimes associated with hot/sour fluid in the back of the throat and nocturnal awakening. The patient denies difficulty swallowing, pain on swallowing, or weight loss. The symptoms have been present for 6 weeks; the patient has gained 20 lb in the past 2 years. Which of the following is the most appropriate initial approach?

A. Therapeutic trial of ranitidine or omeprazole
B. Exercise test with thallium imaging
C. Esophagogastroduodenoscopy
D. CT scan of the chest
E. Coronary angiography

Explanation: In the absence of alarm symptoms (such as dysphagia, odynophagia, weight loss, or gastrointestinal bleeding), a therapeutic trial of acid reduction therapy is reasonable. Mild to moderate GERD symptoms often respond to H2 blockers. More severe disease, including erosive esophagitis, usually requires proton pump inhibitor therapy for 8 weeks to ensure healing. If the patient has recurrent symptoms or symptomatic GERD for over 5 years, endoscopy is indicated to rule out Barrett esophagus (intestinal metaplasia of the lower esophagus). Barrett esophagus is a premalignant condition, and most patients receive surveillance EGD every 2 to 3 years, although evidence of mortality benefit from this approach is not available. In the absence of alarm symptoms, a therapeutic trial is generally favored over more expensive diagnostic studies (endoscopy, CT scan). Classic symptoms of GERD do not mandate an evaluation for coronary artery disease unless other features suggest this diagnosis.

Q7: A 32-year-old white woman complains of abdominal pain off and on since the age of 17. She notices abdominal bloating relieved by defecation as well as alternating diarrhea and constipation. She has no weight loss, GI bleeding, or nocturnal diarrhea. On examination, she has slight LLQ tenderness and gaseous abdominal distension. Laboratory studies, including CBC, are normal. Which of the following is the most appropriate initial approach?

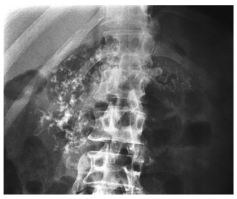
A. Recommend increased dietary fiber, antispasmodics as needed, and follow-up examination in 2 months.
B. Refer to gastroenterologist for colonoscopy.
C. Obtain antiendomysial antibodies.
D. Order UGI series with small bowel follow-through.
E. Order small bowel biopsy.

Explanation: This patient meets the Rome II criteria for irritable bowel syndrome. The major criterion is abdominal pain relieved with defecation and associated with change in stool frequency or consistency. In addition, these patients often complain of difficult stool passage, a feeling of incomplete evacuation, and mucus in the stool. In this young patient with long-standing symptoms and no evidence of organic disease on physical and laboratory studies, further evaluation (ie, colonoscopy or small bowel studies for sprue) is unnecessary. Irritable bowel syndrome is a motility disorder associated with altered sensitivity to abdominal pain and distension. It is the commonest cause of chronic GI symptoms and is three times more common in women than in men. Associated lactose intolerance may cause similar symptoms and should be considered in all cases. Patients older than 40 years with new symptoms, weight loss, or positive family history of colon cancer should have further workup, usually with colonoscopy.

Answers: Q6: A | Q7: A

Abdominal pain

Q8: A 42-year-old man is evaluated in the hospital for a 1-year history of postprandial abdominal pain that radiates to the back, is worse after eating, and is associated with bloating and nausea. He has not lost weight. The patient has had at least five alcohol-containing drinks a day for 20 years. On physical examination, vital signs are normal; BMI is 21. There is mild epigastric tenderness with no guarding or rebound and normal bowel sounds. Laboratory studies reveal a normal complete blood count and normal glucose and liver chemistry tests; amylase is 221 U/L and lipase is 472 U/L. A plain film of the abdomen is shown. Which of the following is the most likely diagnosis?



A. Acute cholangitis
B.Chronic pancreatitis
C. Diverticulitis
D. Peptic ulcer disease

Explanation: The diagnosis of chronic pancreatitis should be strongly considered in the appropriate clinical setting, such as a patient with a history of alcoholism who presents with chronic upper abdominal pain radiating to the back, diabetes, and steatorrhea. Such patients may not need additional testing. However, most patients have only nonspecific abdominal pain and elevated pancreatic enzyme levels and require diagnostic radiographic imaging studies. The presence of pancreatic calcifications on plain films or CT scan confirms the diagnosis. Plain films of the abdomen will show pancreatic calcifications in some patients, as it did in this patient. Most patients, however, require abdominal CT scans to detect the calcifications and to exclude other causes of pain.
Acute cholangitis is associated with biliary obstruction and is characterized by the triad of pain, fever, and jaundice, which are absent in this patient. If biliary obstruction involves the pancreatic duct as well, pancreatic enzymes may be elevated. Acute cholangitis is not compatible with an illness lasting 1 year.
Diverticulitis is another acute illness characterized by left lower quadrant pain, fever, and localized abdominal tenderness. Neither acute cholangitis nor diverticulitis is associated with pancreatic calcifications. Acute diverticulitis is not associated with pancreatic enzyme elevations.
Pain associated with peptic ulcer disease is likely to be epigastric, is usually described as burning or gnawing, and tends to occur during fasting or at night. It is not associated with elevated pancreatic enzyme levels or pancreatic calcifications.

Key Point The diagnosis of chronic pancreatitis should be strongly considered in patients with a history of alcoholism presenting with chronic upper abdominal pain radiating to the back, diabetes, steatorrhea, and pancreatic calcifications on abdominal radiographs.

Q9: A 41-year-old man is evaluated for an 8-month history of mid-epigastric pain that is worse after eating and six to eight oily bowel movements a day usually occurring after a meal. He has lost 6.8 kg (15 lb) over the past 6 months. The patient drinks six to eight cans of beer a day, and he has been admitted to the hospital twice with acute pancreatitis. He takes no medications. On physical examination, BMI is 21. He has normal bowel sounds and mid-epigastric tenderness but no evidence of hepatosplenomegaly or masses. Rectal examination reveals brown stool that is negative for occult blood. The remainder of the examination is normal. Plain radiograph of the abdomen shows a normal bowel gas pattern and is otherwise normal. Which of the following tests is most likely to establish the diagnosis in this patient?

A. Colonoscopy
B. CT scan of the abdomen
C. Measurement of serum antiendomysial antibodies
D. Stool for leukocytes, culture, ova, and parasites

Fasting plasma glucose	124 mg/dL (6.9 mmol/L)
Aspartate aminotransferase	191 U/L
Alanine aminotransferase	82 U/L
Amylase	132U/L
Lipase	289 U/L

Explanation: The test most likely to establish the diagnosis is CT scan of the abdomen. This patient has chronic pancreatitis secondary to alcohol abuse, which has resulted in malabsorption. The three classic findings in chronic pancreatitis are abdominal pain that is usually mid-epigastric, postprandial diarrhea, and diabetes mellitus secondary to pancreatic endocrine insufficiency. Malabsorption occurs in patients with chronic pancreatitis when approximately 80% of the pancreas is destroyed. Malabsorption presents with diarrhea and steatorrhea, weight loss, and deficiencies of fat-soluble vitamins because the damaged pancreatic gland is no longer producing the pancreatic exocrine enzymes to absorb food. Additional clues to the diagnosis include elevated pancreatic enzyme levels and liver chemistry tests. Patients with a typical presentation may not need additional testing. However, most patients with chronic pancreatitis have only nonspecific abdominal pain (and normal pancreatic enzyme concentrations) and require diagnostic radiographic imaging studies. The presence of pancreatic calcifications on radiographs confirms the diagnosis. Plain films of the abdomen will show pancreatic calcifications in approximately 30% of patients. Most patients, however, require abdominal CT scans, which are able to detect pancreatic calcification in up to 90% of patients. CT scanning can also exclude other causes of pain. Antiendomysial antibodies are a marker for celiac disease, which is unlikely in this patient with an evident history of pancreatic malabsorption. Although colonoscopy is indicated as a screening tool for average risk asymptomatic patients beginning at the age of 50 years and for patients with a change in bowel habits and weight loss, this patient's history suggests pancreatic malabsorption, and colonoscopy is less likely than abdominal CT scan to confirm the diagnosis. Stool studies are appropriate for determining the cause of an acute infectious diarrhea, but this patient has had diarrhea for 8 months, and infectious diarrhea is not usually associated with such a degree of weight loss or elevation of pancreatic enzymes.

Key Point Patients with chronic pancreatitis present with abdominal pain and, in more severe cases, malabsorption and endocrine insufficiency.

Answers: Q8: B | Q9: B

Abdominal pain

Q10: A 30-year-old woman is evaluated for a 9-month history of cramping midepigastric discomfort that is relieved by defecation; the discomfort is sometimes accompanied by bloating. The stool is often watery. She has not had fever, chills, or weight loss. The patient is otherwise healthy and takes no medications; there is no family history of gastrointestinal disease. On physical examination, the patient is afebrile; blood pressure is 105/70 mm Hg, pulse rate is 72/min, and respiration rate is 14/min; BMI is 23. The abdomen is soft and not tender or distended; the stool is brown and negative for occult blood. Complete blood count and serum biochemistry studies, including liver studies, vitamin B12, vitamin D, and thyroid-stimulating hormone, are normal. A flexible sigmoidoscopy is normal. Which of the following is the most appropriate management for this patient?

A. Colonoscopy
B.CT enteroscopy
C. Gluten-free diet
D. Symptomatic management

Explanation: The most appropriate management for this patient is symptom control. Irritable bowel syndrome (IBS) is the most common gastrointestinal condition diagnosed in the United States. This patient presents with symptoms that meet the Rome III criteria for IBS. The Rome criteria were developed to establish consensus guidelines for diagnosis of functional bowel disorders. Criteria for IBS are symptoms of recurrent abdominal pain or discomfort and a marked change in bowel habit for at least 6 months, with symptoms experienced on at least 3 days a month for at least 3 months. Two or more of the following must also apply: (1) pain is relieved by a bowel movement; (2) onset of pain is related to a change in frequency of stool; and/or (3) onset of pain is related to a change in the appearance of stool. In this otherwise healthy young woman, reassurance that she has a chronic but not a life-threatening disease with recommendation of a high-fiber diet should be the initial therapy. CT enteroscopy or colonoscopy would be premature at this point given the absence of alarm symptoms: fever, weight loss, blood in stool, abnormal physical examination, family history of inflammatory bowel disease or colon cancer, or pain or diarrhea that awakens/interferes with sleep. This patient does not have evidence of malabsorption, anemia, or weight loss to suggest a diagnosis of celiac disease; therefore, an empiric gluten-free diet would be inappropriate. An empiric gluten-free diet is never appropriate without first establishing the histological diagnosis of celiac disease with a small-bowel biopsy.

Key Point Irritable bowel syndrome is a clinical diagnosis of exclusion and, in the absence of alarm symptoms, invasive workup is not necessary.

Q11: A 59-year-old woman is evaluated in the emergency department for a 9-hour history of epigastric pain, nausea, and vomiting. She had been previously healthy. On physical examination, the patient appears ill. Temperature is 36.5°C (97.8°F), blood pressure is 148/84 mm Hg, pulse rate is 112/min, and respiration rate is 14/min. BMI is 30. Abdominal examination reveals diffuse tenderness. Ultrasonography shows cholelithiasis and a dilated common bile duct. Which of the following is the most appropriate next step in the management of this patient?

Leukocyte count	28,200/μL (28.2 × 10^9/L)
Total bilirubin	3.4 mg/dL (58.1 μmol/L)
Alkaline phosphatase	164 U/L
Alanine aminotransferase	224 U/L
Aspartate aminotransferase	142 U/L
Amylase	410 IU/L
Lipase	360 IU/L

A- Emergency laparoscopic cholecystectomy
B- Endoscopic retrograde cholangiopancreatography (ERCP)
C- Jejunal enteral feedings
D- Magnetic resonance cholangiopancreatography (MRCP)

Explanation: The most appropriate next step in management is ERCP. Patients with acute pancreatitis usually have the sudden onset of epigastric pain, often radiating to the back. These symptoms are often accompanied by nausea, vomiting, fever, and tachycardia. The physical examination shows epigastric tenderness, abdominal distension, hypoactive bowel sounds, and occasional guarding. The diagnosis is confirmed by laboratory results showing serum concentrations of amylase and lipase at least three times the upper limit of normal. Abdominal ultrasonography should be used to detect cholelithiasis in patients with suspected gallstone pancreatitis. ERCP is recommended in patients with evidence of gallstone pancreatitis and suspected biliary obstruction. Biliary obstruction is suspected if cholelithiasis or choledocholithiasis is present, bile ducts are dilated, and liver enzymes are elevated. Aminotransferase concentrations rise initially in gallstone pancreatitis, with subsequent rise of alkaline phosphatase and bilirubin if obstruction persists. ERCP with sphincterotomy has been shown to lower morbidity and mortality in these patients, significantly reducing rates of cholangitis and biliary sepsis.
Although elective cholecystectomy will be required in the future, ERCP is the preferred immediate intervention for removing obstructing stones in acute pancreatitis. MRCP may be used to evaluate biliary obstruction if ultrasonography is nondiagnostic. In a patient with choledocholithiasis identified by ultrasonography, MRCP is unlikely to provide additional diagnostic information and cannot be used therapeutically to remove the obstructing stone. Finally, definitive treatment should not be delayed to obtain further imaging studies. Jejunal enteral feedings are indicated in patients with severe pancreatitis when it is anticipated the patient will not be able to eat for a prolonged period of time. In this case, it is likely the patient will be able to resume oral intake after the obstructing stone is removed.

Key Point ERCP with sphincterotomy and stone extraction is the initial treatment of choice for gallstone pancreatitis.

Answers: Q10: D | Q11: B

Abdominal pain

Q12: A 34-year-old woman is evaluated for continued severe mid-epigastric pain that radiates to the back, nausea, and vomiting 5 days after being hospitalized for alcohol-related pancreatitis. She has not been able eat or drink since being admitted. On physical examination, temperature is 38.2°C (100.8°F), blood pressure is 132/84 mm Hg, pulse rate is 101/min, and respiration rate is 20/min. There is no scleral icterus or jaundice. The abdomen is distended and diffusely tender with hypoactive bowel sounds but no peritoneal signs. CT scan of the abdomen shows a diffusely edematous pancreas with multiple peripancreatic fluid collections and no evidence of pancreatic necrosis. Which of the following is the most appropriate next step in the management of this patient?

A- Begin prednisone
B- Enteral nutrition with nasojejunal feeding tube
C- Intravenous imipenem
D- Pancreatic debridement

Aspartate aminotransferase	189 U/L
Alanine aminotransferase	151 U/L
Bilirubin (total)	1.1 mg/dL (18.8 µmol/L)
Amylase	388 U/L
Lipase	924 U/L

Explanation: The most appropriate management step is enteral nutrition with nasojejunal tube feeding. This patient has moderate to severe acute pancreatitis and after 5 days remains febrile, continues to be in pain, and cannot take in any oral nutrition. The patient will likely have an extended period before being able to take in oral nutrition. Two routes are available for providing nutrition in patients with severe acute pancreatitis: enteral nutrition and parenteral nutrition. Enteral nutrition is provided through a feeding tube, ideally placed past the ligament of Treitz so as not to stimulate the pancreas. Parenteral nutrition is provided through a large peripheral or central intravenous line. Enteral nutrition is preferred over parenteral nutrition because of its lower complication rate. Enteral nutrition is associated with a significantly lower incidence of infections, reduced surgical interventions to control complications of pancreatitis, and a reduced length of hospital stay. Imipenem therapy is only helpful in acute pancreatitis when there is evidence of pancreatic necrosis. Pancreatic necrosis is diagnosed by a contrast-enhanced CT scan that shows nonenhancing pancreatic tissue. In patients with noninfected pancreatic necrosis, antibiotics may decrease the incidence of sepsis, systemic complications (for example, respiratory failure), and local complications (for example, infected pancreatic necrosis or pancreatic abscess). There is no benefit from antibiotic use in acute pancreatitis without pancreatic necrosis, and such treatment may lead to development of nosocomial infections with resistant pathogens. Similarly, pancreatic debridement is recommended only in patients with pancreatitis and infected pancreatic necrosis. There is no role for corticosteroid therapy in patients with acute pancreatitis of any etiology. Corticosteroid use may increase the risk for nosocomial related infections and metabolic complications such as hyperglycemia.

Key Point Enteral feeding is the preferred route for providing nutrition in patients with severe acute pancreatitis.

Q13: A 61-year-old man is evaluated for a 3-week history of abdominal discomfort and early satiety. During this time, he has experienced a 1.4-kg (3-lb) weight loss. For the past 10 days he has treated these symptoms with an over-the-counter proton pump inhibitor with partial relief of symptoms. He takes no other medications. On physical examination, temperature is 37°C (98.6°F), blood pressure is 132/76 mm Hg, pulse rate is 68/min, and respiration rate is 12/min. His abdominal examination reveals a rounded, soft abdomen with active bowel sounds. No masses are palpable. Deep epigastric palpation results in mild tenderness. Upper endoscopy reveals a 9-mm ulcer in the gastric antrum proximal to the pylorus. Which of the following is the most appropriate management for this patient's ulcer?

A- Biopsy
B- Omeprazole, amoxicillin, and clarithromycin
C- Rapid urease test
D- Urea breath test

Explanation: The most appropriate management for this patient's gastric ulcer is biopsy. Biopsies of all gastric ulcers should be performed, because even small, benign-appearing gastric ulcers may harbor malignancy. In benign ulcers, biopsies can also provide evidence for the presence of Helicobacter pylori infection and guide appropriate therapy. Testing for H. pylori is indicated in patients with active peptic ulcer disease (duodenal or gastric) and in patients with a history of peptic ulcer disease who have not been previously treated for H. pylori infection. The most commonly used endoscopic tests include biopsy and histologic assessment and the rapid urease test. The sensitivity of the rapid urease test can be reduced by as much as 25% in patients who have taken a proton pump inhibitor (PPI), such as omeprazole, within 2 weeks or bismuth or antibiotic therapy within 4 weeks of the endoscopy; therefore, biopsy followed by histologic evaluation for evidence of H. pylori infection is the endoscopic test of choice for this patient. The sensitivity of urea breath testing, like that of the rapid urease test, is reduced by medications that affect urease production such as a PPI. Treatment for peptic ulcer disease is guided by the biopsy and presence of H. pylori infection. In the presence of documented infection, triple therapy consisting of a PPI, amoxicillin, and clarithromycin is the most commonly used initial treatment. Triple therapy is not indicated in the absence of documented infection. In this patient, triple therapy should be withheld pending documentation of infection.

Key Point Biopsies of all gastric ulcers should be performed, because even small, benign-appearing gastric ulcers may harbor malignancy.

Answers: Q12: B | Q13: A

Abdominal pain

Q14: A 65-year-old woman is evaluated 1 week after undergoing an esophagogastroduodenoscopy for persistent abdominal pain. The procedure showed a 1-cm, clean-based ulcer in the duodenal bulb and scattered antral erosions. Biopsy specimens from the stomach showed nonspecific gastritis but no evidence of Helicobacter pylori infection. Serum antibody testing for H. pylori was also negative. Proton pump inhibitor therapy was started, and the patient's symptoms were alleviated. The patient has a history of mild osteoarthritis and osteoporosis. Medications are over-the-counter ibuprofen for arthritis and a calcium supplement, vitamin D, and alendronate. On physical examination, vital signs are normal. The abdominal examination reveals no tenderness, hepatomegaly, or palpable masses. Complete blood count is normal. Which of the following is the most appropriate next step in the management of this patient?

A- Measure serum gastrin
B- Perform fecal antigen test for Helicobacter pylori
C- Repeat endoscopy and ulcer biopsy
D- Stop the alendronate
E- Stop the ibuprofen

Explanation: The most appropriate next step in the management of this patient is to stop the ibuprofen. The two most common causes of peptic ulcer disease are NSAIDs and Helicobacter pylori infection, which account for more than 90% of cases. This patient has a history of arthritis for which she takes over-the-counter ibuprofen; many patients who take such nonprescription medications are unaware that they are taking an NSAID that can cause ulcer disease. H. pylori infection has been ruled out in this patient by the negative histology for the organism as well as negative serum antibody testing; therefore, no further testing for H. pylori is needed. Measuring serum gastrin should be considered in a patient in whom there is a suspicion of an acid hypersecretion state, such as a gastrinoma (Zollinger-Ellison syndrome), clinical features of which include multiple peptic ulcers, ulcers in unusual locations, severe esophagitis, or fat malabsorption, none of which this patient has. Malignancy always needs to be considered in a patient with a gastric ulcer; therefore, biopsies of the ulcer and follow-up endoscopy to ensure ulcer healing would be recommended. However, this patient has a duodenal ulcer, which is much less likely to represent a malignancy, and biopsy of the ulcer or follow-up endoscopy to assess for healing is not needed. Alendronate therapy for osteoporosis has been associated with esophagitis and rare cases of gastric or duodenal ulcers; however, stopping alendronate without considering the more common causes of peptic ulcer disease would not be appropriate at this time.

Key Point The two most common causes of peptic ulcer disease are NSAIDs and Helicobacter pylori infection, which account for more than 90% of cases.

Q15: A 46-year-old man is evaluated for a 5-month history of intermittent midabdominal discomfort that occurs after eating. Each episode lasts between 30 minutes and1 hour. The discomfort is described as fullness; he reports no symptoms characteristic of esophageal reflux or biliary colic. He has no vomiting, dysphagia, or changes in bowel habits. He has gained approximately 4.5 kg (10 lb) during the past 5 months. Medical history includes low back pain for which he takes ibuprofen. He has no family history of malignancy. On physical examination, vital signs are normal. BMI is 28. The remainder of the physical examination is normal. A metabolic panel and complete blood count are normal. What is the most appropriate next management step for this patient?

A- Start metoclopramide
B- Stop ibuprofen
C- Obtain an upper endoscopy
D- Test for Helicobacter pylori infection

Explanation: For a patient with dyspepsia who is taking nonsteroidal anti-inflammatory drugs (NSAIDs) and has no concerning alarm features, stopping the NSAID is the most appropriate next step. NSAIDs are the drugs most frequently associated with dyspepsia. If stopping or changing the NSAID is not a viable option, initiation of a proton pump inhibitor is warranted. Metoclopramide is a treatment that may have efficacy in patients with dysmotility-like dyspepsia. However, this diagnosis is based on patient symptoms (early satiety, nausea), a normal upper endoscopy, and absence of other more common causes of dyspepsia such as NSAID use.
NSAID use is a much more common cause of dyspepsia than Helicobacter pylori infection. Testing for H. pylori before stopping the ibuprofen may lead to unnecessary treatment or misdiagnosis in this patient. Simply stopping or changing the NSAID may obviate the need for further testing for H. pylori and unnecessary treatment if the patient's dyspepsia improves. If symptoms continue after stopping the NSAID, testing for H. pylori is warranted.
Alarm features such as unexplained iron deficiency anemia, unintentional weight loss, dysphagia, odynophagia, palpable abdominal masses, or jaundice would necessitate an urgent upper endoscopy. Because the incidence of malignancy is significantly greater in patients older than 55 years, upper endoscopy is indicated in any patient older than 55 years with new-onset dyspepsia even without alarm features. This patient has no indication for upper endoscopy.

Key Point NSAIDs are potential causes of dyspepsia and should be stopped or changed in patients with dyspeptic symptoms.

Answers: Q14: E | Q15: B

Abdominal pain

Q16: A 58-year-old woman is evaluated for a 3-month history of burning midepigastric pain after eating and early satiety. The pain feels the same as a gastric ulcer she had 10 years ago. She reports no associated sour taste, belching, bloating, or worsening symptoms with recumbency or at night. She has no nausea, vomiting, painful swallowing, changes in bowel habits, or weight loss. She is otherwise in good health and has no symptoms of anxiety or depression. On physical examination, vital signs are normal. Mild midepigastric tenderness is present, but her physical examination is otherwise normal. A thyroid-stimulating hormone level, complete blood count, and metabolic panel are normal. An upper endoscopy is performed and it is normal. Testing for H. pylori is negative. Which of the following is the most appropriate management for this patient?

A- Ambulatory esophageal pH monitoring
B- Psychiatric evaluation
C- Surgical evaluation
D- Trial of a proton pump inhibitor (PPI)

Explanation: The most appropriate management for this patient is an empiric trial with a proton pump inhibitor (PPI). Functional dyspepsia is defined as chronic or recurrent discomfort in the epigastrium with no organic cause determined. Upper endoscopy is necessary to rule out organic causes, and only after this is performed can the diagnosis of functional dyspepsia be distinguished from organic dyspepsia (e.g., dyspepsia caused by peptic ulcer disease, reflux esophagitis, malignancy). Because this patient's functional dyspepsia symptoms are ulcer-like, an empiric trial of a PPI is the recommended treatment. Ambulatory esophageal pH monitoring, which consists of inserting a pH monitor in the distal esophagus and recording the results over a period of 24 hours, is the most accurate means to confirm the diagnosis of gastroesophageal reflux disease (GERD). The technique also allows determination of an association between symptoms and the amount and pattern of esophageal acid exposure. This procedure may be helpful when the diagnosis of GERD is in doubt or appropriate GERD therapy is nonsuccessful. This patient's symptoms are not compatible with GERD and ambulatory pH monitoring is not indicated. Functional dyspepsia does not have an apparent organic cause that requires surgery. Therefore, surgical consultation is not indicated. With no other signs or symptoms to suggest a psychiatric illness, psychiatric consultation is not warranted.

Key Point An empiric trial of a proton pump inhibitor is indicated for ulcer-like functional dyspepsia.

Q17: A 46-year-old man is evaluated for a 5-month history of intermittent midabdominal discomfort that occurs after eating. Each episode lasts between 30 minutes and1 hour. The discomfort is described as fullness; he reports no symptoms characteristic of esophageal reflux or biliary colic. He has no vomiting, dysphagia, or changes in bowel habits. He has gained approximately 4.5 kg (10 lb) during the past 5 months. Medical history includes low back pain for which he takes ibuprofen. He has no family history of malignancy. On physical examination, vital signs are normal. BMI is 28. The remainder of the physical examination is normal. A metabolic panel and complete blood count are normal. What is the most appropriate next management step for this patient?

A- Start metoclopramide
B- Stop ibuprofen
C- Obtain an upper endoscopy
D- Test for Helicobacter pylori infection

Explanation:

Gastrointestinal bleeding

Q1: You see an 80-year-old man who presents to accident and emergency with epigastric pain. The pain started 3 days ago and today he noticed that the colour of his stools has changed to a 'tarry-black' colour. Associated symptoms include nausea and lethargy. The patient is a smoker of 20 cigarettes a day and has recently finished eradication treatment for a duodenal ulcer. The patient is alert and orientated with a pulse rate of 99 and blood pressure of 98/69, respiratory rate of 18, oxygen saturations of 98 per cent on room air and temperature of 37.2°C. On examination, the abdomen is soft with marked tenderness in the epigastric region and bowel sounds are present. The rectum is empty, on PR examination, with some traces of malaena. The patient has been started on high flow oxygen and has been given some oral analgesia. The most appropriate next step in managing this patient is:

A. Keep nil by mouth and arrange endoscopy
B. Request an erect chest x-ray
C. Intravenous pantoprazole
D. ECG
E. Intravenous cannulation and fluids

Explanation: The patient's symptoms of epigastric pain and malaena point to a diagnosis of an upper GI bleed which can also present with haematemesis. The cause could possibly be due to a (recurrent) bleeding duodenal ulcer. The initial assessment/management of any acute medical condition should follow the 'ABC' (airway, breathing and circulation) route. Answers A–E are all steps in managing an upper GI bleed but, in this question, the most appropriate next step in management would be to insert two large bore cannulae and commence IV fluids (E). In addition, although not mentioned in the answer, taking blood for investigations (e.g. FBC, U&Es, coagulation screen, group and save, amylase and liver function tests) would also be performed when the cannulae are inserted. Once the patient has been stabilized haemodynamically (with IV fluids or blood if required in cases of severe anaemia), he/she is usually placed nil by mouth and an upper GI endoscopy is arranged to identify, and treat, any sites of bleeding. The Rockall score can be used to assess: (1) Risk of rebleeding/mortality pre-endoscopy; and (2) Risk of rebleeding/mortality post-endoscopy.

Q2: You see a 75-year-old man with an acute episode of haematemesis, who was admitted the night before and is awaiting an upper GI endoscopy. You are asked on the ward round about the common causes of upper GI bleeding. From the list below, which of the following is the most common cause of upper GI bleeding?

A. Mallory–Weiss tear
B. Peptic ulcers
C. Oesophageal varices
D. Drug induced
E. Malignancy

Explanation: Approximately 80 per cent of upper GI bleeds have known identifiable causes, some of which include:

- peptic ulcers – approximately 35–50 per cent of bleeds (B);
- Mallory–Weis tears – 15 per cent (A);
- oesophagitis – 5–15 per cent;
- gastritis and gastric erosions – 5–15 per cent;
- oesophageal varices – 5–10 per cent (C);
- drugs (e.g. NSAIDs, steroids, anticoagulants) – 5 per cent (D);
- upper GI malignancy – 5 per cent (E);
- rarer causes (<5 per cent):
- Dieulafoy's lesion;
- angiodysplasia;
- haemobilia;
- aorto-enteric fistula.

Answers: Q1: E | Q2: B

Gastrointestinal bleeding

Q3: A 65-year-old man is admitted with rectal bleeding. He noticed a significant amount of blood in the toilet after going to the bathroom this morning and had some mild cramping just before that bowel movement. His past medical history is positive for coronary artery disease (has had stents placed and is on aspirin and clopidogrel) and osteoarthritis for which he has been taking ibuprofen. He denies weight loss and has no previous history of bleeding. On examination he is slightly diaphoretic. Vital signs are BP 124/72 and pulse 88 with the patient supine, BP 94/52 and pulse 110 with the patient standing. Abdomen is nontender and nondistended. NG aspirate is negative for occult blood. After establishing two large- bore intravenous lines, administering an IV fluid bolus and otherwise stabilizing the patient, what will be the most important study to perform?

A. Upper endoscopy
B. Air-contrast barium enema
C. Colonoscopy
D. X-ray of the abdomen—flat and upright
E. CT scan of the abdomen

Explanation: This patient has ischemic colitis. It typically occurs in people older than 50. Risk factors include atherosclerotic disease, including peripheral vascular disease and coronary artery disease. Episodes of bleeding can be preceded by abdominal pain and watery diarrhea. Colonoscopy will reveal inflammatory changes (sometimes patchy) from the splenic flexure to the sigmoid colon with sparing of the rectum. Nonsteroidal induced colitis is also a possibility and could be evaluated by colonoscopy. Given the history of red blood per rectum, upper endoscopy would not be the first choice of examination. An air-contrast barium enema could be obtained if colonoscopy were unavailable, in order to evaluate for colitis and to rule out a carcinoma. Plain x-rays of the abdomen occasionally show thumbprinting from edematous mucosal folds but are less sensitive than colonoscopy. A CT of the abdomen would be unrevealing in a case of ischemic colitis and would be unlikely to detect a small carcinoma if present.

Q4: A 30-year-old male smoker presents to the emergency room complaining of chest pain and hematemesis, having vomited up two cups of blood. He admits to drinking too much that same evening and having vomited repeatedly after drinking shots of vodka with his friends following a sporting event. His chest pain is worse after each episode of vomiting; he has never had a cardiac problem in the past. His past history is important for only for hypertension controlled with hydrochlorothiazide. He denies any previous history of alcohol abuse. On examination he is anxious and diaphoretic. His supine pulse is 90, with a blood pressure of 110/90. Heart and lungs are normal, and he has mild epigastric tenderness. His hemoglobin is 11. Stool is hemoccult positive. EKG and initial cardiac enzymes are normal. You admit the patient to the intensive care unit and consult a gastroenterologist. What is the most likely outcome of this patients gastrointestinal bleeding?

A. Spontaneous resolution of the acute upper GI bleeding within 24 to 48 hours
B. Recurrent massive upper GI bleeding within a few hours
C. Continued slow bleeding
D. Mental status deterioration within a few hours
E. Development of fever and intense right lower quadrant pain within a few hours

Explanation: This patient has a Mallory-Weiss tear, which is the cause of bleeding in approximately 5% of patients with an acute upper GI bleed. Most of these tears heal spontaneously within 24 to 48 hours with supportive therapy. If there is ongoing bleeding, IV vasopressin or injection of a sclerotic agent via endoscopy may be required. Surgical intervention with oversewing of the bleeder is rarely needed. The history is not suggestive of chronic alcoholism which may be associated with esophageal varices and hence a higher risk of recurrent massive bleeding as well as mental status deterioration. Acute appendicitis rarely presents with UGI bleeding.

Answers: Q3: C | Q4: A

Gastrointestinal bleeding

Q5: A 75-year-old woman is evaluated in the emergency department for the acute onset of passage of bright red blood per rectum. This morning she had crampy abdominal pain and had two episodes of diarrhea after which she passed bright red blood. The patient has a history of hypertension and coronary artery disease. Medications are aspirin, ramipril, metoprolol, and simvastatin. She had a colonoscopy 6 months ago, which was normal. On physical examination, the patient is not in acute distress; temperature is 36.8°C (98.2°F), blood pressure is 130/80 mm Hg, pulse rate is 70/min, and respiration rate is 14/min. The heart and lungs are normal. The abdomen is soft with tenderness in the left lower quadrant without rebound or guarding. Rectal examination shows the presence of bright red blood. Laboratory studies reveal a hemoglobin level of 11.9 g/dL (119 g/L), a leukocyte count of 8400/µL (8.4 × 109/L), and platelet count 246,000/µL (246 × 109/L). Serum electrolytes, glucose, creatinine, and urea nitrogen are normal. CT scan of the abdomen and pelvis shows segmental thickening in the sigmoid colon. Which of the following is the most likely diagnosis?

A. Crohn disease
B. Irritable bowel syndrome
C. Ischemic colitis
D. Peptic ulcer disease

Explanation: This patient likely has ischemic colitis, the most frequent form of ischemia of the gastrointestinal tract. This type of ischemia usually affects the elderly with atherosclerotic disease, and in most cases is transient and resolves with conservative management. Patients with acute colonic ischemia usually present with rapid onset of abdominal pain and tenderness over the affected bowel. Rectal bleeding or bloody diarrhea usually develops within 24 hours of the onset of abdominal pain. The typical finding on CT scan is thickening of the bowel wall in a segmental pattern, which is not specific for ischemia and can be seen in infectious colitis and Crohn disease. The finding of patchy segmental ulcerations on colonoscopy in a patient with a compatible history establishes the diagnosis. Colonic strictures are a rare complication. The patient's acute onset of symptoms with bloody diarrhea is not consistent with Crohn disease. Patients with Crohn disease commonly present with a chronic history of abdominal pain, diarrhea, and weight loss. Peptic ulcer disease could present with bright red rectal bleeding but only in the setting of a large and rapid bleed and could not explain the findings on the CT scan. Irritable bowel syndrome is a diagnosis of exclusion and does not present with rectal bleeding and the changes noted on the CT scan.

Key Point Ischemic colitis presents most commonly in elderly patients with atherosclerotic vascular disease with crampy abdominal pain and bloody stool; in most cases it is self- limited.

Q6: A 60-year-old man with alcoholic liver disease was admitted with an upper GI bleed secondary to oesophageal varices. The patient undergoes endoscopic variceal banding and is discharged after 2 weeks in-hospital stay. Which of the following medications would act as prophylaxis in preventing a rebleed from his oesophageal varices?

A. Frusemide
B. Amlodipine
C. Ramipril
D. Propranolol
E. Irbesartan

Explanation: Oesophageal varices arise as a result of portal hypertension (>10 mmHg) which leads to dilated collateral veins at sites of portosystemic anastomsis (e.g. the lower oesophagus). The causes of portal hypertension can be divided into: (1) Pre-hepatic: portal-vein thrombosis, splenic vein thrombosis; (2) Hepatic: cirrhosis (accounts for 80 per cent of causes of portal hypertension), shistosomiasis (most common cause worldwide), sarcoidosis, myeloproliferative disease, congenital hepatic fibrosis; and (3) Post-hepatic: Budd–Chiari syndrome, right heart failure, constrictive pericarditis, veno-occlusive disease. Once portal pressures are >12 mmHg, variceal bleeding may develop. Prophylaxis for the prevention of variceal bleeding can be divided into: (1) Primary: non-selective β-blockade (e.g. propranolol) and/or endoscopic banding ligation; (2) Secondary (i.e. after an initial variceal bleed: non-selective β-blockade, endoscopic banding ligation, transjugular intrahepatic portosystemic shunting (TIPPS) for varices resistant to banding or surgical shunts if TIPPS is not possible.

Answers: Q5: C | Q6: D

Gastrointestinal bleeding

Q7: A 65-year-old man attends your clinic with a three-month history of weight loss of approximately 9 kg despite a normal appetite. A full blood count reveals that his haemoglobin is 9.0 g/dL (previous haemoglobin was 13.5 g/dL one year ago) and the MCV is 71 fL. Abdominal examination is unremarkable and per rectum exam is nil of note. The patient states that he has normal bowel habits and has been feeling quite tired lately. The most appropriate management is:

A. Reassure and discharge
B. Arrange an upper and lower GI endoscopy
C. Prescribe iron tablet supplementation
D. Arrange an abdominal ultrasound
E. Arrange an abdominal x-ray

Explanation: This patient is suffering from iron deficiency anaemia which could potentially be secondary to an upper or lower GI malignancy. The fact that there has been drastic weight loss despite no change in appetite suggests a cachectic process. In addition, there has been a 4.5 g/dL drop in the patient's haemoglobin. Tying in these clinical findings, ruling out a malignancy should be the priority. Therefore, from the list of answers above, the most appropriate plan of management would be to arrange an upper and lower GI endoscopy (B).

For each case scenario, select the most likely diagnosis. Each lettered option may be used once, more than once, or not at all.

Q8: An 88-year-old white woman with osteoarthritis has noticed mild epigastric discomfort for several weeks. Naproxen has helped her joint symptoms. She suddenly develops hematemesis and hypotension.

Q9: A 76-year-old white man presents with painless hematemesis and hypotension. He has no previous GI symptoms but did have resection of an abdominal aortic aneurysm 12 years previously. Emergency EGD shows no bleeding source in the stomach or duodenum.

Q10: A 56-year-old man reports intermittent blood stains on his toilet tissue, mild abdominal pain, and increasing weakness and fatigue. He has never had a colonoscopy. He has lost approximately 10 lb over the past 2 months without trying. Iron deficiency anemia is present.

A. Mallory-Weiss tear
B. Aortoenteric fistula
C. Gastric ulcer
D. Esophageal varices
E. Hereditary hemorrhagic telangiectasia (HHT)
F. Adenocarcinoma of the colon
G. Dieulafoy lesion

Explanation: Nonsteroidal anti-inflammatory drugs, even over-the-counter brands, are common causes of GI bleeding. Preceding symptoms may be mild before the bleeding occurs. Cotreatment with misoprostol decreases GI bleeding but is quite expensive. Selective COX-2 inhibitors decrease the incidence of GI bleeding, but have been shown to increase cardiovascular events and to carry the same risk of renal dysfunction, edema, and blood pressure elevation as nonselective NSAIDs.

Erosion of the proximal end of a woven aortic graft into the distal duodenum or proximal jejunum can occur many years after surgery for abdominal aortic aneurysm. Often, the patient will have a smaller herald bleed, which is then followed by catastrophic bleeding. A high index of suspicion is necessary, as timely surgery can be lifesaving.

Colorectal cancer is the third most common cancer among men and women in the United States and the second leading cause of cancer mortality. About 6% of North Americans will develop the colon cancer, but it is preventable if screened for aggressively. Typical presenting symptoms of the disease include weight loss and blood in the stool. Iron deficiency anemia suggests colon cancer (as opposed to colon polyps or hemorrhoids). Surgical resection of limited stage colon cancers is curative, and long-term survival is likely. Advances in chemotherapeutic regimens have extended median survival to beyond 2 years in patients with disease not amenable to surgical cure.

A Mallory-Weiss tear occurs when there is a tear in the mucosa in the lower portion of the esophagus following retching. Esophageal varices due to portal hypertension usually bleed without warning pain. Blood loss in both Mallory-Weiss tears and esophageal varices can be massive. Hereditary hemorrhagic telangiectasia or Osler-Weber-Rendu syndrome is a cause of nosebleeds, GI bleeding, and skin lesions.
The associated arteriovenous malformations can appear in the brain, lungs, liver, and intestines.

A Dieulafoy lesion is a tortuous arteriole in the stomach that can erode and bleed; it can be difficult to find on endoscopy.

Answers: Q7: B | Q8: C | Q9: B | Q10: F

Gastrointestinal bleeding

Q11: A 68-year-old man is evaluated in the emergency department for a 6-hour history of nausea and vomiting with some bright-red emesis. For the past 2 hours he has felt lightheaded and weak. On physical examination, temperature is 37.0°C (98.6°F), blood pressure is 88/51 mm Hg, pulse rate is 114/min, and respiration rate is 18/min. Nasogastric aspiration shows a mixture of coffee grounds and dark blood. The abdomen is not tender, and bowel sounds are normal. Laboratory studies reveal a hemoglobin level of 9.4g/dL (94 g/L); all other tests are normal. Intravenous omeprazole therapy is begun, and the patient is stabilized with infusion of normal saline and transfusion of two units of packed erythrocytes. Which of the following is the best management option for this patient?

A- Esophagogastroduodenoscopy
B- Immediate surgical intervention
C- Observation
D- Octreotide infusion
E- Ranitidine infusion

Explanation: Upper endoscopy should be performed at the time of an upper gastrointestinal bleed after appropriate volume resuscitation to provide a diagnosis as to the cause of bleeding, provide a prognosis, and perform endoscopic guided therapy if required. For example, an ulcer with a visible vessel has an approximately 50% risk of rebleeding if not treated endoscopically. These ulcers can be effectively treated with injection therapy, thermal coagulation via endoscopic probes, or mechanical modalities such as endoclips. Clean- based ulcers rebleed in less than 5% of cases and do not require endoscopic therapy.
There is a 5% to 10% rebleeding rate for endoscopic hemostasis. In these patients, endoscopic therapy may be repeated if the patient remains hemodynamically stable. If repeat endoscopy is unsuccessful or the bleeding vessel is inaccessible or too large, surgical consultation should be obtained. However, endoscopic intervention is the first management choice for upper gastrointestinal bleeding.
Intravenous omeprazole has been shown to reduce the risk of recurrent upper gastrointestinal bleeding in peptic ulcers after endoscopic hemostasis. Oral omeprazole also may decrease rebleeding. A meta-analysis showed that adjuvant high-dose proton pump inhibitor therapy following endoscopic hemostasis for ulcers at high risk of rebleeding reduces rebleeding, surgery, and mortality. Octreotide may have a marginal benefit by decreasing the rate of nonvariceal bleeding but is inferior to intravenous proton pump inhibitors. Ranitidine, a histamine H2 blocker, is inferior to proton pump inhibitors as an adjunct to endoscopic therapy, and there is no benefit of adding a histamine H2 blocker to proton pump inhibitor therapy.

Key Point Upper endoscopy should be performed at the time of an upper gastrointestinal bleed after appropriate volume resuscitation to provide a diagnosis as to the cause of bleeding, provide a prognosis, and perform endoscopic guided therapy if required.

Q12: A 60-year-old man hospitalized for advanced cirrhosis complicated by ascites and encephalopathy is evaluated for massive hematemesis and hypotension. The patient's medications are spironolactone, propranolol, furosemide, and lactulose. On physical examination, temperature is 35.6°C (96.1°F), blood pressure is 80/50 mm Hg, pulse rate is 146/min, and respiration rate is 20/min. The patient has just vomited red blood. Laboratory studies show a hemoglobin level of 9g/dL (90 g/L), a platelet count of 60,000/µL (60 × 109/L), and an INR of 3. Which of the following is the most appropriate initial management of this patient?

A- Arteriography
B- Esophagogastroduodenoscopy
C- Intravenous nadolol
D- Rapid volume replacement

Explanation: The first step in the management of acute variceal hemorrhage is the restoration of the intravascular volume using a large bore peripheral intravenous line or a central line. Packed erythrocytes are used as needed to replace blood loss and clotting factors are replaced as needed. Platelet transfusions may be indicated if values fall below 50,000/µL (50 × 109/L). Following restoration of the intravascular volume, this patient should undergo urgent esophagogastroduodenoscopy and band ligation of esophageal varices. Band ligation has been shown to be as effective as sclerotherapy for preventing early rebleeding. Therapy should also be started with intravenous octreotide, which reduces portal venous blood inflow through inhibition of the release of vasodilatory hormones and is more effective for controlling bleeding than placebo; however, its ultimate effect on survival is unknown. Arteriography is not first-line therapy in patients with a variceal bleed from venous portal hypertension, and no intervention should take precedence over restoration of the intravascular volume. Arteriography is reserved for patients with a presumed arterial source of bleeding as can be seen in peptic ulcer disease or tumors anywhere along the gastrointestinal tract. In such cases, arteriography can be used to identify and embolize the specific vessel involved. This method is usually reserved for cases in which the patient is actively bleeding and either endoscopic therapy has failed to stop the bleeding or the presence of active bleeding interferes with identification of the bleeding site and the patient is unstable. Intravenous nadolol is not appropriate because this patient is hypotensive and needs volume replacement and endoscopic intervention rather than medical therapy. A nonselective β-blocker is useful in the primary and secondary prevention of variceal bleeding but not as acute therapy.

Key Point Volume restoration is a priority management intervention for gastrointestinal bleeding in hemodynamically unstable patients.

Answers: Q11: A | Q12: D

Gastrointestinal bleeding

Q13: A 51-year-old woman has a 3-month history of intermittent rectal bleeding and pain on defecation. Bloody streaks cover the stool, and the toilet paper is also bloody. She is otherwise well and takes no medications. One month before the bleeding developed, she underwent an elective orthopedic surgical procedure and required narcotic drugs for several weeks postoperatively. The narcotics caused significant constipation. The patient had her first screening colonoscopy less than 1 year ago, and results were normal. At that time, a retroflexed view of the rectum revealed small internal hemorrhoids. Visual inspection of the anal opening reveals small external hemorrhoids and several anal skin tags. Hemoglobin is 13.9 g/dL (139 g/L). Which of the following is most likely causing this patient's rectal bleeding and pain?

A- Anal fissure
B- Colon cancer
C- Colonic diverticula
D- Rectal cancer

Explanation: This patient most likely has an anal fissure that is causing rectal outlet bleeding and pain with defecation and that is probably due to her recent constipation. An anal fissure is a tear in the lining of the anal canal. Careful rectal examination by gently spreading the buttocks apart may reveal the fissure, but this finding may not always be present. The patient may have too much pain to allow digital rectal examination or anoscopy. Chronic fissures are often accompanied by external skin tags, as seen in this patient. Recurrent or nonhealing fissures should raise concern for underlying diseases, particularly Crohn disease.
Rectal cancer and colon cancer must always be considered in someone with new-onset rectal outlet bleeding. However, this patient underwent colonoscopy less than 1 year ago, and results were normal. Even if this patient had colonic diverticula, the fact that her bleeding occurs with painful defecation and has been present over a 3-month period is not typical of diverticular bleeding, which tends to cause significant acute painless hematochezia that often stops spontaneously.

Key Point Anal fissures generally cause rectal outlet bleeding and pain with defecation.

Answers: Q13: A

Chronic diarrhea

Q1: You see a 25-year-old woman who presents with a 24-hour history of watery diarrhoea. She states that she has opened her bowels 11 times since her onset of symptoms. Associated symptoms include nausea and vomiting with abdominal cramps and pain which started in the evening following a barbeque meal in the afternoon that day. The patient is alert and orientated and her observations include a pulse rate of 69, blood pressure of 124/75 and temperature of 37.1°C. On examination, her abdomen is soft, there is marked tenderness in the epigastric region and bowel sounds are hyperactive. The patient is normally fit and well with no past medical history. The most likely diagnosis is:

A. Irritable bowel syndrome
B. Gastroenteritis
C. Ulcerative colitis
D. Laxative abuse
E. Crohn's disease

Explanation: The history of the acute onset of diarrhoea coupled with nausea and vomiting a few hours after a meal is highly suggestive of a clinical diagnosis of gastroenteritis (B). Irritable bowel syndrome (A) sufferers usually experience chronic diarrhoea alternating with constipation. There is no history of blood-stained or mucus-based diarrhoea, which is usually seen in inflammatory bowel disease (C and E) (ulcerative/Crohn's colitis). With regard to the clinical scenario, the patient has no past medical history which therefore makes laxative abuse (D) very unlikely.

Q2: A 35-year-old woman presents with a 24-hour history of watery diarrhoea. She has opened her bowels nine times since the onset of her symptoms. You diagnose gastroenteritis after learning that the patient and her family all ate at a new restaurant and the rest of her family have had similar problems. The most appropriate management is:

A. Oral rehydration advice, anti-emetics and discharge home
B. Oral antibiotic therapy and discharge home
C. Admission for intravenous fluid rehydration
D. Admission for intravenous antibiotic therapy
E. No treatment required

Explanation: Gastroenteritis is usually a self-limiting disease that often does not require pharmacological therapy. The mainstay of treatment is to advise patients to increase oral fluid intake (A) to compensate for the water lost from diarrhoea and vomiting. However, in some circumstances, where severe dehydration secondary to profuse diarrhoea exists (leading to confusion and hypotension) patients may warrant admission for intravenous fluid rehydration (C). Antibiotic therapy (B) and (D) is usually not indicated for gastroenteritis unless a bacterial organism has been isolated. The fact that the patient's observations are within the normal range and she is not systemically unwell, the most appropriate answer here would be to advise the patient on oral fluid rehydration and prescribe antiemetics (e.g. metocloperamide), followed by discharge.

Q3: A 56-year-old man presents with a 2-week history of diarrhoea which has not settled following an episode of 'food poisoning'. Which of the following would be the most appropriate investigation?

A. Full blood count
B. Urea and electrolytes
C. Stool sample for microscopy, culture and sensitivities
D. Abdominal x-ray
E. Liver function tests

Explanation: The most appropriate investigation for this patient would be to obtain a stool sample (C), especially if there is a history of travel. Performing tests such as full blood count (A), urea and electrolytes (B), abdominal x-ray (D) and liver function tests (E) would not change the management of this patient and hence in this scenario would not be indicated. A stool sample would enable the physician to isolate the causative organism (if present), which would consequently determine if antibiotic therapy is required.

Answers: Q1: B | Q2: A | Q3: C

Chronic diarrhea

Q4: You are questioned by your registrar regarding bacteria responsible for causing blood-stained diarrhoea. From the list below, select the organism which is not responsible for causing blood-stained diarrhoea.

A. Campylobacter spp.
B. Salmonella spp.
C. Escherichia coli
D. Shigella spp.
E. Stapylococcus spp.

Explanation: All of the organisms listed are known to cause diarrhoea in patients with gastroenteritis. From the list of answers, Campylobacter (A), Salmonella (B), E. coli (C) and Shigella (D) are bacteria known to cause bloody diarrhoea.

Q5: A 48-year-old woman presents with a 2-month history of change in bowel habit and 10-lb weight loss despite preservation of appetite. She notices increased abdominal gas, particularly after fatty meals. The stools are malodorous and occur two to three times per day; no rectal bleeding is noticed. The symptoms are less prominent when she follows a clear liquid diet. Which of the following is the most likely histological abnormality associated with this patient's symptoms?

A. Signet ring cells on gastric biopsy
B. Mucosal inflammation and crypt abscesses on sigmoidoscopy
C. Villous atrophy and increased lymphocytes in the lamina propria on small bowel biopsy
D. Small, curved gram-negative bacteria in areas of intestinal metaplasia on gastric biopsy
E. Periportal inflammation on liver biopsy

Explanation: The patient's history suggests malabsorption. Weight loss despite increased appetite goes with either a hypermetabolic state (such as hyperthyroidism) or nutrient malabsorption. The gastrointestinal symptoms support the diagnosis of malabsorption. Patients may notice greasy malodorous stools, increase in stool frequency, stools that are tenacious and difficult to flush, as well as changes in bowel habit according to the fat content of the diet. In the United States, celiac sprue (gluten-sensitive enteropathy) and chronic pancreatic insufficiency are the commonest causes of malabsorption. The histological pattern described in option c is associated with celiac sprue. IgA antiendomysial antibodies and antibodies against tissue transglutaminase provide supporting evidence. Signet ring cells are seen with gastric cancer. This lesion causes weight loss through anorexia or early satiety but would not cause malabsorption. Colonic mucosal inflammation and crypt abscesses are associated with ulcerative colitis; since this disease affects only the colon, small bowel absorption is not affected. Helicobacter pylori (which appears as curved gram-negative rods on gastric biopsy) is not associated with malabsorption. Periportal inflammation is seen in chronic hepatitis but does not cause malabsorption.

Q6: You see a 40-year-old woman who was diagnosed with Crohn's disease ten years ago. Due to a severe attack of Crohn's which failed to respond to medical therapy, she had a small bowel resection. Your registrar tells you that she is at risk of developing vitamin B12 deficiency as a result of her surgery. Which part of the small bowel is responsible for the absorption of vitamin B12?

A. Jejunum
B. Proximal ileum
C. Duodenum
D. Terminal ileum
E. None of the above

Explanation: The terminal ileum is responsible for the absorption of vitamin B12. If this vitamin is not supplemented, the patient will experience symptoms of glossitis, neuropathy, macrocytic anaemia. The proximal ileum is responsible for absorption of vitamin B2 and vitamin C. The jejunum is responsible for the absorption of vitamin D folic acid and nicotinamide. The duodenum is responsible for the absorption of the minerals calcium and iron.

Answers: Q4: E | Q5: C | Q6: D

Chronic diarrhea

Q7: A 74-year-old woman is evaluated in the emergency department with a 2-day history of diarrhea characterized by ten bowel movements daily, with worsening abdominal pain and fever. Five weeks ago, the patient was hospitalized with necrotizing fasciitis of the right thigh for which she underwent debridement, received nafcillin and clindamycin therapy, and was discharged after 2 weeks. On discharge, she was prescribed a 2-week course of nafcillin, which she completed 1 week ago. On physical examination, temperature is 38.6°C (101.5°F), blood pressure is 90/55 mm Hg, pulse rate is 122/min, and respiration rate is 24/min. The abdomen is distended and tender to palpation, and bowel sounds are absent. Laboratory studies indicate a leukocyte count of 32,500/μL (32.5 × 109/L). Stool, blood, and urine samples are obtained for culture. Which of the following is the most likely diagnosis?

A. Clostridium difficile infection
B. Crohn disease
C. Diverticulitis
D. Diverticulosis
E. Ischemic colitis

Explanation: This patient most likely has severe Clostridium difficile infection (CDI). CDI typically presents with watery diarrhea, although the range of symptoms span an asymptomatic carrier state to severe fulminant colitis with toxic megacolon. Patients with CDI and associated colitis typically have diarrhea up to 10 or 15 times daily, lower abdominal pain, cramping, fever, and leukocytosis that often exceeds 15,000/μL (15 × 109/L). CDI with colitis is most commonly associated with prior antibiotic administration. The colitis is produced by two toxins, A and B. These have different mechanisms of action, but both are highly potent and cause cytotoxicity at extremely low concentrations. The toxins can be detected in the clinical laboratory and the presence of either toxin confirms the diagnosis. Treatment of severe CDI with colitis consists of oral vancomycin and intravenous metronidazole. The typical presentation of Crohn disease is abdominal pain, diarrhea, and weight loss that occurs over a period of months, if not years. This patient's severe and rapidly progressive course is not consistent with Crohn disease. Patients with uncomplicated diverticulitis present with abdominal pain and fever. Physical examination discloses left lower quadrant abdominal tenderness. Leukocytosis is present, and urinalysis may show sterile pyuria due to inflammation close to the bladder. The patient's 2 day history of severe diarrhea is not consistent with diverticulitis. Diverticulosis consists of the presence of diverticula in the colon. Diverticulosis is common in aging Western populations and is not associated with pain or diarrhea. Ischemic colitis symptoms include left lower quadrant abdominal pain and bloody diarrhea, which are often self-limited. Treatment is supportive and includes intravenous fluids and bowel rest. Most symptoms resolve within 48 hours. This patient's progressive symptoms are not consistent with a diagnosis of ischemic colitis.

Key Point Patients with previous exposure to antibiotics may develop Clostridium difficile, infection and associated colitis, which is characterized by diarrhea up to 10 or 15 times daily, lower abdominal pain, cramping, fever, and leukocytosis.

Q8: A 47-year-old woman has been experiencing a four-month history of diarrhoea and bloating. Associated symptoms include lethargy and weight loss. Full blood count reveals haemoglobin of 9.3 d/gL and MCV 70 fL. Which of the following investigations would be helpful in the patient's diagnosis?

A. Anti-mitochondrial antibodies
B. Anti-smooth muscle antibodies
C. Anti-tissue transglutaminase antibodies
D. Anti-nuclear antibodies
E. Anti-neutrophil cytoplasmic antibodies

Explanation: The patient is suffering from coeliac disease which is a T-cell mediated autoimmune disease of the small bowel characterized by intolerance to alcohol-soluble proteins in wheat, barley, rye and oats (also known as prolamin) leading to villous atrophy and malabsorption.

Patients may present with steatorrhoea, diarrhoea, abdominal pain and bloating, nausea and vomiting, signs of microcytic anaemia (secondary to iron deficiency) or macrocytic anaemia (secondary to vitamin B12 or folate deficiency), weight loss, failure to thrive in children.

Diagnosis is made by:
• testing for antibodies: α-gliadin, tissue transglutaminase and anti-endomysial (an IgA antibody which is 95 per cent specific for coeliac disease unless the patient is IgA deficient);
• duodenal biopsy which can be performed at upper GI endoscopy. Aim of treatment is to completely avoid gluten-containing food. From the list of answers, (C) is therefore the correct answer.

Answers: Q7: A | Q8: C

Chronic diarrhea

Q9: A 34-year-old white woman is treated for a UTI with amoxicillin. Initially she improves, but 5 days after beginning treatment she develops recurrent fever, abdominal bloating, and diarrhea with six to eight loose stools per day. What is the best diagnostic test to confirm your diagnosis?

A. Identification of Clostridium difficile toxin in the stool
B. Isolation of C difficile in stool culture
C. Stool for white blood cells (fecal leukocytes)
D. Detection of IgG antibodies against C difficile in the serum
E. Visualization of gram-positive rods on microscopic examination of stool

Explanation: Clostridium difficile is an important cause of diarrhea in patients who receive antibiotic therapy. Clostridium difficile proliferates in the gastrointestinal tract when the normal enteric bacteria are altered by antibiotics. Commonly implicated antibiotics include ampicillin, clindamycin, cephalosporins, and trimethoprim-sulfamethoxazole. The diarrhea is usually mild to moderate, but can be profuse. Other clinical findings include fever, abdominal pain, abdominal tenderness, leukocytosis, and serum electrolyte abnormalities. The diagnosis is made by demonstration at sigmoidoscopy of yellowish plaques (pseudomembranes) that cover the colonic mucosa or by detection of C difficile toxin in the stool. The pseudomembranes consist of a tenacious fibrinopurulent mucosal exudate that contains extruded leukocytes, mucin, and sloughed mucosa. Isolation of C difficile from stool cultures is nonspecific because of asymptomatic carriage, particularly in infants. Testing for fecal leukocytes is also nonspecific and may be negative in C difficile colitis. Serological tests are not clinically useful for diagnosing this infection. Although Clostridia are indeed gram-positive bacilli, they cannot be distinguished microscopically from numerous other anaerobic organisms in stool. Pseudomembranous colitis demands discontinuation of the offending antibiotic. Antibiotic therapy for moderate or severe disease includes oral metronidazole or vancomycin. Cholestyramine can be used therapeutically to bind the diarrheogenic toxin.

Answers: Q9: A

Liver cirrhosis

Q1: A 69-year-old man present with a 2-week history of abdominal pain which has worsened over the last few days. On examination, the patient is jaundiced and the abdomen is distended with tenderness in the epigastric region. In addition, there is a smooth hepatomegaly and shifting dullness. Which of the following is a cause of hepatomegaly?

A. Iron deficiency anaemia
B. Budd–Chiari syndrome
C. Ulcerative colitis
D. Crohn's disease
E. Left-sided heart failure

Explanation: From the answers above, Budd–Chiari syndrome (B) (which presents with a triad of symptoms: acute abdominal pain, hepatomegaly and ascites), is the most likely cause of hepatomegaly. The condition results from hepatic vein outflow obstruction of which:
• there is no known cause in 50 per cent of sufferers;
• of the remaining 50 per cent of patients diagnosed with Budd–Chiari syndrome, 75 per cent of these are due to thrombosis of the hepatic vein (primary Budd–Chiari syndrome) and 25 per cent are due to external compression of the hepatic vein (secondary Budd–Chiari syndrome).

The causes of hepatomegaly can be classified according to:
1 Maligancy: primary (e.g. HCC) or secondary.
2 Hepatic congestion secondary to: right heart failure, Budd–Chiari syndrome.
3 Infection: hepatitis (secondary to viruses, malaria, shistosomiasis, amoebic abscess, hydatid cyst), infectious mononucleosis.
4 Haematological: leukaemia, lymphoma, myeloproliferative disorders, such as myelofibrosis, sickle-cell disease, haemolytic anaemias.
5 Anatomical: Riedel's lobe.
6 Other causes include early cirrhosis, fatty liver, porphyria, amyloidosis, Gaucher's disease.

Q2: A 58-year-old man with cirrhosis and ascites caused by chronic hepatitis C is hospitalized because of subtle personality change that develops into frank mental status changes with confusion. The patient's wife reports that his stools have been darker than usual and that he has been unsteady upon arising the last few days. She also reports that he has been reluctant to take several of his medications recently as he has been reading about natural remedies. On physical examination, the patient is lethargic, disoriented, and uncooperative. He is afebrile, has clear lungs, normal heart, distended abdomen with shifting dullness, and no meningeal or focal neurologic findings. There is mild hyperreflexia and a nonrhythmic flapping tremor of the wrists. Stool is heme positive. CT scan of the head is normal. What is the best initial therapy to address this patient's mental status changes?

A. Quetiapine 25 mg orally tid
B. Lorazepam 1 mg orally tid
C. Haloperidol 2 mg intramuscularly q 4 hours prn agitation
D. Omeprazole 20 mg orally tid
E. Lactulose 30 cc orally, titrated to three to four stools daily

Explanation: This patient has hepatic encephalopathy. Precipitating factors include azotemia, acute liver decompensation, use of sedatives or opioids, GI hemorrhage, hypokalemia, constipation, infection, a high-protein diet, and recent placement of a portosystemic shunt (TIPS). The most effective medical treatment is lactulose, a nonabsorbable disaccharide. Antibiotics such as neomycin, metronidazole, and rifaximin can also reduce symptoms. The other listed medications have not been shown to be effective in treating patients with hepatic encephalopathy. Quetiapine is used for psychosis and depression, lorazepam is useful in alcohol withdrawal and anxiety, haloperidol in psychosis, and omeprazole in peptic ulcer disease.

Answers: Q1: B | Q2:E

Liver cirrhosis

Q3: A 56-year-old chronic alcoholic has a 1-year history of ascites. He is admitted with a 2-day history of diffuse abdominal pain and fever. Examination reveals scleral icterus, spider angiomas, a distended abdomen with shifting dullness, and diffuse abdominal tenderness. Paracentesis reveals slightly cloudy ascitic fluid with an ascitic fluid PMN cell count of 1000/µL. Which of the following statements about treatment is true?

A. Antibiotic therapy is unnecessary if the ascitic fluid culture is negative for bacteria.
B. The addition of albumin to antibiotic therapy improves survival.
C. Repeated paracenteses are required to assess the response to antibiotic treatment.
D. After treatment of this acute episode, a second episode of spontaneous bacterial peritonitis would be unlikely.
E. Treatment with multiple antibiotics is required because polymicrobial infection is common.

Explanation: Spontaneous bacterial peritonitis is the occurrence of bacterial infection in preexisting ascitic fluid without bowel wall perforation. It is almost always caused by a single species; isolation of multiple species would suggest a bowel wall perforation. The typical patient has preexisting cirrhosis and ascites, and presents with fever and abdominal pain. Acute deterioration of liver function and hepatic encephalopathy are common. An ascitic fluid PMN cell count of greater than 250/µL confirms the diagnosis, even if the culture is negative. Standard antibiotic therapy is a fluoroquinolone or third-generation cephalosporin for 7 to 10 days. Response to therapy can be judged clinically, and repeated paracentesis is not usually necessary. The addition of albumin to antibiotic therapy has been shown to improve survival. Recurrence rates are high, and long-term prophylactic therapy with a fluoroquinolone is recommended.

Q4: A 40-year-old white man complains of slowly progressive generalized weakness, weight loss, abdominal pain, and wrist and knee pain over the past several months. He was told at an urgent care visit that his blood sugar was a little higher than normal. There is a family history of liver disease on his father's side. On examination, the patient has diffuse hyperpigmentation and a palpable liver edge. Mild polyarthritis of the wrists is also noted. What is the best test or combination of tests to help you diagnose this patient's problem?

A. Complete blood count with differential and a comprehensive metabolic panel
B. Hemoglobin A1C
C. Iron, total iron-binding capacity, and ferritin
D. Alpha-1-antitrypsin level
E. Liver-spleen scan

Explanation: Hemochromatosis is an autosomal recessive condition that causes increased intestinal absorption of iron and excessive total body iron stores. The cause is a defect in the HFE or related gene; it affects Caucasians most frequently at a rate of about 1 in 250 persons. Clinically, the liver is usually enlarged, and excessive skin pigmentation is present in 90% of symptomatic patients at the time of diagnosis. Diabetes occurs secondary to direct damage to the pancreas by iron deposition. Arthropathy develops in 25% to 50% of cases. Initial screening involves transferrin saturation (iron/total iron binding capacity) and ferritin levels. A transferrin saturation of over 45% or a ferritin over 150 would be consistent with the diagnosis and would suggest the need for referral and genetic testing. A simple CBC would not suggest the diagnosis. The hemoglobin A1C is helpful in diagnosing and monitoring diabetes. Patients with alpha-1-antitrypsin deficiency have liver disease but not diabetes or arthropathy. A liver-spleen scan could detect cirrhosis but would not be specifically helpful in determining whether or not the patient has hemochromatosis as the cause.

Answers: Q3: B | Q4: C

Liver cirrhosis

Q5: A 46-year-old woman presents to your clinic with a week's history of jaundice. Her past medical history includes longstanding atrial fibrillation and hypertension. Physical examination reveals hepatomegaly. You assess her liver function which shows a bilirubin of 41 iu/L, AST 111 iu/L, ALT 55 iu/L and ALP 98 iu/L. There is no history of travel. You have a look at the patient's medication history. Which of the following drugs below is likely to have caused the derangement in the patient's liver function?

A. Aspirin
B. Ramipril
C. Amiodarone
D. Bendroflumethiazide
E. Amlodipine

Explanation: This patient is suffering from drug-induced liver cirrhosis secondary to chronic amiodarone therapy. Amiodarone (C) along with other drugs, such as methyldopa and methotrexate, are known to induce liver cirrhosis. Liver cirrhosis is characterized, histologically, by a loss of the normal hepatic architecture coupled with bridging fibrosis and nodular regeneration. The causes of liver cirrhosis include chronic alcoholism, non-alcholic steatohepatitis, chronic hepatitis B and C infections, autoimmune conditions (e.g. autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis), genetic disorders (e.g. haemachromatosis, Wilson's disease), cryptogenic (in approximately 20 per cent), Budd–Chiari syndrome. In some cases, patients do not present with clinical signs although LFTs may show derangement. Some patients may show signs of chronic liver disease such as leuconychia, clubbing, palmer erythema, hyperdynamic circulation, Dupuytren's contracture, spider naevi, xanthelasma, gynaecomastia, atrophic testes, loss of body hair, hepatomegaly (occurs in initial stages then shrinks in late disease).

Investigations include:
- blood: FBC, LFTs, clotting studies (there is a decline in synthetic function of the liver leading to an elevated INR), iron studies, hepatitis serology, immunoglobulins, autoantibodies, AFP, caeruloplasmin , α1-antitrypsin;
- liver ultrasound and duplex;
- MRI;
- ascitic tap for MC&S (spontaneous bacterial peritonitis (SBP)), protein content, LDH, glucose, cell count and biochemistry;
- liver biopsy – confirms diagnosis.

Complications of liver cirrhosis include: (1) Hepatic failure leading to conditions such as coagulopathy, encephalopathy, hypoalbuminaemia, sepsis and hypoglycaemia; (2) Portal hypertension leading to ascites, splenomegaly, oesophageal varices and other portosystemic shunts; (3) Increased risk of hepatocellular carcinoma. Management is targeted towards stopping/removing the underlying causative factor and to treat symptoms (e.g. colestyramine can be used for pruritus, interferon-α treatment for HCV-induced cirrhosis, penicillamine for Wilson's disease). Ascites can be managed through fluid restriction, low salt diet, diuretics (e.g. spironolactone). If SBP is suspected (i.e. on a clinical basis before the MC&S results of the ascitic tap are obtained), antibiotic treatment should commence. Definitive treatment for liver cirrhosis is liver transplantation which increases the five-year survival from 20 to 70 per cent in end-stage disease.

Q6: A 47-year-old man presents complaining of weight gain, on examination there is an abdominal distension with a fluid thrill. Which of following is not a cause of ascites secondary to venous hypertension?

A. Congestive heart failure
B. Cirrhosis
C. Constrictive pericarditis
D. Budd–Chiari syndrome
E. Nephrotic syndrome

Explanation: Ascites can be described as the pathological accumulation of fluid in the abdominal cavity. Ascites occur secondary to:
- conditions leading to venous hypertension (e.g. cirrhosis, congestive heart failure, constrictive pericarditis, Budd–Chiari syndrome, portal vein thrombosis);
- hypoalbuminaemia (e.g. nephrotic syndrome, malnutrition);
- malignant disease (e.g. secondary metastases of carcinomas of breast, ovary, colon);
- infections (e.g. tuberculosis);
- others (e.g. pancreatic disease, ovarian disease, myxoedema).

Answers A–D are all known causes of ascites that occur secondary to venous hypertension. Nephrotic syndrome (E), however, leads to ascites secondary to hypoalbuminaemia.

Answers: Q5: C | Q6: A

Liver cirrhosis

Q7: A 56-year-old man, diagnosed with emphysema, presents with a one-month history of jaundice and ascites. Your registrar suspects that this patient may have liver disease secondary to α1-antitrypsin deficiency. Select the most likely mode of inheritance from the list below:

A. Autosomal dominant
B. X-linked dominant
C. Autosomal recessive
D. Polygenic
E. None of the above

Explanation: α1-antitrypsin deficiency is an autosomal recessive disorder (C), which results from single amino acid substitutions at positions 264 and 342 on chromosome 14. α1-antitrypsin is a serine protease, synthesized in the liver, required in controlling inflammatory cascades. The lack of this serine protease results in emphysema (75 per cent), chronic liver disease and hepatocellular carcinoma, asthma, pancreatitis, gallstones, Wegener's granulomatosis.
Patients with liver disease secondary to α1-antitrypsin deficiency usually present with dyspnoea (from emphysema), liver cirrhosis, cholestatic jaundice. Investigations include: serum α1-antitrypsin levels, liver biopsy, genetic phenotyping and DNA analysis at prenatal diagnosis. Management involves quitting smoking, augmentation therapy with α1-antitrypsin pooled from human plasma and liver transplantation is the treatment of choice in decompensated cirrhosis.

Q8: A patient on your ward is diagnosed with hepatocellular carcinoma. You are asked to perform a tumour marker level on this patient. Which of the following tumour markers are elevated in hepatocellular carcinoma?

A. α-fetoprotein
B. Carcinoembryonic antigen (CEA)
C. CA 15-3
D. HcG
E. CA 125

Explanation: Fifty to 80 per cent of hepatocellular carcinomas are associated with high serum levels of α-fetoprotein (AFP), a tumour marker, which is also linked to, and elevated in, testicular carcinomas. Serum levels of AFP can be monitored either post-surgical resection (if the tumour is solitary) or post chemotherapy; falling or rising levels post treatment could be indicative of disease remission or progression, respectively. CEA (B) is primarily linked with colorectal carcinoma. CA 15-3 (C) is linked with breast carcinoma. HcG(D) and CA 125 (E) are usually associated with ovarian carcinoma.

Q9: A 45-year-old woman is evaluated during a routine office visit. She was diagnosed with chronic active hepatitis B infection 10 years ago. She has no symptoms and no other medical problems. A liver biopsy performed 3 years ago revealed changes consistent with chronic active inflammation with no cirrhosis. She is taking interferon alfa. On physical examination, vital signs are normal. No evidence of telangiectasias or other stigmata of chronic liver disease is present. The abdomen is unremarkable without evidence of hepatomegaly, liver tenderness, or ascites. The remainder of the examination findings are normal. Serum aspartate aminotransferase is 200 U/L and alanine aminotransferase is 100 U/L. (unchanged from 6 months ago). Prothrombin time and activated partial thromboplastin time are normal. Hepatitis C antibody is negative. Which of the following is the most appropriate screening strategy for hepatocellular carcinoma in this patient?

A- α-Fetoprotein
B- Abdominal ultrasonography
C- CT of the liver with contrast
D- Screening is not indicated

Explanation: The most appropriate screening strategy for hepatocellular carcinoma in this patient is liver ultrasonography. Hepatocellular carcinoma is the most common primary intrahepatic tumor and the fastest growing cause of cancer-related death in men in the United States. The cancer usually develops in patients with cirrhosis. The most common causes of cirrhosis leading to hepatocellular carcinoma are chronic hepatitis B and hepatitis C viral infections and alcoholic liver disease; however, patients with chronic hepatitis B infection in the absence of cirrhosis may develop hepatocellular carcinoma. Patients with a compatible ultrasound imaging study and a subsequent serum α- fetoprotein level greater than 500 ng/mL (500 µg/L) can be diagnosed with hepatocellular carcinoma without a biopsy. The optimal time to initiate a screening program and its ideal frequency are unknown. Combined use of α-fetoprotein measurement and ultrasonography increases the sensitivity of detection but at the expense of increased false-positive results. α-Fetoprotein is not specific for hepatocellular carcinoma and should not be used alone as a screening test unless ultrasound is not available. Liver CT scanning exposes the patient to unnecessary radiation, particularly if screening is performed frequently. Key Point Patients with chronic hepatitis B infection in the absence of cirrhosis may develop hepatocellular carcinoma and should undergo periodic screening.

Answers: Q7: C | Q8: A | Q9: B

Liver cirrhosis

Q10: A 43-year-old woman has a 3-month history of gradually increasing abdominal distention and jaundice. She has no other symptoms, and her medical history is noncontributory. On physical examination, the patient has jaundice, palmar erythema, and spider angiomata. Abdominal examination discloses hepatosplenomegaly and moderate ascites. Abdominal ultrasonography shows hepatomegaly, a coarse echotexture of the liver, patent portal and hepatic veins, mild splenomegaly, moderate ascites, and no bile duct dilatation. Paracentesis is performed. The ascitic fluid leukocyte count is 80/µL, and albumin is 0.7 g/dL (7 g/L). Gram stain and culture are pending. Which of the following is the most likely cause of the ascites?

Aspartate aminotransferase	53 U/L
Alanine aminotransferase	47 U/L
Alkaline phosphatase	123 U/L
Total bilirubin	3.2 mg/dL (54.7 µmol/L)
Albumin	2.9 g/dL (29 g/L)

A- Cirrhosis
B- Nephrotic syndrome
C- Ovarian cancer
D- Tuberculosis

Explanation: This patient has cirrhosis with ascites. Ascites is the most common complication of portal hypertension secondary to cirrhosis. Any patient who develops new-onset ascites should undergo diagnostic paracentesis. Initial evaluation of ascitic fluid should include measurement of albumin and cell count with differential, Gram stain, and culture. The serum-to-ascites albumin gradient (SAAG) is calculated by subtracting the ascitic fluid albumin level from the serum albumin level. A gradient greater than 1.1 g/dL (11 g/L) indicates that the patient has portal hypertension with a high degree of accuracy. In addition to cirrhosis, other causes of portal hypertension, such as constrictive pericarditis, right-sided heart failure, and the Budd-Chiari syndrome, should be considered. A gradient of less than 1.1 g/dL (11 g/L) is not associated with portal hypertension but with conditions that can cause ascites by other mechanisms, including infection, inflammation, or low serum oncotic pressure, such as the nephrotic syndrome, malignancy, or tuberculosis. Analysis of this patient's ascitic fluid shows a SAAG of 2.2 g/dL (22 g/L), which is consistent with ascites due to sinusoidal hypertension from a chronic liver disease such as cirrhosis.

Key Point Ascitic fluid analysis showing a serum-to-ascites albumin gradient greater than 1.1 g/dL is consistent with ascites caused by chronic liver disease, such as cirrhosis, right-sided heart failure, and the Budd-Chiari syndrome.

Q11: A 45-year-old man is evaluated in the emergency department for lethargy and disorientation. The patient has a history of alcoholic cirrhosis complicated by esophageal variceal bleeding, ascites, and edema. His medications are furosemide, spironolactone, propranolol, and lactulose. He has been sober for 1 year. On physical examination, the patient is somnolent but arousable. He is afebrile; blood pressure is 100/78 mm Hg, pulse rate is 65/min, and respiration rate is 12/min. There are no focal neurologic deficits; the pupils are equal and reactive to light. There is shifting abdominal dullness and 2+ lower extremity edema. The stool is negative for occult blood. Urinalysis is positive for leukocytes. Urine dipstick is positive for 3+ leukocyte esterase and nitrites. CT scan of the head is normal. A diagnostic peritoneal fluid tap excludes spontaneous bacterial peritonitis. Diuretics are discontinued and empiric antibiotic therapy is started. Which of the following is the most appropriate management for this patient?

Leukocyte count	5600/µL (5.6 × 10^9/L)
Glucose (random)	112 mg/dL (6.2 mmol/L)
Creatinine	1.8 mg/dL (159.1 µmol/L)
Sodium	135 meq/L (135 mmol/L)
Potassium	3.5 meq/L (3.5 mmol/L)
Chloride	100 meq/L (100 mmol/L)
Bicarbonate	28 meq/L (28 mmol/L)
Bilirubin (total)	4.0 mg/dL (68.4 µmol/L)
Aspartate aminotransferase	78 U/L
Alanine aminotransferase	45 U/L
Albumin	2.7 g/dL (27 g/L)
Ammonia	230 µg/dL (135 µmol/L)

A- Corticosteroids
B- Hemodialysis
C- Increase lactulose therapy
D- Transjugular intrahepatic portosystemic shunt

Explanation: The most appropriate management for this patient is to increase the lactulose therapy. This patient has severe encephalopathy manifested by worsening somnolence. Encephalopathy progresses from subtle findings, such as reversal of the sleep-wake cycle or mild mental status changes, to irritability, confusion, slurred speech, and ultimately coma if not recognized and treated. There can be multiple inciting causes of encephalopathy in patients with cirrhosis, including dehydration, infection (especially spontaneous bacterial peritonitis), diet indiscretions, gastrointestinal bleeding, and medications. This patient likely became worse with the development of the urinary tract infection. The best course of management is to treat the infection and to discontinue the diuretics and increase the lactulose to respond to the encephalopathy. The dose of lactulose should be titrated to achieve two to three soft stools per day with a pH below 6.0. Approximately 70% to 80% of patients with hepatic encephalopathy improve on lactulose therapy, and treatment is usually well tolerated. Corticosteroids have no role in the reversal of hepatic encephalopathy. Transjugular intrahepatic portosystemic shunt (TIPS) is not appropriate because placement of TIPS is likely to precipitate worsening hepatic encephalopathy as more blood is bypassed through the shunt rather than processed by the liver. There is no role for hemodialysis in the treatment of hepatic encephalopathy and there appear to be no other indications for dialysis (severe acidosis, hyperkalemia, renal failure with hypervolemia).

Key Point First-line therapy for hepatic encephalopathy is lactulose.

Answers: Q10: A | Q11: C

Liver cirrhosis

Q12: A 45-year-old man with alcoholic cirrhosis is admitted to the hospital for worsening ascites and abdominal pain. His medications are propranolol, lactulose, spironolactone, and furosemide.
On physical examination, temperature is 37.2°C (99.0°F), blood pressure is 110/60 mm Hg, pulse rate is 56/min, and respiration rate is 16/min. Tense ascites is present, and the abdomen is tender to palpation. The remainder of the examination is noncontributory. Admission serum creatinine is 0.8 mg/dL (70.7 µmol/L). A diagnostic paracentesis reveals 350 leukocytes/µL. Cefotaxime and albumin infusions are begun. On hospital day 3 the patient is oliguric. Laboratory studies reveal a blood urea nitrogen level of 15 mg/dL (5.4 mmol/L) and a serum creatinine level of 2.0 mg/dL (176.8 µmol/L). Urinalysis reveals a spot urine sodium of 10 meq/L (10 mmol/L). Furosemide and spironolactone are discontinued and infusions of normal saline and albumin are initiated, but he remains oliguric. Kidney ultrasound shows normal kidney size, and there is no hydronephrosis. Which of the following is the most likely cause of his acute kidney injury?

Leukocyte count	5600/µL (5.6×10^9/L)
Glucose (random)	112 mg/dL (6.2 mmol/L)
Creatinine	1.8 mg/dL (159.1 µmol/L)
Sodium	135 meq/L (135 mmol/L)
Potassium	3.5 meq/L (3.5 mmol/L)
Chloride	100 meq/L (100 mmol/L)
Bicarbonate	28 meq/L (28 mmol/L)
Bilirubin (total)	4.0 mg/dL (68.4 µmol/L)
Aspartate aminotransferase	78 U/L
Alanine aminotransferase	45 U/L
Albumin	2.7 g/dL (27 g/L)
Ammonia	230 µg/dL (135 µmol/L)

A- Hepatorenal syndrome
B- Obstructive nephropathy
C- Prerenal azotemia
D- Renal artery stenosis

Explanation: This patient most likely has hepatorenal syndrome, which is defined as development of kidney failure in patients with portal hypertension and normal renal tubular function. Intense renal vasoconstriction leads to a syndrome of acute kidney dysfunction characterized by increased renal sodium avidity, a relatively normal urine sediment, and oliguria in some patients. This condition is diagnosed after other causes of acute kidney injury such as prerenal azotemia, renal parenchymal disease, or obstruction have been excluded. Spontaneous bacterial peritonitis, vigorous diuretic therapy, paracentesis without volume expansion, and gastrointestinal bleeding also may precipitate hepatorenal syndrome. The most effective treatment for hepatorenal syndrome is liver transplantation.
Although patients with complete obstruction have significantly decreased urine output, those with partial obstruction may have polyuria caused by loss of tubular function or excretion of excess retained solute. Kidney ultrasonography in most patients with obstruction reveals hydronephrosis and was absent in this patient.
This patient had no signs of hypovolemia such as hypotension or tachycardia, and his kidney dysfunction did not improve after discontinuation of diuretics and administration of volume replacement with normal saline albumin. This makes prerenal azotemia an unlikely diagnosis. The diagnosis of renal artery stenosis as the cause of this acute kidney injury is unlikely considering his end-stage cirrhosis, no evidence of hypertension, and no signs of diffuse vascular disease.

Key Point The hepatorenal syndrome is defined as development of kidney dysfunction in patients with portal hypertension after exclusion of prerenal azotemia, renal parenchymal disease, or obstruction.

Answers: Q12: A

Abnormal liver enzymes

Q1: You see a 54-year-old woman, referred to accident and emergency through her GP, with a week's history of jaundice and right upper quadrant abdominal pain. Associated symptoms include dark urine and pale stools. There is no history of weight loss and the patient does not consume alcohol. Her liver function tests reveal a bilirubin of 40 µmol/L, ALT of 40 iu/L, AST 50 iu/L and ALP of 350 iu/L. The most likely diagnosis is:

A. Gallstones
B. Viral hepatitis
C. Alcoholic hepatitis
D. Carcinoma of the head of the pancreas
E. Autoimmune hepatitis

Explanation: From the history, it is clear that the patient is suffering conjugated hyperbilirubinaemia with symptoms of jaundice coupled with dark urine and pale stools. The liver function tests support a diagnosis of cholestasis – bilirubin of 40 µmol/L, with an unparalleled rise in ALP (350 iu/L). AST and ALT are mildly elevated in comparison. Therefore, from the list of possible answers, gallstones (A) are the most likely diagnosis. With viral (B), alcoholic hepatitis (C) and autoimmune hepatitis (E) one would expect elevation in ALT and AST enzymes due to hepatocellular damage. There is no history of weight loss which makes pancreatic carcinoma (D) unlikely.

Q2: You are asked by your registrar to request an imaging investigation for a 49-year- old woman with jaundice and abdominal pain. She has a past medical history of gallstones and you suspect this is a recurrence of the same problem. The most appropriate imaging investigation is:

A. Abdominal x-ray
B. Abdominal ultrasound
C. Abdominal CT
D. Magnetic resonance imaging (MRI)
E. Endoscopic retrograde cholangiopancreatography (ERCP)

Explanation: The most appropriate imaging modality for the investigation of gallstones is abdominal ultrasound (B). This remains the imaging modality of choice. It is highly sensitive (gallstones are echogenic and will usually cast a 'shadow' on US), fast, non-invasive, free from radiation exposure and is relatively cheap compared to CT and MRI. Although patients who are admitted via accident and emergency with an acute abdomen will usually have an abdominal x-ray (B), this investigation is not done in attempting to detect gallstones as only 10 per cent are radiopaque. CT scanning (C) has been shown to be less sensitive than ultrasound scanning in the detection of gallstones and, in addition, delivers a very large quantity of radiation which can be avoided in this case. MRI (D) is not routinely performed for gallstone detection as it is costly, time consuming and, again, not as sensitive as ultrasound scanning. ERCP (E) is useful in the detection of gallstones within the common bile duct, but cannot clearly identify stones within the gallbladder and, being quite an invasive procedure, would not be recommended as first-line imaging in this scenario.

Q3: You see a 47-year-old woman who presents with a 3-day history of jaundice. You assess her liver function tests (LFTs) and see that the ALP iu/L is raised at 350 iu/L, AST 45 iu/L, ALT 50 iu/L and bilirubin 50 iu/L. The patient feels well in herself, although she has noticed that her urine has become quite dark and her stools quite pale. You assess her medication history. Which of the following drugs from the patient's medication history may be responsible for the cholestasis?

A. Co-amoxiclav
B. Bendroflumethiazide
C. Ramipril
D. Amlodipine
E. Aspirin

Explanation: Drugs which are known to cause cholestasis include:
• Clavulanic acid
• Penicillins
• Oestrogens
• Erythromycin
• Chlorpromazine
Therefore, (A) would be the most likely drug to cause cholestasis. The drugs mentioned in answers B–E are not known to cause cholestasis.

Answers: Q1: A | Q2: B | Q3: A

Abnormal liver enzymes

Q4: A 70-year-old man presents with a complaint of fatigue. There is no history of alcohol abuse or liver disease; the patient is taking no medications. Scleral icterus is noted on physical examination; the liver and spleen are nonpalpable. The patient has a normocytic, normochromic anemia. Urinalysis shows bilirubinuria with absent urine urobilinogen. Serum bilirubin is 12 mg/dL, AST and ALT are normal, and alkaline phosphatase is 300 U/L (three times normal). Which of the following is the best next step in evaluation?

A. Ultrasound or CT scan of the abdomen
B. Viral hepatitis profile
C. Reticulocyte count
D. Serum ferritin
E. Antimitochondrial antibodies

Explanation: Patients with jaundice should be characterized as having unconjugated (indirect reacting) or conjugated (direct) hyperbilirubinemia. Causes of unconjugated hyperbilirubinemia include hemolysis, ineffective erythropoiesis, or enzyme deficiencies (the commonest in adults being Gilbert syndrome). The patient, however, has conjugated hyperbilirubinemia, which almost always indicates significant liver dysfunction, either hepatocellular or cholestatic (obstructive); this patient's predominant elevation of alkaline phosphatase suggests a cholestatic pattern. Normal transaminases rule out hepatocellular damage (such as viral or alcoholic hepatitis). Instead, a disease of bile ducts or a cause of impaired bile excretion should be considered. Ultrasound or CT scan will evaluate the patient for an obstructing cancer or stone disease versus intrahepatic cholestasis. Ferritin values would evaluate for hemochromatosis, but this disease typically causes transaminase elevation and hepatomegaly. Primary biliary cirrhosis (PBC, evaluated by the antimitochondrial antibody test) might be considered if imaging studies show a nondilated biliary system (suggesting intrahepatic cholestasis), but PBC is usually seen in middle-aged women.

Q5: A 24-year-old man is evaluated for a 6-day history of malaise, fatigue, and jaundice following a camping trip in rural Mexico 3 weeks ago. His alcohol consumption is approximately 6 beers per week, never exceeding more than 2 beers per occasion. Two weeks ago he participated in a marathon race and finished the race without incident. His sister was recently diagnosed with primary biliary cirrhosis. The remainder of his history is unremarkable. On examination, temperature is 37.8°C (100.0°F), blood pressure is 132/72 mm Hg, pulse rate is 104/min, and the respiration rate is 16/min. BMI is 21. Examination shows sclera icterus and hepatomegaly. The remainder of the examination findings are normal. Which of the following patterns of hepatic injury is present?

A. Cholestatic injury
B. Hepatocellular injury
C. Mixed hepatocellular and cholestatic injury
D. Nonhepatic injury pattern (muscle injury)

Bilirubin (total)	4.6 mg/dL (78.7 µmol/L)
Bilirubin (direct)	3.5 mg/dL (59.9 µmol/L)
Aspartate aminotransferase	1123 U/L
Alanine aminotransferase	1350 U/L
Alkaline phosphatase	185 U/L

Explanation: This patient has acute hepatocellular damage associated with mild hyperbilirubinemia that could be caused by acute hepatitis. Hepatocellular injury most often results in an elevation of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) concentrations, which reflect release of intracellular enzymes from injured hepatocytes. AST is also released from other tissues, such as the heart and skeletal muscle. Therefore, elevations of ALT, which is minimally produced in nonhepatic tissues, are more specific for diagnosing liver disease. Hepatocyte dysfunction is often associated with conjugated hyperbilirubinemia, in which the direct bilirubin fraction is greater than 50%. Cholestatic injury (cholestasis), which consists of a lack of or an abnormality in the flow of bile, is indicated primarily by an elevation of serum alkaline phosphatase and relatively minimal elevations of AST and ALT. Cholestasis may occur without jaundice because of the capacity of the liver to continue to secrete bile sufficiently until the injury to the bile ducts is significant. Profound disruption of the bile secretory mechanisms is likely to result in conjugated hyperbilirubinemia with elevation of the direct fraction of serum bilirubin. The first evaluative step in a patient with a cholestatic pattern of injury is to obtain an ultrasound study to determine if intrahepatic or extrahepatic biliary obstruction is present. Liver disorders can also present with a mixed pattern of liver injury that is characterized by moderate to severe elevations of aminotransferase, alkaline phosphatase, and bilirubin levels. Hepatitis B and C are examples of conditions that can occasionally present with a mixed liver injury pattern. This patient's predominantly elevated aminotransferase levels with mildly elevated alkaline phosphatase concentration and direct bilirubin fraction clearly points to a hepatocellular injury pattern. A nonhepatic injury pattern, such as muscle injury, would be associated with striking elevations of AST, lesser elevations of ALT, and would not be associated with elevations of conjugated bilirubin.

Key Point Hepatocellular injury most often results in an elevation of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) concentrations and often is associated with direct hyperbilirubinemia.

Answers: Q4: A | Q5: B

Abnormal liver enzymes

Q6: A 30-year-old woman is evaluated because of an abnormal serum total bilirubin level detected when she had a life insurance examination. Medical history is unremarkable. Her only medication is an oral contraceptive agent. Physical examination is normal. Which of the following is the most appropriate management at this time?

A. Discontinue the oral contraceptive agent
B. No further intervention required
C. Obtain a reticulocyte count and haptoglobin level
D. Repeat the liver chemistry tests in 3 months
E. Schedule abdominal ultrasonography

Hemoglobin	13.9 g/dL (139 g/L)
Mean corpuscular volume	88 fL
Red cell distribution width	10.8%
Serum total bilirubin	2.4 mg/dL (41.0 µmol/L)
Serum direct bilirubin	0.2 mg/dL (3.4 µmol/L)
Serum aspartate aminotransferase	23 U/L
Serum alanine aminotransferase	22 U/L
Serum alkaline phosphatase	82 U/L

Explanation: This patient has indirect (unconjugated) hyperbilirubinemia, which in an asymptomatic patient with a normal hemoglobin level and otherwise normal liver tests is suggestive of Gilbert syndrome. Bilirubin is measured as conjugated (direct) and unconjugated (indirect) fractions. In patients with cholestatic diseases leading to jaundice, approximately half of the bilirubin is measured as the conjugated fraction. Predominance of the unconjugated fraction indicates either the overproduction of bilirubin (as occurs in hemolysis) or impairment of bilirubin conjugation. The latter is relatively common, given the 5% prevalence of Gilbert syndrome in the general population. This benign syndrome, also known as constitutional hepatic dysfunction and familial nonhemolytic jaundice, is characterized by total bilirubin concentrations up to 3.0 mg/dL (51.3 mmol/L) resulting from a reduced expression of the enzyme that conjugates bilirubin. Gilbert syndrome is the most common inherited disorder of bilirubin metabolism. In adults, it is a benign disorder, and no additional diagnostic studies or therapy is required at this time. Cholestasis due to an oral contraceptive agent will cause conjugated (direct) hyperbilirubinemia and an elevated serum alkaline phosphatase level, neither of which this patient has. Patients with hemolysis significant enough to cause unconjugated hyperbilirubinemia generally have a low hemoglobin level and abnormal values for mean corpuscular volume (low) and red cell distribution width (high). Abdominal ultrasonography may be a helpful study for patients with direct hyperbilirubinemia, which is usually associated with liver disease, but is not indicated in this patient who has indirect hyperbilirubinemia and no evidence of liver disease.

Key Point The incidental finding of indirect (unconjugated) hyperbilirubinemia in an asymptomatic patient with a normal hemoglobin level and otherwise normal liver tests is indicative of Gilbert syndrome.

Q7: A 42-year-old man is evaluated for a 1-month history of progressive jaundice, pruritus, and dark urine. The patient has a 15-year history of ulcerative colitis. He is treated with mesalamine and occasionally requires corticosteroid therapy. He takes no other medications. On physical examination, vital signs are normal. There is jaundice and hepatomegaly but no splenomegaly, ascites, or abdominal tenderness. There is no asterixis. Which of the following is the most likely diagnosis?

A. Gilbert syndrome
B. Hepatitis A
C. Hepatitis C
D. Primary sclerosing cholangitis

Hemoglobin	14 g/dL (140 g/L)
Aspartate aminotransferase	150 U/L
Alanine aminotransferase	180 U/L
Bilirubin (total)	4.2 mg/dL (71.8 µmol/L)
Alkaline phosphatase	450 U/L

Explanation: This patient likely has primary sclerosing cholangitis, a chronic cholestatic liver disease associated with inflammatory bowel disease and characterized by fibrosis, inflammation, and stricturing of the biliary tree. Up to 85% of affected patients have underlying inflammatory bowel disease, but less than 5% of patients with inflammatory bowel disease have primary sclerosing cholangitis. Cholestatic liver diseases primarily cause elevation of serum alkaline phosphatase values and minor elevations of the aminotransferase levels. The disorder is more common in patients with ulcerative colitis than with Crohn disease. Most patients are diagnosed while asymptomatic with abnormal results on liver biochemistry tests, but jaundice and pruritus can occur in patients with advanced disease. The diagnosis is usually made by endoscopic retrograde cholangiopancreatography, which is especially useful in advanced disease where histologic samples can be taken to rule out cholangiocarcinoma and stents can be placed if there is a dominant stricture. Magnetic resonance cholangiopancreatography can also be used.
Gilbert syndrome is a common disorder associated with indirect hyperbilirubinemia. Patients with this syndrome generally have a serum total bilirubin level of less than 3.0 mg/dL (51.3 µmol/L), whereas the serum direct bilirubin level is less than or equal to 0.3 mg/dL (5.1 µmol/L). A presumptive diagnosis of Gilbert syndrome can be made in an otherwise healthy patient who has indirect hyperbilirubinemia, normal liver enzyme values, and a normal hemoglobin concentration (which excludes hemolysis). This patient does not fulfill the criteria for Gilbert syndrome. Patients with acute hepatitis C are usually asymptomatic and therefore rarely present clinically, but 60% to 85% of persons who acquire acute hepatitis C develop chronic infection. The cholestatic picture in the absence of other signs of advanced liver disease is inconsistent with chronic hepatitis C. Patients with acute hepatitis A often have fatigue, nausea, mild upper abdominal pain, and jaundice. Serum aspartate aminotransferase and alanine aminotransferase values are usually greater than 500 U/L. Hepatitis A does not present with a cholestatic biochemical profile as seen in this patient.

Key Point Patients with acute hepatitis have a marked elevation of aminotransferases, whereas patients with primary sclerosing cholangitis have a cholestatic pattern (primary elevation of bilirubin and alkaline phosphatase levels)

Answers: Q6: B | Q7: D

Abnormal liver enzymes

Q8: You see a 56-year-old man in your clinic with suspected alcoholic liver disease. Liver function tests reveal a bilirubin of 36 iu/L, AST of 150 iu/L, ALT 75 iu/L and ALP 100 iu/L. Which of the following blood test parameters would support a diagnosis of alcoholic-related liver disease?

A. Normal mean cell volume (MCV)
B. Low MCV
C. Normal mean cell haemoglobin (MCH)
D. Low MCH
E. Raised MCV

Explanation: Macrocytosis, i.e. an elevated MCV (>96 fL) of which the causes can be seen in:
• megaloblastic anaemia secondary to vitamin B12 and folic acid deficiency;
• chronic alcoholism and/or alcoholic liver disease (most common causes of all causes of macrocytosis), pregnancy, hypothyroidism, reticulocytosis, aplastic anaemia, myelodysplastic syndromes and can also be caused by drugs that inhibit DNA synthesis (e.g. azathioprine);
an elevated MCV would suggest, along with the deranged LFTs, and support a diagnosis of alcoholic liver disease. Therefore answers A–D are incorrect.

Q9: You see a 52-year-old woman with rheumatoid arthritis in your clinic. She was referred by her GP after her ALP levels were found to be abnormally high at 300 iu/L. In addition, she was also found to be serum anti-mitochondrial antibody (AMA) positive. The most likely diagnosis is:

A. Primary biliary cirrhosis
B. Wilson's disease
C. Heriditary haemochromotosis
D. Primary sclerosing cholangitis
E. Alcoholic liver disease

Explanation: This patient is suffering from primary biliary cirrhosis (PBC) (A) which is characterized by chronic granulomatous inflammation leading to damage of interlobular bile ducts. This chronic inflammatory process leads to cholestasis, cirrhosis and portal hypertension. The cause of PBC is thought to be of autoimmune origin (women being more affected than men) and is associated with various autoimmune conditions. Patients are often asymptomatic and diagnosis is usually made when abnormal LFTs are detected with an abnormal rise in serum ALP. Symptoms include lethargy and pruritus which can occur before the presentation of jaundice. Signs include jaundice, xanthelasma, xanthomata, skin pigmentation, splenomegaly and hepatomegaly. Investigations include blood tests: (1) LFTs (raised ALP, γ-GT, with mildly elevated AST and ALT. In late disease there is a raised bilirubin level and low levels of albumin with an increase in the prothrombin time); (2) Ninety-eight per cent of patients with PBC are anti-mitochondrial antibody (AMA) positive. ANA, SMA and ANCA autoantibodies may also be present but at low titres; (3) IgM (usually raised); (4) Raised levels of TSH and cholesterol may be present. Performing radiological imaging, such as ultrasound, will exclude extrahepatic cholestasis and liver biopsy will confirm granulomas (not specific to PBC) surrounding the bile ducts, progressing to cirrhosis.

Treatment is divided into:
• symptomatic – for symptoms of pruritus (e.g. colestyramine) , diarrhoea (e.g. codeine phosphate) and osteoporosis (e.g. bisphosphonates);
• specific – vitamin A, D, K supplementation, ursodeoxycholic acid for improving jaundice and ascites;
• liver transplantation for end-stage liver disease.

Wilson's disease (B) is an autosomal recessive disorder (of gene on chromosome 13 that codes for copper transporting ATPase) resulting in toxic accumulation of copper in the liver and central nervous system. Twenty-four hour urinary copper excretion is high (>100 µg/24 h with normal levels being <40 µg) with low copper and caeruloplasmin levels. Diagnosis can be confirmed by genetic testing and liver biopsy. Patients present with signs of liver disease. Kayser–Fleischer rings are pathognomonic (copper deposits in iris). Hereditary haemochromatosis (C) is an inherited condition characterized by a disorder in iron metabolism. There is increased intestinal iron absorption which is deposited in multiple organs such as the liver, heart, pancreas, etc. LFTS are usually elevated with raised ferritin and serum iron levels, and low total iron-binding capacity (TIBC). Diagnosis can be confirmed with HFE (mutation in HFE gene is responsible for hereditary haemochromatosis) genotyping and liver biopsy. Patients are initially asymptomatic then eventually experience arthralgia and tiredness with slate-grey skin pigmentation with late disease progression. Iron deposition also occurs in the pancreas leading to impaired insulin secretion and eventually diabetes (also known as bronze diabetes). Primary sclerosing cholangitis (D) is a condition of unknown cause which is defined by non- malignant, non-bacterial inflammation, fibrosis and strictures of the intra- and extrahepatic bile ducts. It is serum AMA negative but ANA, SMA and ANCA may be positive. Diagnosis is made with MRCP and liver biopsy. Patients are initially asymptomatic and may present with jaundice, pruritus, abdominal pain and fatigue. Alcoholic liver disease (E) is incorrect here as there is no mention, in the clinical scenario, of raised AST/ALT levels which would signify hepatocellular damage.

Answers: Q8: E | Q9: A

Abnormal liver enzymes

Q10: You see a 56-year-old woman who presents with a two-month history of jaundice. Associated symptoms include lethargy and polyarthralgia. Her LFTs reveal a bilirubin of 46 iu/L, AST 200, ALT 175, ALP 104. On examination, the patient is jaundiced and has finger clubbing. There are several spider naevi on the front and back of the trunk. Her abdomen is soft and there is a smooth hepatomegaly. Prior to her onset of symptoms, the patient has been fit and well. Viral serology is normal and anti-soluble liver antigen (SLA) is detected. You decide to start this patient on treatment. The most appropriate treatment is:

A. Liver transplantation
B. Methotrexate
C. Prednisolone
D. Cyclosporin
E. Antivirals

Explanation: This patient has symptoms of chronic liver disease secondary to auto- immune hepatitis (AIH) which is indicated from the history (no history of excessive alcohol consumption), negative viral serology and positive SLA autoantibody. AIH is an inflammatory liver disease of unknown cause which is characterized by suppressor T-cell defects which are directed against hepatocyte surface antigens. Three types of AIH have been identified according to the various autoantibodies detected (e.g. Type-1: anti-smooth muscle antibodies, antinuclear antibodies; type-2: anti-liver/kidney microsomal type 1 antibodies; and type-3: antibodies against soluble liver antigen or liver–pancreas antigen). AIH is known to affect women (young and middle-aged) with 25 per cent presenting with acute hepatitis and signs of autoimmune disease (e.g. polyarthralgia, glomerulonephritis, pernicious anaemia, PSC). The remaining patients are asymptomatic and are diagnosed when signs of chronic liver disease develop. Investigations include: (1) Blood: LFTs, immunoglobulins (e.g. IgG), auto-antibodies (see above) and FBC (may show low WCC and platelets); (2) liver biopsy may reveal mononuclear infiltration, fibrosis or cirrhosis; and (3) MRCP to exclude PSC. Management involves: (1) Symptomatic treatment for chronic liver disease; (2) immunosuppressant therapy: Corticosteroid therapy (e.g. prednisolone) or steroid-sparing agent such as azathioprine can be used; and (3) liver transplantation is indicated for decompensated liver cirrhosis or failure to respond to medical treatment.

Q11: You are told by your registrar that one of your inpatients has been diagnosed with primary sclerosing cholangitis (PSC). Your registrar suspects that the patient may have an associated condition. Primary sclerosing cholangitis is associated with which of the following diseases?

A. Thyroid disease
B. Systemic sclerosis
C. Rheumatoid arthritis
D. Ulcerative colitis
E. Irritable bowel syndrome

Explanation: Eighty to 100 per cent of patients with PSC will have ulcerative colitis (D). On the other hand, 3 per cent of patients with ulcerative colitis will have PSC. Thyroid disease (A), systemic sclerosis (B) and rheumatoid arthritis (C) are associated with primary biliary cirrhosis.

Q12: A 68-year-old man presents to his GP with signs of drastic weight loss. He is known to have PSC. The GP suspects an underlying malignancy. Which of the following tumours would a patient with primary sclerosing cholangitis be more at risk of developing?

A. Hepatocellular carcinoma
B. Cholangiocarcinoma
C. Hepatic fibroma
D. Hepatic haemangioma
E. Pancreatic carcinoma

Explanation: Twenty to 30 per cent of patients diagnosed with PSC are more likely to develop cholangiocarcinoma, which is defined as a malignancy of the biliary tree. Other causes include flukes (in the East), congenital biliary cysts and N-nitroso toxins. Patients may present with fever, abdominal pain with or without ascites, and jaundice. LFTs show raised bilirubin with highly elevated ALP. Ultrasound scanning may be performed to detect lesions and ERCP and biopsy is diagnostic. Seventy per cent of cholangiocarcinomas cannot be surgically resected. Of those treated through the surgical route (hepatectomy and extrahepatic bile duct excision and caudate lobe resection), 76 per cent recur. For tumours that cannot be surgically treated, palliative stenting may be conducted to improve quality of life. Hepatocellular carcinoma (A) is a malignant tumour of hepatocytes and accounts for approximately 90 per cent of primary liver tumours. Causes include viral hepatitis, cirrhosis (related to alcohol, PBC, haemochromotosis), aflatoxin, parasites such as Clonorchis sinensis and anabolic steroids. Hepatic fibroma (C) and haemangiomas (D) are benign liver tumours which do not usually require treatment. They are not related with PSC. Pancreatic carcinoma (E), although a possible answer, is unlikely here as patients with PSC do not have an increased chance of developing this condition.

Answers: Q10: C | Q11: D | Q12: B

Abnormal liver enzymes

Q13: A 64-year-old woman attends your clinic with a 2-week history of jaundice. Over the last three months the patient has lost 10 kg. Associated symptoms include decreased appetite, dark urine and pale stools. On examination, the patient is jaundiced, her abdomen is soft and you can palpate a painless mass in the right upper quadrant. From the list of answers below, select the initial most appropriate investigation that you would request for this patient:

A. Abdominal x-ray
B. Abdominal CT
C. MRI of the abdomen
D. Abdominal ultrasound
E. ERCP

Explanation: The patient is exhibiting Courvoisier's law which states that a palpable gallbladder in the presence of painless jaundice is unlikely due to gallstones. In this scenario, it is likely that the patient's symptoms of painless jaundice, dark urine and pale stools coupled with drastic weight loss point to a diagnosis of carcinoma of the head of the pancreas. Risk factors include smoking, chronic excessive alcohol consumption, diabetes mellitus, high fat diet and chronic pancreatitis. Patients usually present with symptoms of painless cholestatic jaundice, weight loss, diabetes or acute pancreatitis. Some rare features include thrombophlebitis migrans, hypercalcaemia, portal hypertension and nephrosis. Signs include jaundice, palpable gallbladder, epigastric mass, hepatomegaly, splenomegaly, lymphadenopathy and ascites. Investigations include blood tests (FBC, LFTs), imaging modalities such as abdominal ultrasound and abdominal CT (B) (which can also be used for guided biopsies of lesions and staging before surgical intervention), ERCP (E) (may be able to localize site of obstruction leading to cholestasis) and endoscopic sonography (has been shown to be the most accurate diagnostic and staging tool). Referring to the question, the most appropriate answer would be to initially request an abdominal ultrasound (B) which would provide non-invasive imaging of the pancreas.

Q14: A 27-year-old woman is found to have a positive hepatitis C antibody at the time of plasma donation. Physical examination is normal. Liver enzymes reveal ALT of 62 U/L (normal < 40), AST 65 U/L (normal < 40), bilirubin 1.2 mg/dL (normal), and alkaline phosphatase normal. Hepatitis C viral RNA is 100,000 copies/mL. Hepatitis B surface antigen and HIV antibody are negative. Which of the following statements is true?

A. Liver biopsy is necessary to confirm the diagnosis of hepatitis C.
B. Most patients with hepatitis C eventually resolve their infection without permanent sequelae.
C. This patient should not receive vaccinations against other viral forms of hepatitis.
D. Serum ALT levels are a good predictor of prognosis.
E. Patients with hepatitis C genotype 2 or 3 are more likely to have a favorable response to treatment with interferon and ribavirin.

Explanation: This patient has chronic hepatitis C. A positive test for hepatitis C viral RNA confirms the diagnosis. Liver biopsy is not necessary for confirmation, but may be useful in predicting need for treatment. Chronic hepatitis C rarely resolves spontaneously. Untreated, about 15% of patients with hepatitis C will eventually develop cirrhosis. The levels of ALT and viral RNA correlate poorly with histologic disease and eventual prognosis. Treatment with pegylated interferon and ribavirin is aimed at preventing cirrhosis. Females, patients under age 40, patients with minimal or no cirrhosis, and those infected with genotypes 2 and 3 are more likely to respond to treatment. All patients with chronic hepatitis C should receive vaccination against hepatitis A and B, which can cause fulminant hepatic failure in patients with preexisting hepatitis C.

Answers: Q13: D | Q14: E

Abnormal liver enzymes

Q15: A 22-year-old college student has recently returned from a 3-month anthropology course in Thailand where she lived with a local village family. She has a 2-week history of fatigue and nausea with occasional vomiting and a 2-day history of jaundice. She was previously well, takes no medications, and has no history of liver disease, injection drug use, blood transfusions, sexual exposures, or known exposure to anyone with hepatitis. She took malarial prophylaxis and her hepatitis B vaccination status is current. She does not recall vaccination for hepatitis A. Physical examination is significant only for jaundice and a slightly enlarged, nontender liver. There are no spider angiomata or signs of encephalopathy. Which of the following is the most likely diagnosis?

A- Hepatitis A
B- Hepatitis B
C- Hepatitis C
D- Hepatitis D

Aspartate aminotransferase	1586 U/L
Alanine aminotransferase	1897 U/L
Total bilirubin	6.2 mg/dL (106.0 µmol/L)

Explanation: This patient most likely has acute hepatitis A. The patient has clinical symptoms and laboratory findings consistent with acute hepatitis (fatigue, jaundice, aminotransferase concentrations >1000 U/L). The major routes of transmission are ingestion of contaminated food or water and contact with an infected person. Groups at particularly high risk include people living in or traveling to underdeveloped countries, children in day care centers, men who have sex with men, and perhaps people who ingest raw shellfish. Although any of the hepatitis viruses can cause symptomatic acute hepatitis, hepatitis A is the most likely infection in a traveler to an undeveloped country without other risk factors. Hepatitis A is almost always a self-limited infection, although acute hepatitis A may rarely present as fulminant hepatitis that may require liver transplantation. The clinical course may include a prolonged cholestatic phase characterized by persistence of jaundice for up to 6 months. Treatment of acute hepatitis A is supportive. Serum immune globulin should be administered to all household and intimate contacts within 2 weeks of exposure. Hepatitis A virus vaccine should be offered to travelers who go to underdeveloped countries, men who have sex with men, injection drug users, and patients with chronic liver disease. Hepatitis B, C, and D are less likely without a history of parenteral exposure. Hepatitis D virus (HDV or delta agent) depends upon the presence of HBsAg for its replication and, therefore, cannot survive on its own. In a patient infected with hepatitis B, HDV infection may present as an acute hepatitis (in which case it is a coinfection) or an exacerbation of preexisting chronic hepatitis (in which case it is a superinfection). Patients with a history of injection drug use are at greatest risk for acquiring HDV infection. Finally, acute hepatitis C rarely causes symptoms.

Key Point Patients with acute hepatitis generally have fatigue, nausea, vomiting, jaundice, and aminotransferase values greater than 1000 U/L.

Q16: A 55-year-old man is hospitalized for a 2-week history of jaundice and altered mental status. The patient has a 10-year history of alcohol dependence. His family reports that he had been drinking heavily every day until about 3 weeks ago. On physical examination, the patient is confused and lethargic; temperature is 38.0°C (100.4°F), blood pressure is 90/60 mm Hg, pulse rate is 120/min, and respiration rate is 30/min. Examination reveals scleral icterus. There is no guarding on palpation of the abdomen. The liver edge is tender and palpable. There is no ascites, edema, or evidence of bleeding. Ultrasonography shows an enlarged, fatty liver with no nodules, ascites, pericholecystic fluid, or bile duct dilatation. Which of the following is the most likely diagnosis?

A- Alcoholic hepatitis
B- Autoimmune hepatitis
C- Hepatitis A
D- Hepatitis B
E- Hepatitis C

INR	4.0
Bilirubin (total)	37.0 mg/dL (632.7 µmol/L)
Aspartate aminotransferase	175 U/L
Alanine aminotransferase	73 U/L
Hepatitis B surface antigen	Negative
Hepatitis B surface antigen antibody	Positive
Hepatitis C antibody	Negative
Hepatitis A antibody (IgM)	Negative
Hepatitis A antibody (IgG)	Positive
Antinuclear antibody titer	Negative

Explanation: This patient has severe alcoholic hepatitis. Excessive alcohol intake may cause liver disease directly or may increase the risk of an unfavorable outcome in patients with preexisting liver disease. This patient with chronic alcohol abuse has many of the characteristic findings of alcoholic hepatitis: a history of recent heavy alcohol use, elevated serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) values (usually less than 500 U/L and frequently less than 300 U/L), AST to ALT ratio greater than 2 to 1, elevated alkaline phosphatase concentration, jaundice, coagulopathy, and encephalopathy. Moreover, other major causes of acute and chronic liver disease have been excluded. The patient's serology tests confirm past infection with hepatitis B virus and current immunity (positive hepatitis B surface antigen antibody). Similarly, the serologic tests for hepatitis A are compatible with past infection and current immunity (positive IgG hepatitis A antibody). The negative hepatitis C antibody serology rules out chronic hepatitis C virus infection. Autoimmune hepatitis is an inflammatory condition of the liver of unknown cause. It primarily develops in persons 20 to 40 years of age, but all age groups and most ethnic groups are affected. Women develop autoimmune hepatitis more often than men. Most patients present with features of chronic liver disease. Antinuclear antibody, anti- smooth-muscle antibody, or antibody to liver/kidney microsome type 1 (anti-LKM1) is present in 87% of patients and helps to support a diagnosis of autoimmune hepatitis. Finally, autoimmune hepatitis does not cause a fatty liver.

Key Point Patients with alcoholic hepatitis have a history of recent heavy alcohol use, elevated serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) concentrations, an AST:ALT ratio greater than 2 to 1, and elevated alkaline phosphatase concentration.

Answers: Q15: A | Q16: A

Abnormal liver enzymes

Q17: A 38-year-old woman is evaluated for abnormal liver chemistry tests detected in an evaluation for new-onset fatigue, joint pains, and jaundice. She has a history of autoimmune hypothyroidism, and her only medications are levothyroxine and a multivitamin. She has never used illicit drugs and does not drink alcohol. Her mother has systemic lupus erythematosus. On physical examination, the patient is afebrile. Blood pressure is 130/75 mm Hg, pulse rate is 80/min, and respiration rate is 14/min. There is scleral icterus; the rest of the examination is normal. Which of the following is the most likely diagnosis?

A- Acute cholecystitis
B- Autoimmune hepatitis
C- Drug-induced liver injury
D- Primary biliary cirrhosis

Bilirubin (total)	6.0 mg/dL (102.6 µmol/L)
Bilirubin (direct)	3.6 mg/dL (61.6 µmol/L)
Aspartate aminotransferase	890 U/L
Alanine aminotransferase	765 U/L
Alkaline phosphatase	100 U/L
Antinuclear antibody	Titer 1:40
Anti-smooth muscle antibody	Titer 1:640
Antimitochondrial antibody	Negative
Viral serologic tests are negative.	

Explanation: This patient has autoimmune hepatitis, a disorder that occurs most commonly in girls and young women. Like this patient with hypothyroidism, many affected patients have other autoimmune disorders and a family history of autoimmunity. These patients usually present with vague symptoms. Fatigue, which occurs in 85% of patients, is the most common presenting symptom, followed by jaundice (46%), anorexia (30%), myalgias (30%), and diarrhea. On physical examination, most patients have an enlarged liver. Patients can have aminotransferase concentrations into the thousands (but typically less than 500 IU at presentation), elevated bilirubin, often near-normal alkaline phosphatase, and hypergammaglobulinemia. Autoimmune serologic tests, specifically antinuclear antibodies, anti-smooth muscle antibodies, and antibody to liver/kidney microsome type 1 (anti-LKM1), may be positive but are not detected in up to 25% of patients. Primary biliary cirrhosis is a chronic progressive cholestatic liver disease of unknown cause. It is an autoimmune disorder that occurs predominantly in women (80% to 90% of cases) between 40 and 60 years of age. The diagnostic triad associated with primary biliary cirrhosis includes a cholestatic liver profile, positive antimitochondrial antibody titers, and compatible histologic findings on liver biopsy. Serum alkaline phosphatase level is usually elevated 10 times or more above normal. The patient's near-normal alkaline phosphatase concentration and negative antimitochondrial antibody essentially rule out primary biliary cirrhosis. Although drug-induced liver injury can cause similar liver test abnormalities, the patient has not taken any new medications recently, making this diagnosis unlikely, and levothyroxine would be a very unusual cause of drug-induced hepatitis. Additionally, drug-induced hepatitis is not associated with positive anti-smooth muscle antibody findings. She has no pain to suggest acute cholecystitis.

Key Point Laboratory findings in patients with autoimmune hepatitis include elevated serum aminotransferase values, hypergammaglobulinemia, mild hyperbilirubinemia, mildly elevated serum alkaline phosphatase values, and the presence of autoantibodies.

Q18: A 32-year-old man is evaluated for a 2-week history of nausea, malaise, low-grade fever, vomiting, and jaundice. Other than having multiple sex partners, he has no other significant medical history and takes only ibuprofen for headache and fever. On physical examination, temperature is 37.6°C (99.7°F), blood pressure is 110/75 mm Hg, pulse rate is 90/min, and respiration rate is 22/min. Examination reveals scleral icterus, jaundice, hepatomegaly, asterixis, and somnolence. There are no stigmata of chronic liver disease. Ultrasonography shows hepatomegaly and increased echogenicity, a normal spleen, and perihepatic ascites. There is no ductal dilatation. Which of the following is the most likely diagnosis?

A- Acute hepatitis A
B- Acute hepatitis B
C- Chronic hepatitis B
D- Hepatitis C

Bilirubin (total)	17.5 mg/dL (299.2 µmol/L)
Aspartate aminotransferase	8790 U/L
Alanine aminotransferase	7650 U/L
INR	2.3
Hepatitis B surface antigen	Positive
Hepatitis B core antigen (IgM)	Positive
Hepatitis C virus RNA	Negative
Hepatitis A IgM antibody	Negative
Hepatitis A IgG antibody	Positive

Explanation: The markedly elevated aminotransferase levels, positive hepatitis B surface antigen, and IgM antibody to hepatitis B core antigen establish the diagnosis of acute hepatitis B infection. Patients at greatest risk for exposure to hepatitis B virus infection are those with a history of multiple sexual partners and injection drug users. Most adult patients will clear their infection after a few months. However, about 5% patients develop acute progressive hepatitis B with hepatic decompensation and need urgent liver transplantation, as does this patient. These patients tend to have an elevated INR and a rising bilirubin level and may develop encephalopathy, a marker of fulminant hepatic failure. Patients with chronic hepatitis B have positive hepatitis B surface antigen and positive IgG antibody to hepatitis B core antigen; IgM antibody to hepatitis B core antigen is negative. In addition, this patient's fulminant course is not compatible with chronic hepatitis B infection. Acute hepatitis A is diagnosed by the presence of IgM antibody to hepatitis A virus (IgM anti-HAV), which appears at the onset of the acute phase of the illness and becomes undetectable in 3 to 6 months. IgG anti-HAV also becomes positive during the acute phase but persists for decades and is a marker of immunity to further infection. A person with a positive IgG anti-HAV titer but a negative titer for IgM anti-HAV has had hepatitis A in the remote past or has received hepatitis A vaccine. Patients with acute hepatitis C are usually asymptomatic and therefore rarely present clinically, but 60% to 85% of persons who acquire acute hepatitis C develop chronic infection. Although determination of antibody to hepatitis C virus (HCV) is a reliable and inexpensive test for diagnosing hepatitis C, the diagnostic "gold standard" is the presence of HCV RNA in serum.

Key Point Positive hepatitis B surface antigen and IgM antibody to hepatitis B core antigen establish the diagnosis of acute hepatitis B infection.

Answers: Q17: B | Q18: B

Abnormal liver enzymes

Q19: A 63-year-old man comes to the emergency department because of significant epigastric pain, nausea, and fever of 24 hours' duration. On physical examination, the patient is jaundiced. Temperature is 38.5°C (101.3°F), blood pressure is 100/68 mm Hg, and pulse rate is 100/min. Abdominal examination discloses significant right upper quadrant tenderness. Abdominal ultrasonography shows a dilated 11-mm common bile duct and a gallbladder containing multiple stones. Which of the following is the most likely diagnosis accounting for all the patient's findings?

Leukocyte count	12,100/μL (12.1 × 10^9/L)
Serum alkaline phosphatase	315 U/L
Serum aspartate aminotransferase	103 U/L
Serum alanine aminotransferase	117 U/L
Serum lipase	240 U/L
Serum total bilirubin	2.9 mg/dL (49.6 μmol/L)

A- Acute cholangitis
B- Acute cholecystitis
C- Acute pancreatitis
D- Cholelithiasis

Explanation: This patient has classic acute cholangitis. The clinical diagnosis is based upon the presence of Charcot triad (fever, jaundice, and right upper quadrant abdominal pain). In this setting, bile duct dilation, with stones in the gallbladder, suggests acute cholangitis due to choledocholithiasis. Broad-spectrum antibiotics to cover aerobic and anaerobic gram- negative bacilli and enterococci should be started immediately. Endoscopic retrograde cholangiopancreatography with sphincterotomy should then be performed to remove impacted stones. Patients with acute cholecystitis may have right upper quadrant pain and gallstones, but the bilirubin level is usually not greater than 2 mg/dL (34.2 μmol/L), and aminotransferase levels are normal. Uncomplicated cholecystitis is not associated with common bile duct obstruction. Patients with simple cholelithiasis are generally asymptomatic. This patient may have pancreatitis that is related to obstruction of the common bile duct and is supported by the finding of elevated lipase level. However, pancreatitis alone cannot explain all of this patient's symptoms and in particular cannot account for the right upper quadrant pain or dilated common bile duct.

Key Point The classic findings of acute cholecystitis are biliary colic, a Murphy sign, fever, leukocytosis, mild bilirubin and aminotransferase elevation, gallstones, pericholecystic fluid, and thickening of the gallbladder wall on ultrasonography

Q20: A 55-year-old woman recently had elevated liver chemistry tests detected on examination for life insurance. She has no symptoms of liver disease and no history of jaundice, ascites, lower extremity edema, or encephalopathy. While in college she received 3 units of blood following a major motor vehicle accident that resulted in a ruptured spleen. She has no other significant medical history and takes no medications. She has had only one sex partner in her lifetime. On physical examination, vital signs are normal. There are spider angiomata on the upper body, and a nodular liver edge is noted. Abdominal CT scan shows changes in the liver consistent with cirrhosis. Which of the following is the most likely diagnosis?

Bilirubin (total)	1.1 mg/dL (18.8 μmol/L)
Aspartate aminotransferase	48 U/L
Alanine aminotransferase	96 U/L
Hepatitis C antibody	Positive
Hepatitis B surface antigen	Negative
Hepatitis A antibody (IgM)	Negative
Hepatitis A antibody (IgG)	Positive

A- Hepatitis A
B- Hepatitis B
C- Hepatitis C
D- Hepatitis D

Explanation: This patient most likely has chronic hepatitis C infection. Hepatitis C virus (HCV) is the most common bloodborne infection in the United States. Although screening of blood products and reduced transmission among injection drug users have resulted in a decreasing number of new HCV infections, the number of deaths is increasing because of the "backlog" of chronic infections and the long duration of chronic infection before cirrhosis develops. Patients with acute hepatitis C are usually asymptomatic and therefore rarely present clinically, but 60% to 85% of persons who acquire acute hepatitis C develop chronic infection. The anti-HCV antibody test is the screening test for at-risk persons; a positive test in a person with one of the risk factors confirms exposure to the virus. The HCV RNA test is required to determine active infection rather than just exposure to the virus. Hepatitis A does not cause chronic liver disease. The patient's serology is compatible with either a past infection with hepatitis A virus or immunization with hepatitis A vaccine. Hepatitis B virus (HBV) causes 20% to 30% of cases of acute viral hepatitis and 15% of cases of chronic viral hepatitis in the United States. Multiple sex partners and injection drug use are the major risk factors for disease acquisition in this country. This patient is negative for hepatitis B surface antigen and therefore does not have chronic hepatitis B infection. Hepatitis D virus (HDV or the delta agent) is a defective virus that requires the presence of HBsAg to replicate. In the United States, injection drug users with hepatitis B are the group at highest risk for acquiring hepatitis D.

Key Point The anti-hepatitis C virus antibody test is the screening test for at-risk persons; a positive test in a person with one of the risk factors confirms exposure to the virus.

Answers: Q19: A | Q20: C

Fatty liver

Q1: A 37-year-old woman presents for evaluation of abnormal liver chemistries. She has long-standing obesity (current BMI 38) and has previously taken anorectic medications but not for the past several years. She takes no other medications and has not used parenteral drugs or had high-risk sexual exposure. On examination, her liver span is 13 cm; she has no spider angiomas or splenomegaly. Several sets of liver enzymes have shown transaminases two to three times normal. Bilirubin and alkaline phosphatase are normal. Hepatitis B surface antigen and hepatitis C antibody are normal, as are serum iron and total iron-binding capacity. Which of the following is the likely pathology on liver biopsy?

A. Macrovesicular fatty liver
B. Microvesicular fatty liver
C. Portal triaditis with piecemeal necrosis
D. Cirrhosis
E. Copper deposition

Explanation: This woman likely has nonalcoholic fatty liver (NAFL), which is associated with macrovesicular accumulation of fat in the liver. If hepatocellular necrosis is present, the condition is termed nonalcoholic steatohepatitis (NASH). This condition is histologically similar to alcoholic hepatitis, and increasing evidence suggests that it too is a precirrhotic condition. With the increasing incidence of obesity in Western societies, NASH may become the commonest cause of cirrhosis and end-stage liver disease. Microvesicular fat is seen in the acute life-threatening conditions of acute fatty liver of pregnancy and Reye syndrome. Portal triaditis and piecemeal necrosis of cells in the hepatic lobule are associated with several disorders, including autoimmune and chronic viral hepatitis. Cirrhosis, characterized by bands of fibrous tissue, regenerating nodules, and disruption of the hepatic architecture, is the final common pathway of various chronic insults to the liver. Copper deposition is seen in Wilson disease.

Q2: A 45-year-old man comes to the physician for a routine health maintenance examination. He feels well. He has type 2 diabetes mellitus. There is no family history of serious illness. He works as an engineer at a local company. He does not smoke. He drinks one glass of red wine every other day. He does not use illicit drugs. His only medication is metformin. He is 180 cm (5 ft 11 in) tall and weighs 100 kg (220 lb); BMI is 31 kg/m2. His vital signs are within normal limits. Examination shows a soft, nontender abdomen. The liver is palpated 2 to 3 cm below the right costal margin. Laboratory studies show an aspartate aminotransferase concentration of 100 U/L and an alanine aminotransferase concentration of 130 U/L. Liver biopsy shows hepatocyte ballooning degeneration, as well as inflammatory infiltrates with scattered lymphocytes, neutrophils, and Kupffer cells. Which of the following is the most likely diagnosis?

A- Primary biliary cirrhosis
B- Alcoholic fatty liver disease
C- Viral hepatitis
D- Nonalcoholic steatohepatitis

Explanation: This patient likely has non-alcoholic fatty liver disease (NAFLD). The term encompasses a wide variety of liver pathology, from steatosis to steatohepatitis to cirrhosis. The pathophysiology of this disease centers around insulin resistance, which is probably present in this obese adolescent with acanthosis nigricans. The diagnosis of NAFLD is suggested by hyperglycemia, hyperlipidemia, elevated transaminases (ALT>AST), and increased echogenicity on liver ultrasound. A recent article on the topic concluded that normal ALT ranges at most children's hospitals are not sensitive for abnormal ALT levels, and that an ALT greater than 25 for boys and 23 girls should raise suspicion for liver disease.

Answers: Q1: A | Q2: D

Esophageal diseases

Q1: A 47-year-old woman presents to your clinic with a three-month history of dysphagia. There is no history of drastic weight loss and the patient experiences symptoms when swallowing solids but not liquids. Which of the following is not an obstructive cause of dysphagia?

A. Pharyngeal carcinoma
B. Oesophageal web
C. Retrosternal goitre
D. Peptic stricture
E. Achalasia

Explanation: Answers A–D are all termed obstructive causes of dysphagia. The causes can be categorized into:

(Obstructive)
- Oesophageal carcinoma
- Peptic strictures (D)
- Oesophageal web/ring (B)
- Gastric carcinoma
- Pharyngeal carcinoma (A)
- Extrinsic pressure from, for example, lung carcinoma, retrosternal goitre (C)

(Oesophageal motility disorders)
- Achalasia (E)
- Systemic sclerosis
- Stroke
- Myasthenia gravis
- Neurological degenerative conditions, e.g. motor neurone disease,Parkinson's disease

(Others)
- Oesophagitis
- Pharyngeal pouch
- Oesophageal candidiasis

Q2: You see a 48-year-old lorry driver, who presents to you with a three-month history of heartburn after meals which has not been settling with antacids and PPIs. You suspect that the patient has a hiatus hernia. The most appropriate investigation for diagnosing a hiatus hernia is:

A. Computer tomography (CT) scan
B. Chest x-ray
C. Upper GI endoscopy
D. Barium meal
E. Ultrasound

Explanation: All the above investigations have been shown to be useful in the diagnosis of a hiatus hernia. However, upper GI barium meals/swallows (D) have been shown to be the most definitive modality in diagnosing hiatus hernias. Chest x-rays (B) may be normal, but in some cases may show an air fluid level above the level of the left hemi-diaphragm. Upper GI endoscopy (C) is commonly used to assess symptoms of dyspepsia and has not been shown to be as sensitive as barium studies in the detection of hiatus hernias. In the UK, CT scanning (A) is not routinely used for the investigation of hiatus hernias, but the latter are incidentally detected on scanning of the abdomen for the investigation of other pathology. Compared to the barium study, CT scanning delivers relatively high levels of radiation. Positive results obtained with ultrasound scanning (E) may lead to inconsistent and false-positive/negative results due to the operator- associated variability regarding technical experience.

Answers: Q1: E | Q2: D

Esophageal diseases

Q3: You see a 56-year-old man who was admitted for an elective upper GI endoscopy due to longstanding GORD which has failed to improve on antacids and PPIs. Your registrar suspects that this patient may have Barrett's oesophagus and asks you to define what this is. The most appropriate description of Barrett's oesophagus is:

A. Metaplasia of the squamous epithelium of the lower third of the oesophagus to columnar epithelium
B. Metaplasia of the columnar epithelium of the upper third of the oesophagus to squamous epithelium
C. Metaplasia of the columnar epithelium of the lower third of the oesophagus to squamous epithelium
D. Metaplasia of the squamous epithelium of the upper third of the oesophagus to columnar epithelium
E. Metaplasia of the squamous epithelium of the middle third of the oesophagus to columnar epithelium

Explanation: Barrett's oesophagus occurs as a result of chronic inflammation of the oesophagus, usually secondary to GORD. Typically, the lower third of the oesophagus is affected whereby the squamous cells are subjected to longstanding acid reflux from the stomach. This gives rise to chronic inflammation of the lower third of the oesophagus and results in metaplastic change of the squamous cells to columnar type which is thought to be an adaptive mechanism in withstanding the erosive action of the stomach acid. This metaplasia is described as a premalignant state and increases the risk of adenocarcinoma of the oesophagus. Diagnosis is made via upper GI endoscopy and biopsy.

Q4: A 65-year-old woman with a complex medical history (including diabetes, hypertension, coronary artery disease, gastroesophageal reflux disease, and ongoing use of alcohol and tobacco) presents with increasing midsternal chest discomfort predominantly when swallowing solid food. Recently, even liquids are becoming problematic. She has not noted blood in her stool or melena, weight loss, or change in her energy level. What is the most likely cause of her dysphagia?

A. Esophageal cancer
B. Peptic esophageal stricture
C. Achalasia
D. Zenker diverticulum
E. Polymyositis

Explanation: Peptic strictures due to chronic, persistent acid reflux cause 80% of esophageal strictures. Diagnostic esophagogastroduodenoscopy followed by dilation is necessary to relieve the dysphagia; the procedure may need to be repeated from time to time as symptoms recur. A patient with esophageal cancer is likely to have weight loss. Patients with achalasia often regurgitate undigested food; achalasia is less common than peptic stricture. A Zenker diverticulum is an outpouching in the posterior wall of the hypopharynx, which allows food retention, causing halitosis, recurrent aspiration, and pneumonia. While patients with polymyositis often have dysphagia, they would typically display weakness of the proximal muscles in addition to dysphagia.

Q5: A 72-year-old woman notices progressive dysphagia to solids and liquids. There is no history of alcohol or tobacco use, and the patient takes no medications. She denies heartburn, but occasionally notices the regurgitation of undigested food from meals eaten several hours before. Her barium swallow is shown. Which of the following is the cause of this condition?

A. Growth of malignant squamous cells into the muscularis mucosa
B. Scarring caused by silent gastroesophageal reflux
C. Spasm of the lower esophageal sphincter
D. Loss of intramural neurons in the esophagus
E. Psychiatric disease

Explanation: The barium swallow shows the dilated baglike proximal esophagus and tapered distal esophageal ring characteristic of achalasia. This is a motor disorder of the esophagus and classically produces dysphagia to both solids and liquids. Structural disorders such as cancer and stricture usually cause trouble swallowing solids as the first manifestation. In achalasia, manometry shows elevated pressure and poor relaxation of the lower esophageal sphincter. In classic achalasia the contractions of the esophagus are weak, although a variant called vigorous achalasia is associated with large-amplitude prolonged contractions. Medications (nitrates, calcium channel blockers, botox injections into the LES) or physical procedures (balloon dilatation or surgical myotomy) that decrease LES pressure are the recommended treatments. Squamous cell carcinoma would not cause esophageal dilation and would be associated with ratty rather than smooth tapering of the esophagus. Achalasia is not associated with gastroesophageal reflux disease. Although anxiety can cause dysphagia and a globus-like sensation in the cricoid region, it would not cause the anatomical changes seen on this barium swallow.

Answers: Q3: A | Q4: B | Q5: D

Esophageal diseases

Q6: A 68-year-old man is evaluated for a 15-year history of acid reflux symptoms and a 6-month history of worsening midsternal burning chest discomfort. The pain is nonexertional and exacerbated by lying down or bending over. He also notes occasional difficulty swallowing solids described as a sensation of food "sticking" at about the level of the lower sternum. The pain is partially alleviated by over-the-counter antacids, but they have no effect on the dysphagia. He does not smoke or drink, he has no other medical problems, and he takes no prescription medications. On physical examination, vital signs are normal. BMI is 27. Cardiopulmonary and abdominal examinations are unremarkable. Which of the following is the most appropriate initial diagnostic test for this patient?

A. Ambulatory esophageal pH monitoring
B. Empiric treatment with omeprazole
C. Helicobacter pylori testing
D. Upper endoscopy

Explanation: The initial diagnostic test for this patient is upper endoscopy. His presentation is typical for GERD: burning pain relieved by antacids and worsened by lying down and bending forward. Response to empiric treatment with a proton pump inhibitor such as omeprazole would be sufficiently sensitive and specific to diagnose GERD; however, this patient also has the alarm symptom of dysphagia. Upper endoscopy should be performed next to evaluate for acid-induced esophageal stricture and esophageal carcinoma. Testing for H. pylori is not indicated for patients with GERD, because the presence or absence of H. pylori does not correlate with the presence or absence of GERD or guide therapy. Ambulatory esophageal pH monitoring is the gold standard for diagnosing GERD and is typically used in patients in whom the diagnosis is uncertain or who are unresponsive to empiric therapy. In this patient who presents with symptoms typical for GERD with alarm symptoms, the primary goal of testing is to establish the presence of a GERD complication such as acid stricture or esophageal carcinoma.

Key Point In patients with gastroesophageal reflux disease, endoscopy is indicated for patients with alarm symptoms.

Q7: A 30-year-old woman is evaluated in the emergency department for abdominal pain and hematemesis. She undergoes upper endoscopy, which demonstrates a 1-cm duodenal ulcer with a clean base. Helicobacter pylori is seen on biopsy, and the patient is discharged home with appropriate therapy for H. pylori. She is adherent to her therapy and her symptoms rapidly resolve. The patient returns to the office 3 months later with 3 weeks of midepigastric abdominal discomfort; regurgitation; and burning chest discomfort that worsens with bending over, lying down, or after eating large meals. Repeat endoscopy demonstrates complete healing of her duodenal ulcer; erosive esophagitis is present. Which of the following is the most appropriate treatment for this patient?

A. Metoclopramide
B. Omeprazole
C. Ranitidine
D. Sucralfate

Explanation: The standard of care for the medical management of gastroesophageal reflux disease (GERD), including patients with erosive esophagitis, is proton pump inhibitor (PPI) therapy. Although histamine2 receptor antagonist therapy relieves symptoms and heals esophagitis in 50% to 60% of patients, PPI therapy provides results in the 80% range. Five PPIs are available in the United States: omeprazole, esomeprazole, lansoprazole, pantoprazole, and rabeprazole; they all have similar efficacy. A promotility agent such as metoclopramide can theoretically be beneficial in the treatment of patients with GERD by increasing lower esophageal sphincter pressure, enhancing gastric emptying, or improving peristalsis. However, promotility agents have significant side effects and the FDA has imposed a black box warning on metoclopramide, and specialty guidelines recommend against the use of metoclopramide because of questionable efficacy and numerous side effects. Sucralfate (aluminum sucrose sulfate) is a topical therapy for peptic ulcer disease and GERD. Sucralfate adheres to the mucosal surface and promotes healing by an unknown mechanism. Sucralfate is approximately as effective as a histamine2 receptor antagonist for the treatment of GERD and nonerosive esophagitis but substantially less effective than a PPI and has no role in the treatment of erosive esophatitis.

Key Point Proton pump inhibitor therapy is the treatment of choice for erosive or severe esophagitis.

Answers: Q6: D | Q7: B

Inflammatory bowel diseases

Q1: Which of the following gastroenterological conditions would give rise to finger clubbing?

A. Hepatocellular carcinoma
B. Ulcerative colitis
C. Irritable bowel syndrome
D. Hepatocellular carcinoma
E. Pancreatic carcinoma

Explanation: Inflammatory bowel disease (e.g. ulcerative colitis and Crohn's disease) is a known gastroenterological cause of finger clubbing along with liver cirrhosis, primary biliary cirrhosis, oesophageal leiyomyoma, coeliac disease and achalasia. Therefore, (B) is the most likely answer here.

Q2: A 28-year-old man undergoes a sigmoidoscopy for longstanding diarrhoea and weight loss. On visualization of the rectum, the mucosa appears inflamed and friable. A rectal biopsy is taken and the histology shows mucosal ulcers with inflammatory infiltrate, crypt abscesses with goblet cell depletion. From the list of answers below, which is the most likely diagnosis describing the histology report?

A. Crohn's disease
B. Pseudomembranous colitis
C. Irritable bowel syndrome
D. Ulcerative colitis
E. No diagnosis – the report is inconclusive

Explanation: The most likely diagnosis is ulcerative colitis (UC) (D) based on the histological results of the rectal biopsy. The findings of inflammatory infiltrates coupled with mucosal ulcers, goblet cell depletion and crypt abscesses are highly suggestive of a diagnosis of UC. UC is described as a relapsing and remitting inflammatory bowel disorder of the colonic mucosa. The condition usually starts at the rectum (proctitis in 50 per cent) and spreads proximally, in a continuous fashion, to affect parts of the colon (e.g. left-sided colitis in 30 per cent) or the entire colonic tract (pancolitis in 20 per cent). UC tends not to spread beyond the ileocaecal valve but may cause a condition called 'backwash ileitis'. Histologically, Crohn's disease (A) is characterized by transmural, non-caseating granulomatous inflammation, coupled with fissuring ulcers, lymphoid aggregates and neutrophil infiltrates. Crohn's disease can affect any part of the GI tract from the mouth to the anus (but favours the terminal ileum in 50 per cent) and is also characterized by skip lesions (unaffected bowel between areas of active disease) whereas in UC, disease spreads from the rectum to the ileocaecal valve in a continuous fashion depending on the stage of disease.
Pseudomembranous colitis (PC) (B) is characterized by the formation of an adherent inflammatory membrane (the pseudomembrane) overlying sites of muscosal injury within the colon. The histology of PC is described as small surface erosions of the superficial colonic crypts coupled with overlying accumulation of neutrophils, fibrin, mucus and necrotic epithelial cells forming a 'summit lesion'. The toxins (toxin A and B) produced by the gram-positive anaerobic bacillus, Clostridum difficile, are meant to be the cause of PC. There is normal histology of the bowel in irritable bowel syndrome (C).

Q3: You are told by your registrar that one of the clinic patients has been admitted with a 'flare up' of ulcerative colitis (UC) which he reports as being severe. From the list of answers below, select the parameters which are likely to reflect a severe flare up of ulcerative colitis:

A. Fewer than four bowel motions per day with large amounts of rectal bleeding
B. Between four and six bowel motions per day with large amounts of rectal bleeding
C. More than four bowel motions per day with large amounts of rectal bleeding
D. More than five bowel motions per day with large amounts of rectal bleeding
E. More than six bowel motions per day with large amounts of rectal bleeding

Explanation: Using the Truelove and Witts criteria, which asseses the severity of UC, patients with UC opening their bowels greater than six times a day, and passing large amounts of blood per rectum, are considered to have severe UC. The other parameters that are recognized under the severe UC category are body temperature >37.8°C, a pulse rate >90 beats per minute, a haemoglobin <10.5 g/dl and an ESR >30 mm/h.
Moderate UC is defined as opening bowels between four and six times a day and passing moderate amounts of blood per rectum, body temperature between 37.1 and 37.8°C, a pulse rate between 70 and 90 beats per minute and haemoglobin between 10.5 and 11 g/dL.
Mild UC is classified as experiencing fewer than four bowel motions per day and passing small amounts, if not no blood, per rectum, normal body temperature, pulse rate <70, haemoglobin of >11 g/dL and an ESR of <30 mm/h.

Answers: Q1: B | Q2: D | Q3: E

Inflammatory bowel diseases

Q4: You read a report which was handwritten in a patient's medical notes who you suspect has inflammatory bowel disease. The report reads, '… there is cobblestoning of the terminal ileum with the appearance of rose thorn ulcers. These findings are suggestive of Crohn's disease'. Select the most likely investigation that this report was derived from:

A. Colonoscopy
B. Sigmoidoscopy
C. Barium follow through
D. Abdominal CT
E. Abdominal ultrasound

Explanation: The appearance of 'cobblestoning' and 'rose thorn ulcers' are radiological descriptions, seen in Crohn's disease, obtained from barium follow-through (A) investigations of the ileum. Lower GI endoscopy is preferred in establishing a diagnosis of IBD (either Crohn's or UC) because the operator is allowed direct visualization of the bowel and biopsies may be taken; skip lesions can be seen on direct visualization but the appearance of 'rose thorn ulcers' have only been described in barium radiograpy studies.

Q5: You are asked to see a 29-year-old woman diagnosed with ulcerative colitis 18 months ago. Over the last 4 days she has been experiencing slight abdominal cramps, opening her bowels approximately 4–5 times a day and has been passing small amounts of blood per rectum. The patient is alert and orientated and on examination her pulse is 67, blood pressure 127/70, temperature 37.3°C and her abdomen is soft with mild central tenderness. PR examination is nil of note. Blood tests reveal haemoglobin of 13.5 g/dL and a CRP of 9 mg/L. The most appropriate management plan for this patient is:

A. Admission to hospital for intravenous fluid therapy and steroids
B. Oral steroid therapy + oral 5-ASA + steroid enemas + discharge
C. Admission and refer to surgeons for further assessment
D. Oral steroid therapy and discharge home
E. Reassurance and discharge home with no treatment required

Explanation: From the patient's symptoms and signs, it is evident that she is experiencing a moderate flare-up of UC (Truelove and Witts criteria in the assessment of severity of UC). Treatment of UC flare-ups is targeted at inducing and maintaining remission. In this question, the patient, although experiencing mild abdominal cramps, frequent bowel motions and passing small amounts of blood per rectum, is systemically well. In addition, her haemoglobin levels are within normal range and her CRP is <10 mg/dL. Therefore, based on the information from the patient's history coupled with the blood test results, hospital admission would not be warranted. This patient can be treated as an outpatient and followed up either in clinic or by her GP. In terms of treatment regimens for moderate UC, patients are usually started on a course of steroids (e.g. 40 mg of prednisolone), which is decreased on a weekly basis coupled with twice daily 5-ASA (e.g. mesalazine) and topical treatment of per rectum steroid foams (e.g. hydrocortisone). If symptoms do not resolve in 10–14 days, the patient is usually treated as severe UC. For mild UC, the aim of treatment again is to induce and maintain remission. This involves commencing a tapering dose of oral steroids with a 5-ASA. In some patients with distal disease, the use of steroid foams per rectum has shown to be of benefit. If symptoms improve, 5-ASA foams can be used instead of steroid foams. However, if symptoms do not improve in 10–14 days, the patient is usually treated as moderate UC. In severe UC, patients are usually admitted for intravenous fluid and steroid (e.g. IV hydrocortisone) therapy. Rectal steroids are also given. Patients are monitored closely and are examined on a twice daily basis to assess for abdominal distension, bowel sounds and abdominal tenderness. Worsening of these signs may be suggestive of toxic dilatation of the colon which would require surgical intervention due to the high risk of bowel perforation. Therefore, (B) is the most appropriate management plan.

Q6: A 29-year-old anxious man is diagnosed with mild Crohn's disease. Due to time constraints, the patient was asked to come back for a follow-up appointment to discuss Crohn's disease in more detail. The patient returns with a list of complications he researched on the internet. Which of the following are not associated with Crohn's disease?

A. Cigarette smoking reduces incidence
B. Fistulae formation
C. Abscess formation
D. Non-caseating granuloma formation
E. Associated with transmural inflammation

Explanation: Answers B–E are all facts that are associated with Crohn's disease, whereas cigarette smoking has been reported to increase the incidence of Crohn's disease but has found to be protective in UC; 70–80 per cent of non- smokers have UC compared to 50–60 per cent of patients who are smokers with Crohn's disease.

Answers: Q4: C | Q5: B | Q6: A

Inflammatory bowel diseases

For each case scenario, select the most likely diagnosis. Each lettered option may be used once, more than once, or not at all.

Q7: A 35-year-old white man presents with diarrhea, weight loss, and RLQ pain. On examination, a tender mass is noted in the RLQ; the stool is guaiac-positive. Colonoscopy shows segmental areas of inflammation. Barium small bowel series shows nodular thickening of the terminal ileum.

Q8: A 75-year-old African American woman, previously healthy, presents with low-grade fever, diarrhea, and rectal bleeding. Colonoscopy shows continuous erythema from rectum to mid-transverse colon. The cecum is normal.

Q9: A 70-year-old white woman presents with LLQ abdominal pain, low-grade fever, and mild rectal bleeding. Examination shows LLQ tenderness. Unprepped sigmoidoscopy reveals segmental inflammation beginning in the distal sigmoid colon through the mid-descending colon. The rest of the examination is negative.

A. Ulcerative colitis
B. Crohn disease
C. Ischemic colitis
D. Diverticulosis
E. Amebic colitis
F. Tuberculoma of the colon

Explanation: Crohn disease can affect the entire GI tract from mouth to anus. Right lower quadrant pain, tenderness, and an inflammatory mass would suggest involvement of the terminal ileum. As opposed to ulcerative colitis (a pure mucosal disease), Crohn disease, with full-thickness involvement of the gut wall, can lead to fistula and deep abscess formation. Skip lesions (ie, segmental involvement) also suggest Crohn disease; granuloma formation on biopsies would also support the diagnosis of Crohn disease.

Although thought of a disease of young adults, ulcerative colitis has a second peak of incidence in the 60- to 80-year age group and should be considered in the differential diagnosis of diarrhea at any age. Colonic involvement starts in the rectum and proceeds toward the cecum in a continuous fashion (ie, no skip lesions). Inflammation is limited to the mucosa; so fistulas, deep abscesses, and granulomas are not seen.

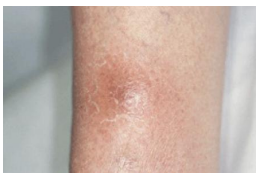
Ischemic colitis usually occurs in the older age group. The ischemia is usually confined to the mucosa, so perforation is unusual. Pain is a prominent complaint and may mimic acute diverticulitis. The finding of segmental inflammation in watershed areas in the vascular distribution of the colon is characteristic. Most patients improve without surgical intervention.

Although acute diverticulitis is associated with lower abdominal pain and fever, diverticulosis is usually asymptomatic until profuse rectal bleeding occurs. Amebic colitis is seen in emigrants from endemic areas and presents with bloody diarrhea. Tuberculomas are rare now that gastrointestinal disease from Mycobacterium bovis has been eradicated from domestic cattle in the United States Tuberculomas are associated with fever, right lower quadrant pain, and hematochezia.

Answers: Q7: B | Q8: A | Q9: C

Inflammatory bowel diseases

Q10: A 24-year-old woman with a 1-year history of Crohn disease is evaluated for tender bumps on her shins. She has been experiencing more abdominal pain and increased bowel movements for the past 3 months. Starting 2 weeks ago, she developed low-grade fever, increased fatigue, and arthralgia. Her only medication is sulfasalazine. On physical examination, vital signs are normal. On abdominal examination, bowel sounds are present and palpation produces slight tenderness in the right lower quadrant. A typical skin lesion found on the lower extremity is shown. Which of the following is the most likely diagnosis for the skin finding?



A- Dermatitis herpetiformis
B- Erythema nodosum
C- Pyoderma gangrenosum
D- Rheumatoid nodule

Explanation: The most likely diagnosis is erythema nodosum. Extraintestinal manifestations occur in approximately 10% to 20% of patients with inflammatory bowel disease at some time in the course of their disease. Erythema nodosum, which manifests as small, exquisitely tender nodules on the anterior tibial surface, is the most common cutaneous manifestation of inflammatory bowel disease and occurs more commonly in Crohn disease, whereas pyoderma gangrenosum is more common in ulcerative colitis. The typical clinical presentation of erythema nodosum is the sudden onset of one or more tender, erythematous nodules on the anterior legs that are more easily palpated than visualized. The eruption is often preceded by a prodrome of fever, malaise, and arthralgia. A residual ecchymotic appearance is common as the lesions age. In patients with inflammatory bowel disease, treating the underlying bowel disease usually results in remission of erythema nodosum.

Dermatitis herpetiformis is characterized by grouped, pruritic, erythematous papulovesicles on the extensor surfaces of the arms, legs, central back, buttocks, and scalp. A genetic predisposition is linked to the same genes associated with celiac disease. Virtually all patients with dermatitis herpetiformis have celiac disease, but gastrointestinal symptoms occur in only about 25% of patients.

Pyoderma gangrenosum occurs in approximately 10% of patients with ulcerative colitis. Pyoderma gangrenosum is an uncommon, neutrophilic, ulcerative skin disease. Lesions tend to be multiple and to appear on the lower extremities. They begin as tender papules, pustules, or vesicles that spontaneously ulcerate and progress to painful ulcers with a purulent base and undermined, ragged, violaceous borders.

Rheumatoid nodules are the most common cutaneous manifestation of rheumatoid arthritis. They may be asymptomatic or painful and interfere with function. Rheumatoid nodules are frequently found in the subcutaneous tissue just distal to the elbow on the extensor surface of the forearm. Nodules also may be found on the extensor surface of the hand and over the Achilles tendons. Rheumatoid nodules and inflammatory bowel disease are not linked.

Key Point Erythema nodosum, which manifests as small, exquisitely tender nodules on the anterior tibial surface, is the most common cutaneous manifestation of inflammatory bowel disease.

Q11: A 52-year-old man is evaluated for a 5-month history of three to four loose, bloody stools a day with mild urgency, abdominal cramping, and fatigue. He has not lost weight during this episode. He is otherwise healthy. On physical examination, vital signs are normal. There is mild lower abdominal tenderness without rebound or guarding; there are no palpable abdominal masses. Examination of the rectum shows gross blood. Colonoscopy shows continuous mild erythema and loss of vascular pattern from the rectum to the transverse sigmoid colon; the rest of the colon and terminal ileum are normal. Biopsy specimens from the abnormal mucosa show cryptitis, crypt abscesses, and distortion of crypt architecture. Which of the following is the most appropriate therapy for this patient?

A- Azathioprine
B- Ciprofloxacin
C- Infliximab
D- Mesalamine
E- Metronidazole

Explanation: The most appropriate treatment is mesalamine. This patient has mild left-sided ulcerative colitis based on his clinical presentation, endoscopic, and histologic findings. Topical therapy is appropriate for distal disease. Options include cortisone foam and mesalamine or corticosteroid suppositories for proctitis and hydrocortisone or mesalamine enemas for left-sided colitis. Oral 5-aminosalicylates, including sulfasalazine, mesalamine, balsalazide, and olsalazine, are appropriate for distal disease that does not respond to topical therapy or for mild to moderate pancolitis. Oral prednisone is used when symptoms do not respond to 5-aminosalicylates. Because prednisone and other corticosteroids have many acute and chronic toxic effects that are dose- and duration-dependent, the lowest effective dose should be given for the shortest time. Azathioprine (AZA) or 6-mercaptopurine (6-MP) may be used for patients who have incomplete disease remission while on corticosteroids. However, because both agents have delayed onset of action, concomitant administration of either AZA or 6- MP together with a 3- to 4-month course of prednisone is often necessary. Antibiotics, including both metronidazole and ciprofloxacin, have not been shown to be effective in ulcerative colitis. Infliximab is a chimeric antibody against tumor necrosis factor α; in patients with severe disease or who do not respond to corticosteroid therapy for remission, infliximab may be effective, but it would not be an appropriate first-line medication for mild ulcerative colitis.
Key Point First-line therapy for induction and maintenance of remission in mild to moderate ulcerative colitis is mesalamine or another 5-aminosalicylate agent.

Answers: Q10: B | Q11: D

Inflammatory bowel diseases

Q12: A 55-year-old man is evaluated for a 4-month history of frequent and urgent defecation with loose and bloody stool, mild abdominal cramping, and fatigue. He has up to eight bowel movements a day and often wakes at night with symptoms. He does not have fever, nausea, or vomiting, but he has lost 3 kg (7 lb). He has mild joint pain in his knees and ankles that also began 4 months ago, is worse in the morning, and resolves somewhat during the day. The patient is a former cigarette smoker but quit smoking 2 years ago. He has no other medical problems. On physical examination, vital signs are normal. There is mild lower abdominal tenderness without rebound or guarding; there are no palpable abdominal masses. Examination of the rectum shows gross blood. Laboratory studies reveal a hemoglobin level of 12.3 g/dL (123 g/L) with a mean corpuscular volume of 76 fL. Fecal leukocytes are present, but stool culture is negative. Colonoscopy shows continuous erythema, friability, and loss of vascular pattern from the rectum to the splenic flexure; the rest of the colon and terminal ileum is normal. Histology shows cryptitis, crypt abscesses, and crypt architecture distortion. Which of the following is the most likely diagnosis?

A- Crohn colitis
B- Infectious colitis
C- Ischemic colitis
D- Microscopic colitis
E- Ulcerative colitis

Explanation: This patient has mild to moderate left-sided ulcerative colitis based on his clinical presentation and endoscopic and histologic findings. His ex-smoking status, microcytic anemia, and the presence of arthritis, which is the most common extraintestinal manifestation of inflammatory bowel disease, further support the diagnosis. Ulcerative colitis typically involves the rectum and extends proximally with contiguous inflammation that is generally limited to the mucosa of the colon and rectum. Patients usually present with bloody diarrhea associated with rectal discomfort, fecal urgency, and cramps. Although most patients have bloody diarrhea, those with proctitis can present with constipation.

Although many colitides can have overlapping clinical, endoscopic, and even histologic features, there are important differences to consider. Microscopic colitis presents with nonbloody diarrhea, and colonoscopy shows normal mucosa macroscopically and histology shows either increased intraepithelial lymphocytes (lymphocytic colitis) or an increased submucosal collagen layer (collagenous colitis). Bleeding is less often a feature of Crohn colitis, and endoscopic inflammatory changes are patchy and generally spare the rectum but can extend throughout the entire gastrointestinal tract; histologic features, however, may be indistinguishable from those of ulcerative colitis. Infectious colitis usually presents with more acute symptoms, and chronic changes such as crypt architecture distortion are absent. Ischemic colitis also generally has a more acute course and spares the rectum because of the dual blood supply to this region and is often associated with other evidence of atherosclerotic vascular disease.

Key Point Ulcerative colitis typically involves the rectum and extends proximally with contiguous inflammation that is generally limited to the mucosa of the colon and rectum.

Answers: Q12: E

General gastroenterology

Q1: During your on-call, you are bleeped to see an 80-year-old woman on the ward who has not opened her bowels for the last 4 days. She is not known to have a history of constipation. On examination, her observations are within normal range, the abdomen is soft and there is mild discomfort at the left iliac fossa. Bowel sounds are present and on PR examination, the rectum is empty. You consult your registrar who asks you to prescribe an osmotic laxative. What is the most appropriate treatment?

A. Ispaghula husk
B. Docusate sodium
C. Lactulose
D. Senna
E. Methylcellulose

Explanation: Osmotic laxatives work by retaining fluid within the bowel. Examples include lactulose (C) (a semi-synthetic dissacharide which produces an osmotic diarrhoea), magnesium salts which are used when rapid bowel evacuation is required, sodium salts and phosphate enemas which are also used for rapid bowel evacuation. Senna (D) and docusate sodium (B), along with bisacodyl, are stimulant laxatives which work by increasing intestinal motility. Stimulant laxatives are not indicated in intestinal obstruction and should not be used for a long duration of time as this may give rise to colonic atony and hypokalaemia. Other forms of stimulant laxatives are the rectal stimulants such as glycerin suppositories. Ispaghula husk (A) and methylcellulose (E) are examples of bulking agents which increase faecal mass resulting in an increase in peristalsis. They are usually mixed with water before ingestion and are contraindicated in patients with intestinal obstruction, faecal impaction and swallowing difficulty.

Q2: A 67-year-old man presents feeling unwell and complaining of general malaise. He mentions a long history of alcohol abuse and his past medical history shows deranged liver function tests. Which of the following clinical signs does not form part of chronic liver disease?

A. Finger clubbing
B. Palmer erythema
C. Spider naevia
D. Koilonychia
E. Jaundice

Explanation: Finger clubbing (A), palmer erythema (B), spider naevi (C) and jaundice (E) are all known clinical signs of chronic liver disease. Others include bruising and liver flap (secondary to hepatic encephalopathy). Koilonychia (D) refers to spooning of the nails and occurs in iron deficiency anaemia. It is leuconychia (whitening of the nails due to hypoalbuminaemia which can occur due to chronic liver disease, nephrotic syndrome, malnutrition) that is seen in chronic liver disease.

Q3: During a ward round, you are questioned about tumours that may arise from the liver parenchyma. Which of the following liver tumours is considered to be benign?

A. Angiosarcoma
B. Fibrosarcoma
C. Adenoma
D. Hepatoblastoma
E. Leiyomyosarcoma

Explanation: Benign primary liver tumours include:
- haemangiomas (most common);
- adenomas (C);
- cysts;
- focal nodular hyperplasia;
- fibromas;
- leiyomyomas.

The malignant primary liver tumours include:
- hepatocellular carcinoma (accounts for 90 per cent of primary liver tumours);
- cholangiocarcinoma;
- angiosarcoma (A);
- hepatoblastoma (D);
- fibrosarcoma (B);
- leiyomyosarcoma (E).

Answers: Q1: C | Q2: D | Q3: C

General gastroenterology

Q4: A 55-year-old white woman has had recurrent episodes of alcohol-induced pancreatitis. Despite abstinence, the patient develops postprandial abdominal pain, bloating, weight loss despite good appetite, and bulky, foul-smelling stools. KUB shows pancreatic calcifications. In this patient, you should expect to find which of the following?

A. Diabetes mellitus
B. Malabsorption of fat-soluble vitamins D and K
C. Guaiac-positive stool
D. Courvoisier sign
E. Markedly elevated amylase

Explanation: Chronic pancreatitis is caused by pancreatic damage from repeated attacks of acute pancreatitis. The classic triad is abdominal pain, malabsorption, and diabetes mellitus. Twenty-five percent of cases are idiopathic. Vitamins D and K are absorbed intact from the intestine without digestion by lipase and are therefore absorbed normally in pancreatic insufficiency. Forty percent of patients, however, develop B12 deficiency. Treatment of the malabsorption with pancreatic enzyme replacement will lead to weight gain, but the pain can be difficult to treat. Courvoisier sign is a palpable, nontender gallbladder in a jaundiced patient. This finding suggests the presence of a malignancy, usually pancreatic cancer. Chronic pancreatitis per se does not produce guaiac-positive stools. Amylase is usually normal in patients with chronic pancreatitis

Match the patient described with the most likely diagnosis. Each lettered option may be used once, more than once, or not at all.

Q5: A 45-year-old diabetic woman presents with 2 days of severe upper abdominal pain that radiates into the back and has been associated with nausea and vomiting. She takes insulin but has been noncompliant for several weeks. She denies alcohol consumption. Her serum is lipemic.

Q6: A 78-year-old white man with coronary artery disease presents with several months of postprandial generalized abdominal pain that typically lasts 30 to 60 minutes. He has become fearful of eating and has lost 15 lb of weight.

Q7: A 68-year-old woman who has had a previous hysterectomy presents with an 8-hour history of cramping periumbilical pain. Each episode of pain lasts 3 to 5 minutes and then abates. Over several hours she develops nausea, vomiting, and abdominal distension. She has been unable to pass stool or flatus for the past 4 hours.

A. Acute diverticulitis
B. Acute pancreatitis
C. Acute cholecystitis
D. Intestinal obstruction
E. Irritable bowel syndrome
F. Mesenteric ischemia

Explanation: Pancreatitis typically causes severe abdominal pain that radiates into the back. It is almost always associated with nausea and vomiting. The most common etiology is heavy alcohol use. Other etiologies include gallstones, hyperlipidemia, certain medications (such as azathioprine and hydrochlorothiazide), trauma, and after ERCP. Serum amylase and lipase are typically elevated. Mild elevation of the amylase can also occur in renal failure, appendicitis, and mumps.

Intermittent mesenteric ischemia occurs from atherosclerotic obstruction of visceral arteries. Patients typically present with postprandial abdominal pain and weight loss (“intestinal angina”). Men are more commonly affected than women and usually have atherosclerotic disease elsewhere. Cigarette smoking is a risk factor. Diagnosis is usually made by Doppler ultrasound of the mesenteric vessels and confirmed by CT angiography. Treatment is usually interventional.

Acute intestinal obstruction is most often associated with adhesive bands from previous surgery. Hysterectomy and appendectomy are the most common preceding surgeries, although any operation associated with entry into the peritoneum can cause adhesions. The patient usually has the classic colicky pain associated with several pain-free minutes before the pain again builds up to maximum intensity. This kind of pain is much more commonly associated with intestinal obstruction than biliary or renal disease (so-called biliary and renal colic are often constant pains).

The pain of acute diverticulitis is usually steady and localized to the left lower quadrant. Acute cholecystitis begins with the severe but ill-localized upper abdominal pain of biliary colic; after the gallbladder wall becomes inflamed, the pain moves to the right upper quadrant and becomes more constant. Pain is the most characteristic symptom of irritable bowel syndrome; it is often cramping and ill-localized. Defecation often relieves the pain of IBS.

Answers: Q4: A | Q5: B | Q6: F | Q7: D

General gastroenterology

Match the clinical description with the most likely disease process. Each lettered option may be used once, more than once, or not at all.

Q8: A 40-year-old white woman complains of pruritus. Physical examination reveals xanthelasma and mild splenomegaly. She has an elevated alkaline phosphatase, but her transaminases are normal. The antimitochondrial antibody test is positive.

Q9: A 58-year-old man with long-standing cirrhosis resulting from hepatitis C develops vague right upper quadrant pain and weight loss. A right upper quadrant mass is palpable. Serum alkaline phosphatase is elevated.

A. Primary biliary cirrhosis
B. Sclerosing cholangitis
C. Hepatocellular carcinoma
D. Hepatitis D
E. Hemochromatosis

Explanation: Primary biliary cirrhosis usually occurs in women between the ages of 35 and 60. The earliest symptom is pruritus, often accompanied by fatigue. Serum alkaline phosphatase is elevated two- to fivefold, and a positive anti- mitochondrial antibody test greater than 1:40 is both sensitive and specific.

Hepatocellular carcinoma is more common in men than women and has a peak incidence between 40 and 60 years of age. A major risk factor is cirrhosis. Hepatitis B and hepatitis C are independent risk factors. The typical patient has preexisting cirrhosis and presents with right upper quadrant pain and a palpable mass. Serum alkaline phosphatase and alpha-fetoprotein are elevated. Diagnosis is confirmed by biopsy. Surgical resection offers the only chance for cure, but most patients do not have resectable disease at presentation.

Primary sclerosing cholangitis leads to beaded narrowing of the extra-hepatic (and often intrahepatic) bile ducts; it usually presents with painless jaundice. Hepatitis D causes acute hepatitis (with transaminase elevation) in patients with chronic hepatitis B. Hemochromatosis causes hepatomegaly and mild transaminase elevation; if treatment is not started before cirrhosis occurs, it can lead to hepatocellular carcinoma

Q10: A 55-year-old woman is evaluated in the hospital for a 2-day history of severe epigastric abdominal pain, nausea and vomiting, and anorexia. The patient has no significant medical history, takes no medications, and does not drink alcohol. On physical examination, temperature is 38.0°C (100.4°F), blood pressure is 124/76 mm Hg, pulse rate is 99/min, and respiration rate is 16/min. There is scleral icterus and jaundice. There is mid-epigastric and right upper quadrant tenderness. Abdominal ultrasonography shows a biliary tree with a dilated common bile duct of 12 mm and cholelithiasis but no choledocholithiasis. Which of the following is the most likely diagnosis?

A- Alcoholic pancreatitis
B- Autoimmune pancreatitis
C- Gallstone pancreatitis
D- Hypertriglyceridemic pancreatitis

Aspartate aminotransferase	656 U/L
Alanine aminotransferase	567 U/L
Bilirubin (total)	5.6 mg/dL (95.8 µmol/L)
Amylase	1284 U/L
Lipase	6742 U/L
Triglycerides	250 mg/dL (2.8 mmol/L)

Explanation: The most likely diagnosis is gallstone pancreatitis. This patient has a classic presentation of acute pancreatitis with the acute onset of epigastric abdominal pain, nausea, and vomiting associated with markedly elevated pancreatic enzymes. About 80% of all cases of acute pancreatitis are due to gallstones and alcohol abuse. About 10% of cases are classified as idiopathic; obstruction, drugs, and metabolic, genetic, infectious, and vascular disorders cause the remaining 10% of cases. The presence of stones in the gallbladder, a dilated bile duct, and elevated aminotransferase levels highly suggest gallstones as the cause of pancreatitis. The scleral icterus, jaundice, and elevated bilirubin level suggest continuing bile duct obstruction. Abdominal ultrasonography has a sensitivity of only 50% to 75% for choledocholithiasis, and a common duct stone should be suspected in the correct clinical situation even when ultrasonography does not show a stone. Endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy and stone removal is the most appropriate procedure in patients with acute gallstone pancreatitis. The absence of alcohol consumption excludes alcoholic pancreatitis. Patients whose serum triglyceride level exceeds 1000 mg/dL (11.3 mmol/L) may develop hypertriglyceridemic pancreatitis, but this patient's triglyceride level is only high normal. Autoimmune pancreatitis is a type of chronic pancreatitis. Findings include hypergammaglobulinemia, diffuse pancreatic enlargement, a mass lesion in the pancreas, an irregular main pancreatic duct, and the presence of autoantibodies such as antinuclear antibody. Patients are usually asymptomatic or have only mild symptoms. This patient's acute onset of pain and evidence of gallstone disease is not compatible with the diagnosis of autoimmune pancreatitis.

Key Point The presence of stones in the gallbladder, a dilated bile duct, and elevated aminotransferase levels highly suggest gallstones as the cause of acute pancreatitis.

Answers: Q8: A | Q9: C | Q10: C

General gastroenterology

Match the clinical description with the most likely disease process. Each lettered option may be used once, more than once, or not at all.

Q11: An African American male patient develops mild jaundice while being treated for a urinary tract infection. Urine bilirubin is negative. Serum bilirubin is 3 mg/dL, mostly unconjugated. Hemoglobin is 7 g/dL.

Q12: A 55-year-old obese Hispanic man with a history of hypertension, diabetes, and hypertriglyceridemia reports intermittent mild right upper quadrant discomfort. He has elevated AST and ALT tests two to three times normal. His abdominal ultrasound shows a normal gallbladder without stones and generalized hyperechogenicity of the liver.

Q13: A young woman complains of 1 week of fatigue, change in skin color, and dark brown urine. She has right upper quadrant tenderness and ALT of 1035 U/L (normal < 40).

A. Hemolysis secondary to G6PD deficiency
B. Pancreatic carcinoma
C. Acute viral hepatitis
D. Crigler-Najjar syndrome
E. Nonalcoholic fatty liver disease f. Gilbert syndrome

Explanation: The young African American male patient with mild jaundice has unconjugated hyperbilirubinemia and an anemia. Unconju-gated bilirubin is bound to albumin in the circulation and is not excreted in the urine; hence the urine bilirubin level is negative. His jaundice may be secondary to G6PD deficiency with hemolysis precipitated by an offending antibiotic (sulfonamide or trimethoprim-sulfamethoxazole). These patients are unable to maintain an adequate level of reduced glutathione in their red blood cells when an antibiotic or other toxin causes oxidative stress to the red cells. The 55-year-old Hispanic man has nonalcoholic fatty liver disease (NAFLD). NAFLD is very common and is estimated to affect up to 20% of the U.S. population. The condition is more common in men than women and more common in whites than blacks. The condition is characterized by triglyceride accumulation in the hepatocytes (steatosis). The underlying pathophysiology is closely linked to insulin resistance and hence to obesity, diabetes, hyperlipidemia and the metabolic syndrome. Most cases are discovered incidentally because of elevated transaminases. Patients may have nonspecific right upper quadrant discomfort and hepatomegaly. Abdominal ultrasound shows hyperechogenicity consistent with fatty infiltration. CT scan is also sensitive in diagnosing the condition (90%). Patients with NAFLD are at risk for progression to nonalcoholic steatohepatitis (NASH) that can lead to fibrosis and cirrhosis. The mainstay of treatment for NAFLD is lifestyle modification with increased exercise (hence increased insulin sensitivity) and weight loss. The young woman's case is most consistent with acute hepatitis—strikingly elevated hepatocellular enzymes and conjugated hyperbilirubinemia. Tenderness of the liver on palpation is common in acute hepatitis.

Pancreatic carcinoma causes painless obstructive jaundice with elevated alkaline phosphatase and normal transaminases. Crigler-Najjar and Gilbert syndromes are both caused by abnormalities in glucuronidation of bilirubin. They cause indirect hyperbilirubinemia without evidence of hemolysis or abnormalities of the other liver enzymes.

Q14: A 65-year-old woman is evaluated for a 6-month history of watery, nonbloody diarrhea; she has from 3 to 20 bowel movements a day. She also has abdominal cramps and bloating and has lost 2.2 kg (5 lb) since the beginning of the episode. She had been previously healthy. She has not traveled recently, been hospitalized, or used antibiotics. On physical examination, the vital signs are normal. The heart rate is regular and the chest is clear. The abdomen is soft with slight distention. Colonoscopy is grossly normal. Multiple biopsy specimens are obtained. Which of the following is the most likely diagnosis?

A- Clostridium difficile colitis
B- Crohn disease
C- Microscopic colitis
D- Tropical sprue
E- Ulcerative colitis

Explanation: This patient most likely has microscopic colitis, which is characterized by chronic watery diarrhea without bleeding. There are two types of microscopic colitis: collagenous colitis and lymphocytic colitis. The average age of onset for collagenous colitis is in the sixth decade of life and it tends to affect more women than men. The average age of onset for lymphocytic colitis is in the seventh decade of life, and women seem to be affected slightly more often than men. The cause of microscopic colitis is unknown. One theory is that the use of NSAIDs may contribute to the development of the disorder. Another theory is that it is caused by an autoimmune response. Colonoscopy in affected patients is grossly normal; to make a diagnosis, several biopsies must be taken from the colon. In collagenous colitis, biopsy specimens show more than normal amounts of collagen beneath the lining of the colon. In lymphocytic colitis, the specimen may also show an increased number of lymphocytes. Loperamide, diphenoxylate, and bismuth subsalicylate, either alone or in combination, are effective and well tolerated when used as initial therapy.
Key Point Microscopic colitis is characterized by chronic watery diarrhea without bleeding; the diagnosis must be made by histologic examination of colonoscopic biopsy specimens.

Answers: Q11: A | Q12: E | Q13: C | Q14: C

General gastroenterology

Q15: A 60-year-old woman is evaluated for a 2-week history of jaundice, weight gain, and increassignificant for type 2 diabetes, hyperlipidemia, and obesity. She drinks 2 twelve-ounce bottles of beer per week and has never exceeded this amount. She was an intravenous drug abuser for 10 years beginning at the age of 20 years but has not used any illicit drugs since then. Her medications are metformin, glyburide, pravastatin, and aspirin. On physical examination, vital signs are normal. BMI is 32. She is jaundiced. Spider angiomata are present over the upper chest. Her abdomen is protuberant and nontender with shifting dullness. The liver and spleen are not palpable. The ankles show pitting edema. Which of the following is the most likely cause of the patient's liver disease?

A- Alcohol
B- Chronic hepatitis B infection
C- Chronic hepatitis C infection
D- Nonalcoholic steatohepatitis
E- Primary biliary cirrhosis

Serum aspartate aminotransferase	165 U/L
Serum alanine aminotransferase	160 U/L
Serum alkaline phosphatase	123 U/L
Total bilirubin	5.6 mg/dL (95.8 µmol/L)
Anti-hepatitis C antibody	Negative
Hepatitis B surface antigen	Negative
Antibody to hepatitis B surface antigen	Positive

Explanation: The most likely cause of this patient's liver disease is nonalcoholic steatohepatitis (NASH). Ascites and elevated aminotransferase and bilirubin levels suggest portal hypertension caused by cirrhosis. Nonalcoholic fatty liver disease (NAFLD) consists of variable degrees of fat accumulation, inflammation, and fibrosis in the absence of significant alcohol intake. Fatty liver disease in the absence of inflammation is more common in women than in men and occurs in 60% of obese patients. NASH is a subcategory of NAFLD defined as the presence of inflammation occurring in about 20% of obese patients of which 2% to 3% will develop cirrhosis. NASH is most commonly seen in patients with underlying consequences of obesity, including insulin resistance, hypertension, and hyperlipidemia (metabolic syndrome). NAFLD is usually diagnosed when patients with characteristic clinical risk factors are found to have mildly to moderately elevated serum aminotransferase concentrations. Imaging with ultrasonography, CT, or MRI can confirm the presence of steatosis. Liver biopsy is sometimes necessary to establish the diagnosis of NASH.
Alcohol and chronic hepatitis C infection are the most common causes of cirrhosis in the United States; however, this patient does not have evidence of hepatitis C infection (negative anti-hepatitis C antibody) nor does she consume alcohol in sufficient quantity to cause cirrhosis (6 alcoholic drinks per day for men and 3 alcoholic drinks per day for women for 10 years). Although chronic hepatitis B infection can lead to cirrhosis, this patient's serologies indicate immunity to hepatitis B (negative hepatitis B surface antigen, positive anti-hepatitis B surface antibody), not chronic hepatitis B infection. Although primary biliary cirrhosis is more common in women than men, it is characterized by marked elevations of the alkaline phosphatase (cholestatic liver disease) not seen in this patient.

Key Point Nonalcoholic steatohepatitis (NASH) is associated with obesity, type 2 diabetes, and hyperlipidemia and is a potential cause of cirrhosis.

Answers: Q15: D