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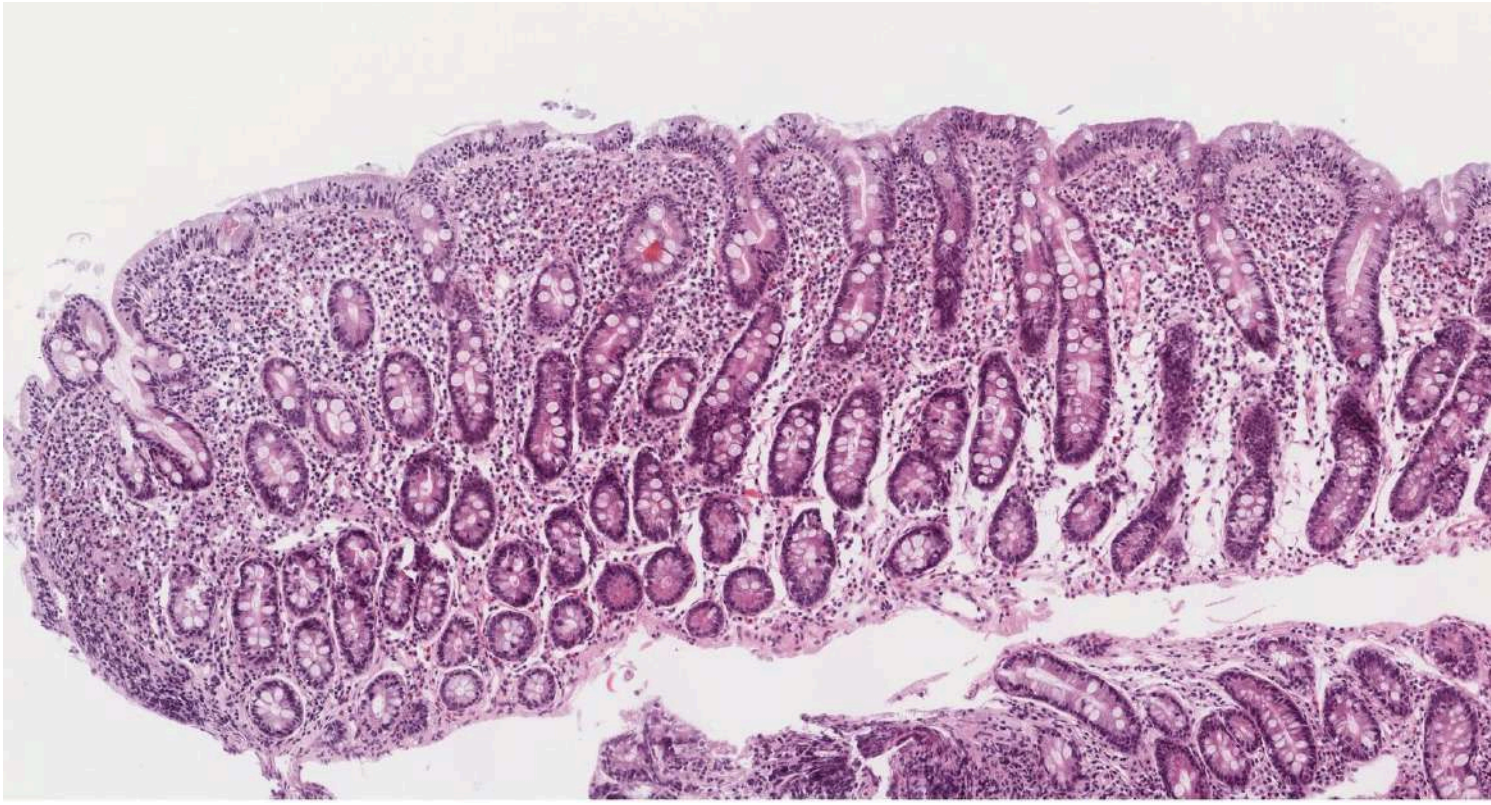
Question # 1

A 34-year-old man comes to the physician because of foul-smelling diarrhea, fatigue, and bloating for 6 months. During this time, he has had a 5-kg (11-lb) weight loss without a change in diet. He has type 1 diabetes mellitus that is well-controlled with insulin. Examination shows conjunctival pallor and inflammation of the corners of the mouth. The abdomen is soft, and there is diffuse tenderness to palpation with no guarding or rebound. His hemoglobin concentration is 10.4 g/dL. The patient undergoes upper endoscopy. A photomicrograph of tissue from an intestinal biopsy is shown. Which of the following is most likely to improve this patient's symptoms?



	Answer	Image
A	Treatment with ceftriaxone	
B	Administration of infliximab	

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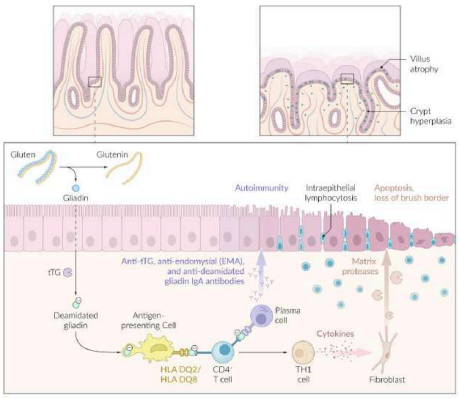
	Answer	Image
C	Avoidance of certain types of cereal grains	
D	Surgical resection of the colon	
E	Reduced intake of milk proteins	
F	Supplemention of pancreatic enzymes	

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Hint

This patient's duodenal biopsy shows villous flattening, elongated and hyperplastic crypts of Lieberkuhn, and lymphocytic infiltration of the lamina propria.

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Correct Answer

A - Treatment with ceftriaxone

Explanation Why

Foul-smelling diarrhea, fatigue, bloating, unintentional weight loss, abdominal tenderness, and signs of iron deficiency anemia (low hemoglobin, conjunctival pallor, angular cheilitis) might raise concern for Whipple disease, which is treated with ceftriaxone. Although duodenal biopsy in Whipple disease may reveal blunting of the villi, it would also show foamy PAS-positive macrophages in the lamina propria rather than the lymphocytic infiltration seen in this patient. Moreover, Whipple disease is also associated with cardiac symptoms (e.g., valve insufficiencies), arthralgias, and neurological findings (e.g., myoclonia, ataxia, oculomotor impairment), none of which are seen in this patient.

B - Administration of infliximab

Explanation Why

Foul-smelling diarrhea, fatigue, bloating, unintentional weight loss, abdominal tenderness, and signs of iron and/or vitamin B_{12} deficiency (low hemoglobin, conjunctival pallor, angular cheilitis) might raise concern for Crohn disease (CD), which can be treated with infliximab. However, CD is not associated with villous atrophy or crypt hyperplasia on intestinal biopsy. Instead, histologic findings of CD include noncaseating granulomas, giant cells, neutrophilic inflammation of the crypts, and distinct lymphoid aggregates within the lamina propria.

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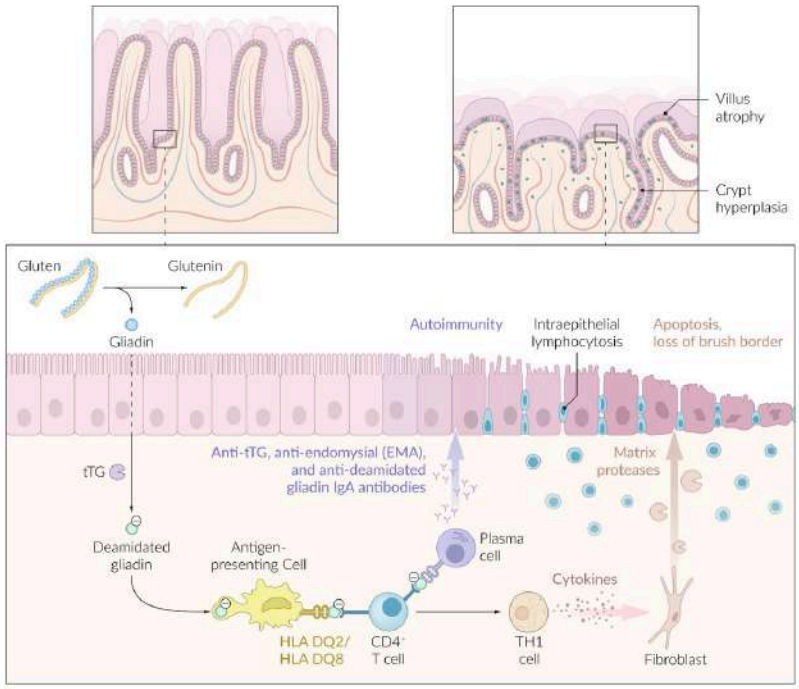
C - Avoidance of certain types of cereal grains

Image



Explanation But

Celiac disease most frequently affects the duodenum (major site of iron absorption) and typically manifests with iron deficiency, as seen in this patient. Whipple disease commonly affects the duodenum and jejunum (major site of folate absorption) and can manifest with iron and folate deficiency. While Crohn disease can affect any part of the gut, it most frequently affects the ileum (major site of vitamin B_{12} absorption) and may therefore manifest with vitamin B12 deficiency.

Explanation Why

Foul-smelling diarrhea, fatigue, bloating, unintentional weight loss, abdominal tenderness, and signs of iron deficiency anemia (low hemoglobin, conjunctival pallor, angular cheilitis) should raise suspicion for celiac disease, for which type 1 diabetes mellitus is a risk factor. The diagnosis is confirmed by the presence of characteristic histology findings together with positive celiac serology. While the disease can occur at any age, the age of onset follows a bimodal distribution; it most often affects infants and adults in the 3rd and 4th decade of life. Treatment consists of a lifelong gluten-free diet, including avoidance of certain types of cereal grains such as wheat, rye, barley, and spelt.

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D - Surgical resection of the colon

Explanation Why

Diarrhea, fatigue, bloating, unintentional weight loss, abdominal tenderness, and signs of iron deficiency anemia (low hemoglobin, conjunctival pallor, angular cheilitis) might raise concern for ulcerative colitis (UC), which can be cured with surgical resection of the affected part of the colon. However, UC typically manifests with bloody diarrhea and only affects the colon, never the small intestine. Colonic biopsy in UC would show mucosal and submucosal inflammation and neutrophilic inflammation of the crypts.

E - Reduced intake of milk proteins

Explanation Why

Foul-smelling diarrhea, bloating, unintentional weight loss, and abdominal tenderness may be consistent with lactose intolerance, which is managed by avoiding or reducing the intake of lactose-containing milk products. However, lactose intolerance is not typically associated with signs of iron deficiency anemia (conjunctival pallor, low hemoglobin, angular cheilitis), which are seen in this patient. Furthermore, intestinal biopsy in lactose intolerance would show normal intestinal architecture, rather than the pathological findings seen in this patient's biopsy.

F - Supplemention of pancreatic enzymes

Explanation Why

Foul-smelling diarrhea, fatigue, bloating, unintentional weight loss, and signs of vitamin B_{12} deficiency (low hemoglobin, conjunctival pallor) might raise concern for exocrine pancreatic insufficiency, which is treated with pancreatic enzyme supplementation. However, in exocrine pancreatic insufficiency, an intestinal biopsy would be normal, with preserved villous architecture.

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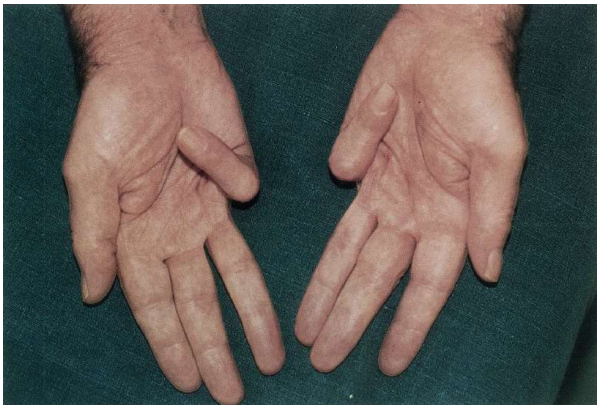
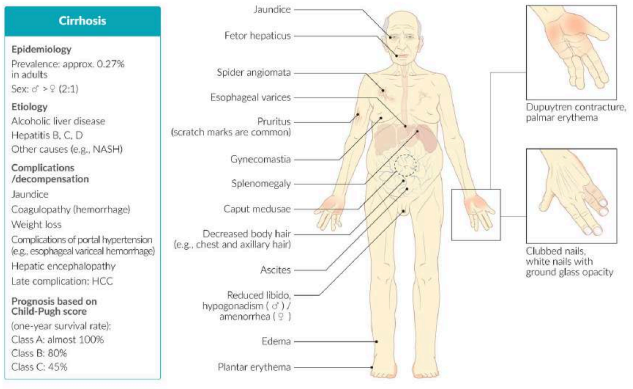
Question # 2

A 59-year-old man with a history of alcoholic cirrhosis is brought to the physician by his wife for a 1-week history of progressive abdominal distension and yellowing of the eyes. For the past month, he has been irritable, had difficulty falling asleep, become clumsy, and fallen frequently. Two months ago he underwent banding for esophageal varices after an episode of vomiting blood. His vital signs are within normal limits. Physical examination shows jaundice, multiple bruises, pedal edema, gynecomastia, loss of pubic hair, and small, firm testes. There are multiple small vascular lesions on his chest and neck that blanch with pressure. His hands are erythematous and warm; there is a flexion contracture of his left 4^{th} finger. A flapping tremor is seen on extending the forearms and wrist. Abdominal examination shows dilated veins over the anterior abdominal wall, the spleen tip is palpated 4 cm below the left costal margin, and there is shifting dullness on percussion. Which of the following pairs of physical examination findings are caused by the same underlying pathophysiology?

	Answer	Image
A	Splenomegaly and Dupuytren contracture	
B	Jaundice and flapping tremor	
C	Palmar erythema and gynecomastia	

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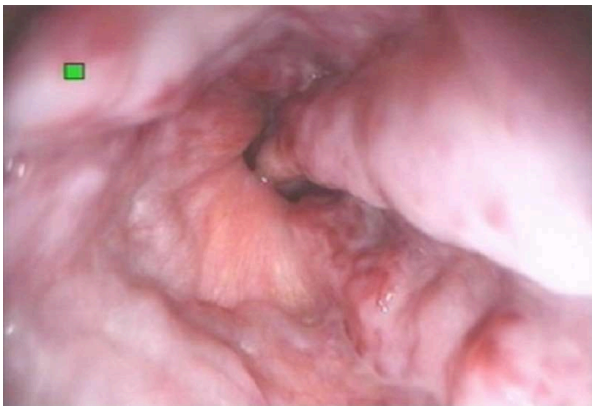
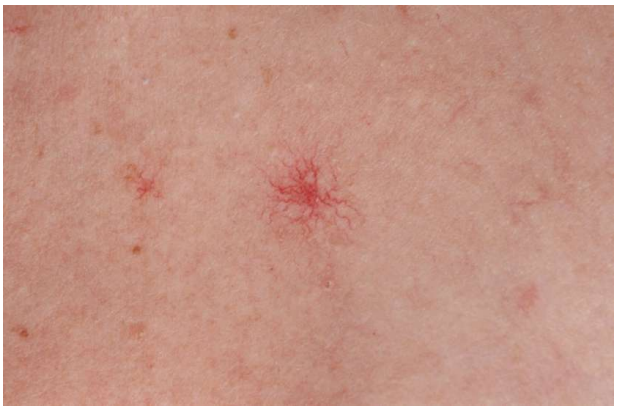
	Answer	Image
D	Esophageal varices and pedal edema	
E	Caput medusae and spider angiomata	
F	Testicular atrophy and abdominal distension	
G	Multiple bruises and loss of pubic hair	

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Hint

Most clinical features of cirrhosis are either due to the failure of the liver to perform its normal functions (e.g., altered bilirubin and sex hormone metabolism, decreased synthesis of proteins, inadequate elimination of nitrogenous waste products) or related to increased pressure within the portal venous system.

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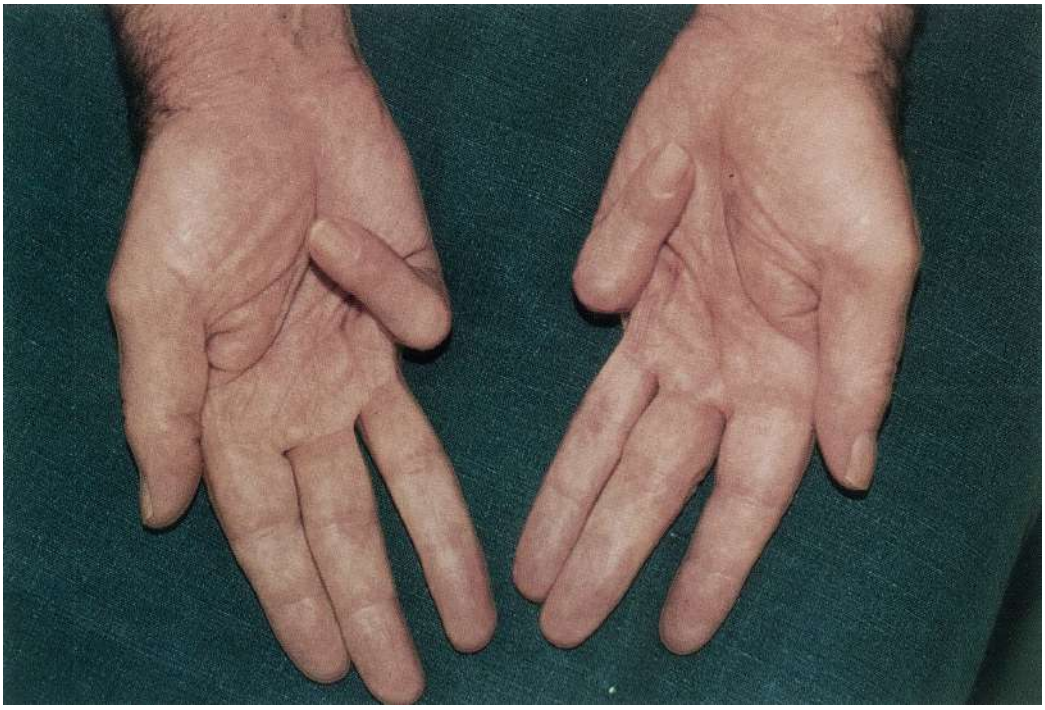
Correct Answer

A - Splenomegaly and Dupuytren contracture

Image



Explanation Why

Although splenomegaly and Dupuytren contracture are both associated with cirrhosis, they have different underlying pathophysiologies. Splenomegaly in cirrhosis is caused by increased pressure within the splenic vein due to portal hypertension. Even though the reason for the thickening of the palmar fascia seen in Dupuytren contracture is still incompletely understood, it is unlikely that portal hypertension would directly cause fibroblastic proliferation and disorderly collagen deposition associated with the contracture.

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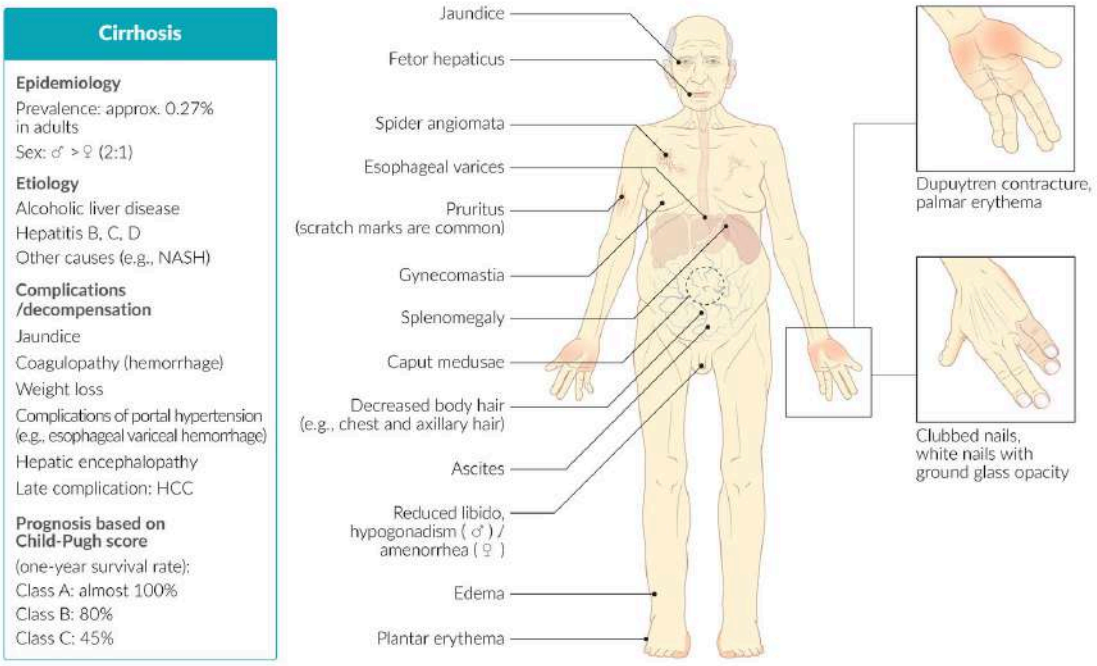
B - Jaundice and flapping tremor

Explanation Why

Although jaundice and flapping tremor are both associated with cirrhosis, they have different underlying pathophysiologies. Jaundice results from the inability of the liver to conjugate bilirubin, which leads to unconjugated hyperbilirubinemia. Flapping tremor is seen in patients with hepatic encephalopathy, in which neurotoxic metabolites like ammonia accumulate in the central nervous system due to impaired hepatic excretion. Consequently, neurotransmission of joint position sense to the brain is impaired.

C - Palmar erythema and gynecomastia

Image



Explanation Why

Palmar erythema and gynecomastia are both features of hyperestrogenism. Cirrhosis can result in a

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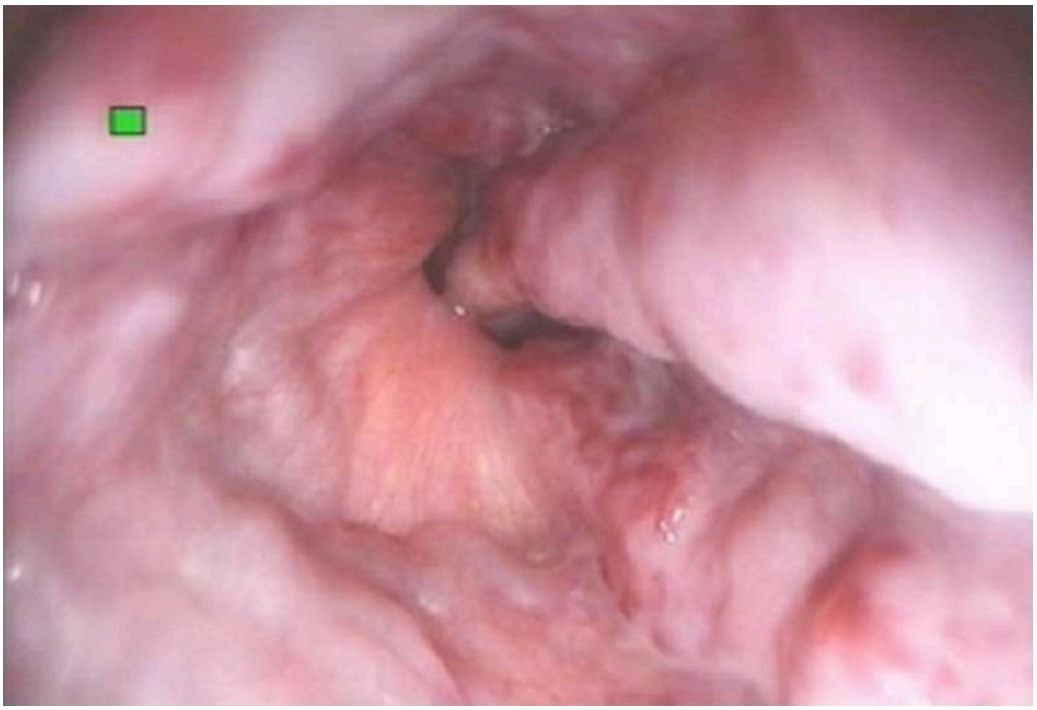
hyperestrogenic state in which there is an increased estrogen/androgen ratio. This is likely due to increased peripheral conversion of androgens to estrogens and decreased hepatic breakdown of estrogen in men with cirrhosis, as well as increased binding and thus inactivation of free testosterone caused by increased amounts of sex-hormone-binding globulin. Other features of hyperestrogenism seen in this patient are spider angiomata and loss of pubic hair.

D - Esophageal varices and pedal edema

Image



Explanation Why

Although esophageal varices and pedal edemas are both associated with cirrhosis, they have different underlying pathophysiologies. Esophageal varices in patients with cirrhosis occur due to portal hypertension because they are a site of portosystemic shunting of blood. Pedal edema can occur as a result of decreased hepatic synthesis of albumin, which decreases the plasma oncotic pressure, causing fluid to shift from the intravascular compartment into the peripheral tissues.

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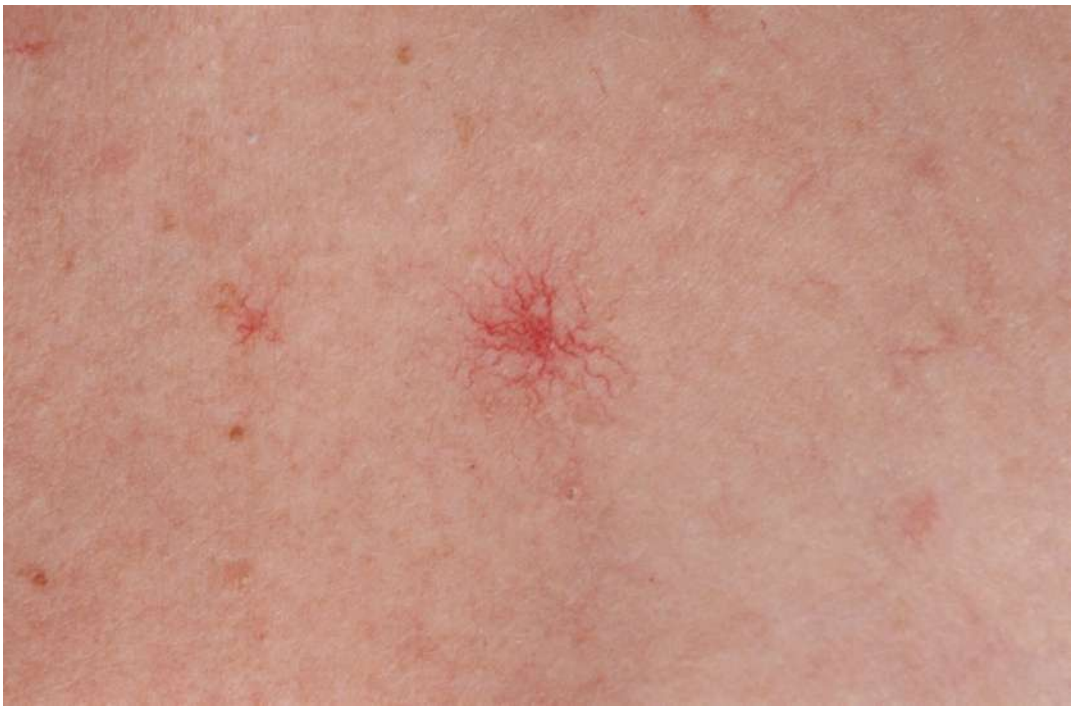
E - Caput medusae and spider angiomata

Image



Explanation Why

Although both caput medusae and spider angiomata are caused by an abnormal dilation of blood vessels and are both associated with cirrhosis, they have different underlying pathophysiologies. Spider angiomata are thought to be caused by hyperestrogenism resulting from an increase in the estradiol/free testosterone ratio. Caput medusae, on the other hand, is a pathognomonic sign of portal hypertension that is caused by portosystemic shunting of blood between the portal paraumbilical veins and the systemic superficial epigastric veins due to increased resistance to portal venous flow in liver cirrhosis.

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F - Testicular atrophy and abdominal distension

Explanation Why

Although testicular atrophy and abdominal distension are both associated with cirrhosis, they have different underlying pathophysiologies. Hypogonadism in cirrhosis, manifesting as testicular atrophy, is thought to be due to multiple factors, including primary gonadal injury, suppression of hypothalamic or pituitary function, as well as binding and inactivation of free testosterone caused by increased amounts of sex-hormone-binding globulin. Abdominal distension, on the other hand, is caused by ascites, a complication of both portal hypertension and decreased hepatic albumin synthesis.

G - Multiple bruises and loss of pubic hair

Explanation Why

Although easy bruising and loss of pubic hair are both associated with cirrhosis, they have different underlying pathophysiologies. In cirrhosis, the hepatic production of coagulation factors is impaired, which can lead to coagulopathy and, consequently, easy bruising. The loss of pubic hair in chronic liver disease, however, is caused by hyperestrogenism resulting from an increase in the estradiol/free testosterone ratio.

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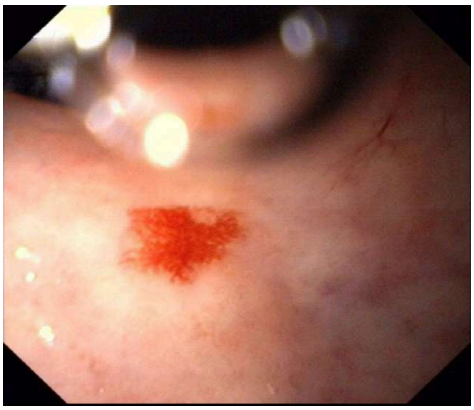
Question # 3

A 79-year-old man with aortic stenosis comes to the emergency room because of worsening fatigue for 5 months. During this time, he has also had intermittent bright red blood mixed in with his stool. He has not had any abdominal pain or weight loss. Physical examination shows pale conjunctivae and a crescendo-decrescendo systolic murmur best heard at the second right intercostal space. The abdomen is soft and non-tender. Laboratory studies show a hemoglobin of 8 g/dL and a mean corpuscular volume of 71 μm^3. Colonoscopy shows no abnormalities. Which of the following is the most likely underlying mechanism of this patient's bleeding?

	Answer	Image
A	Thrombus in the superior mesenteric artery	
B	Transmural inflammation of the large bowel	
C	Atherosclerotic narrowing of the mesenteric arteries	
D	Tortuous submucosal blood vessels	
E	Inherited factor VIII deficiency	

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Hint

This patient has evidence of a chronic, episodic lower GI bleed without mass or diverticula on colonoscopy. His murmur is consistent with aortic stenosis, which is commonly associated with the condition causing his GI bleeding.

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Correct Answer

A - Thrombus in the superior mesenteric artery

Explanation Why

Acute mesenteric ischemia is caused by acute thromboembolism in the mesenteric arteries and typically presents with acute, severe abdominal pain followed by “currant jelly” bloody stools, due to bowel necrosis. This patient's history of intermittent blood in the stool and lack of abdominal pain make this diagnosis an unlikely cause of his gastrointestinal bleeding.

B - Transmural inflammation of the large bowel

Explanation Why

Transmural inflammation of the large bowel is characteristic of Crohn disease. Although Crohn disease can present with anemia, it does not usually cause GI bleeding. Also, the absence of typical features (e.g., chronic diarrhea, abdominal pain, and weight loss) and characteristic findings on colonoscopy (e.g., skipped linear ulcers, aphthous hemorrhagic mucosa, cobblestone appearance of mucosa) make Crohn disease an unlikely diagnosis in this patient.

C - Atherosclerotic narrowing of the mesenteric arteries

Explanation Why

Atherosclerotic narrowing of the mesenteric arteries is seen in chronic mesenteric ischemia. Although this condition also commonly occurs in elderly patients (> 60 years), it is characterized by postprandial pain (abdominal angina) and weight loss, which this patient does not have. In addition, chronic mesenteric ischemia does not typically cause hematochezia, as seen here.

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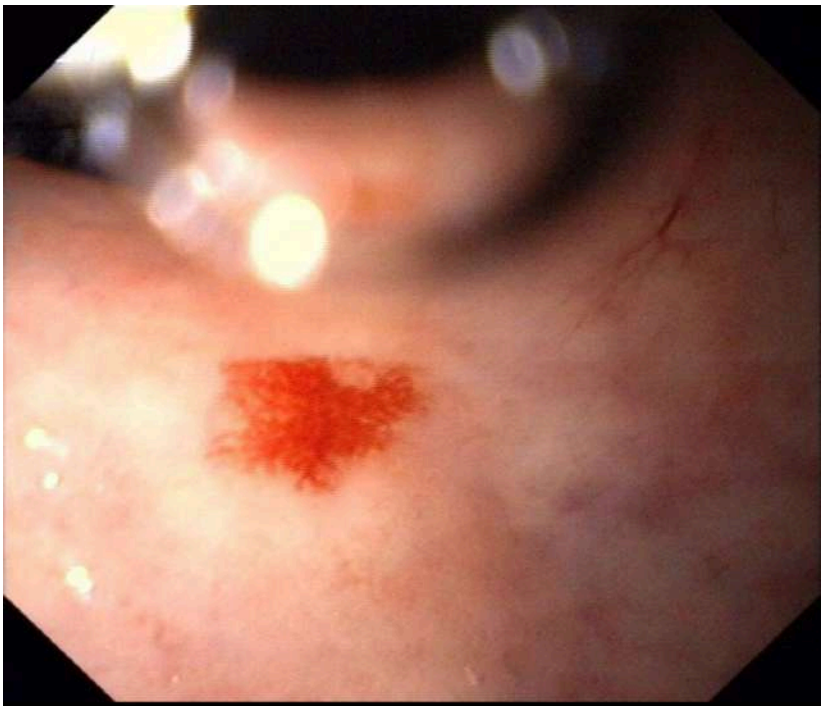
D - Tortuous submucosal blood vessels

Image



Explanation But

Most patients with aortic stenosis who experience bleeding from angiodysplasia have complete resolution of GI bleeding after aortic valve replacement.

Explanation Why

Tortuous and dilated submucosal blood vessels are characteristic of angiodysplasia, which is associated with aortic stenosis (as seen in this patient). The dysplastic vessels seen in angiodysplasia are typically located in the cecum and ascending colon (in > 75% of cases) and classically cause episodic and self-limiting bleeding. Colonoscopic visualization is challenging and definitive diagnosis usually requires angiography. Other conditions associated with angiodysplasia include von Willebrand disease and end-stage renal disease.

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E - Inherited factor VIII deficiency

Explanation Why

Inherited deficiency of factor VIII is characteristic of hemophilia A. Although hemophilia can also cause gastrointestinal bleeding, it is an unlikely etiology in this patient who lacks typical symptoms (e.g., recurrent spontaneous or prolonged episodes of epistaxis and hemarthrosis beginning early in life).

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Question # 4

A 35-year-old woman with irritable bowel syndrome comes to the physician because of increased diarrhea. She has not had any fever, bloody stools, nausea, or vomiting. The increase in stool frequency began when she started a new job. She is started on loperamide, and her symptoms improve. Which of the following is the primary mechanism of action of this drug?

	Answer	Image
A	μ-opioid receptor agonism	
B	5-HT3 receptor antagonism	
C	Acetylcholine receptor antagonism	
D	Physical protection of stomach mucosa	
E	D2 receptor antagonism	
F	H2 receptor antagonism	

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Hint

Loperamide is in the same drug class as diphenoxylate, fentanyl, and dextromethorphan.

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Correct Answer

A - μ-opioid receptor agonism

Explanation Why

Loperamide is an antidiarrheal drug that acts directly on μ-opioid receptors in the GI tract to inhibit propulsive peristalsis and intestinal fluid secretion, and increase anal sphincter tone. Unlike other μ-opioid receptor agonists, loperamide has poor CNS penetration and therefore lacks analgesic properties.

B - 5-HT3 receptor antagonism

Explanation Why

Ondansetron is an antiemetic that blocks serotonin both centrally and peripherally via 5-HT3 receptor antagonism. It is not used to treat diarrhea. Loperamide does not act on 5-HT3 receptors.

C - Acetylcholine receptor antagonism

Explanation Why

Antimuscarinic agents, such as dicyclomine, act on acetylcholine receptors of smooth muscle cells to decrease gastrointestinal spasticity and motility. Although dicyclomine can be used to treat some symptoms of irritable bowel syndrome (e.g., cramping), it is not effective against diarrhea. Loperamide does not act on acetylcholine receptors.

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D - Physical protection of stomach mucosa

Explanation Why

Bismuth subsalicylate protects the GI mucosa via antisecretory, antimicrobial, and anti-inflammatory mechanisms. It can be useful in treating diarrhea, particularly from enterotoxigenic Escherichia coli, but is not commonly used for IBS. Loperamide does not act via this mechanism.

E - D2 receptor antagonism

Explanation Why

Metoclopramide is an antiemetic and prokinetic agent that acts via serotonin receptor antagonism and dopamine receptor antagonism. It functions primarily by blocking D2 receptors in the CNS but also blocks 5-HT3 receptors at higher doses. Metoclopramide increases motility in the GI tract and decreases anal sphincter tone; therefore, diarrhea is a side effect and not an indication for the drug. Loperamide does not act on dopamine receptors.

F - H2 receptor antagonism

Explanation Why

H2 antihistamines (e.g., famotidine, ranitidine) act at gastric parietal cells to inhibit acid secretion. They are used to treat conditions such as GERD and PUD but are not used to treat diarrhea. Loperamide does not act on H2 receptors.

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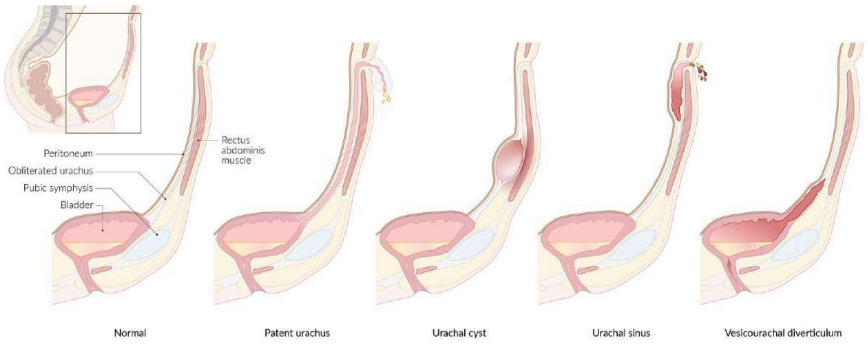
Question # 5

A new imaging modality is being tested to study vitelline duct morphology. A fetus at 20 weeks' gestation is found to have partial obliteration of this duct. Which of the following is the most likely sequela of this condition?

	Answer	Image
A	Protrusion of abdominal viscera into the umbilical cord	
B	Swelling in the genital region	
C	Discharge of meconium from the umbilicus	
D	Dilation of the descending colon	
E	Discharge of urine from the umbilicus	

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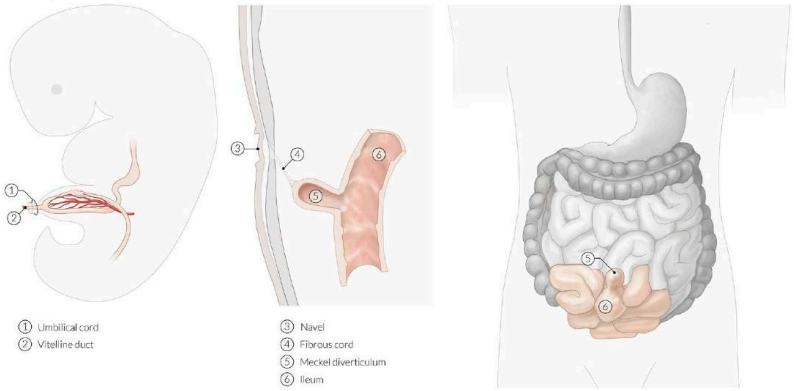
	Answer	Image
F	Bleeding from the gastrointestinal tract	

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Hint

During normal embryonic development, the vitelline duct obliterates completely by the 6^{th} to 7^{th} week of gestation. Incomplete obliteration of the vitelline duct results in a Meckel diverticulum, the most common congenital gastrointestinal tract anomaly.

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Correct Answer

A - Protrusion of abdominal viscera into the umbilical cord

Explanation Why

Protrusion of abdominal viscera into the umbilical cord is characteristic of an omphalocele, which results from failure of the midgut to retract into the abdominal cavity during the 10^{th} week of gestation. Incomplete obliteration of the vitelline duct does not result in herniated loops of bowel.

B - Swelling in the genital region

Explanation Why

Swelling in the genital region is characteristic of a communicating hydrocele, which is caused by a failure of obliteration of the processus vaginalis, not the vitelline duct.

C - Discharge of meconium from the umbilicus

Explanation Why

Discharge of meconium from the umbilicus is a sequela of a vitelline fistula, which occurs if the vitelline duct remains patent. This fetus at 20 weeks' gestation has a partially obliterated vitelline duct.

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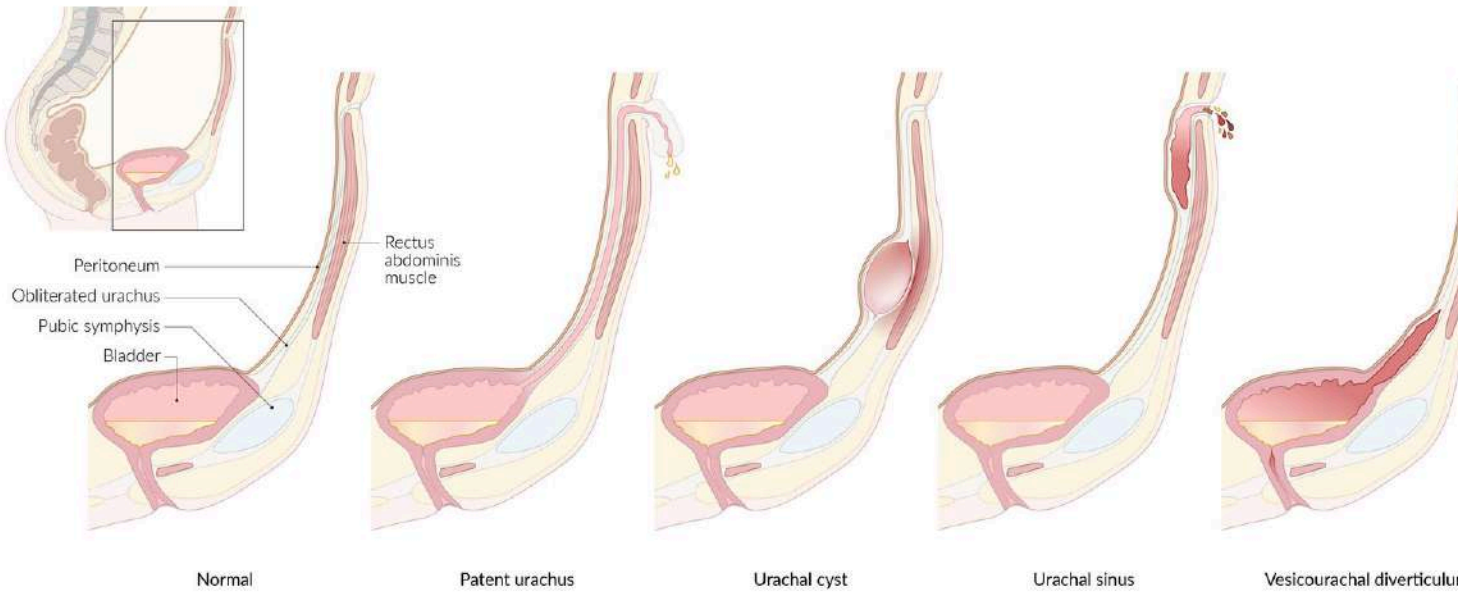
D - Dilation of the descending colon

Explanation Why

This fetus will develop a Meckel diverticulum, which can cause bowel obstruction as as a result of intussusception, volvulus, or a fecolith within the diverticulum. However, the most common location of Meckel diverticulum is the terminal lieum. Therefore, the proximal small bowel is typically dilated and the distal descending colon will be collapsed. Dilation of the descending colon is instead associated with Hirschsprung disease and anal atresia.

E - Discharge of urine from the umbilicus

Image



Explanation Why

Discharge of urine from the umbilicus is caused by a urachal fistula, which results from a failure of the urachus to obliterate, not the vitelline duct.

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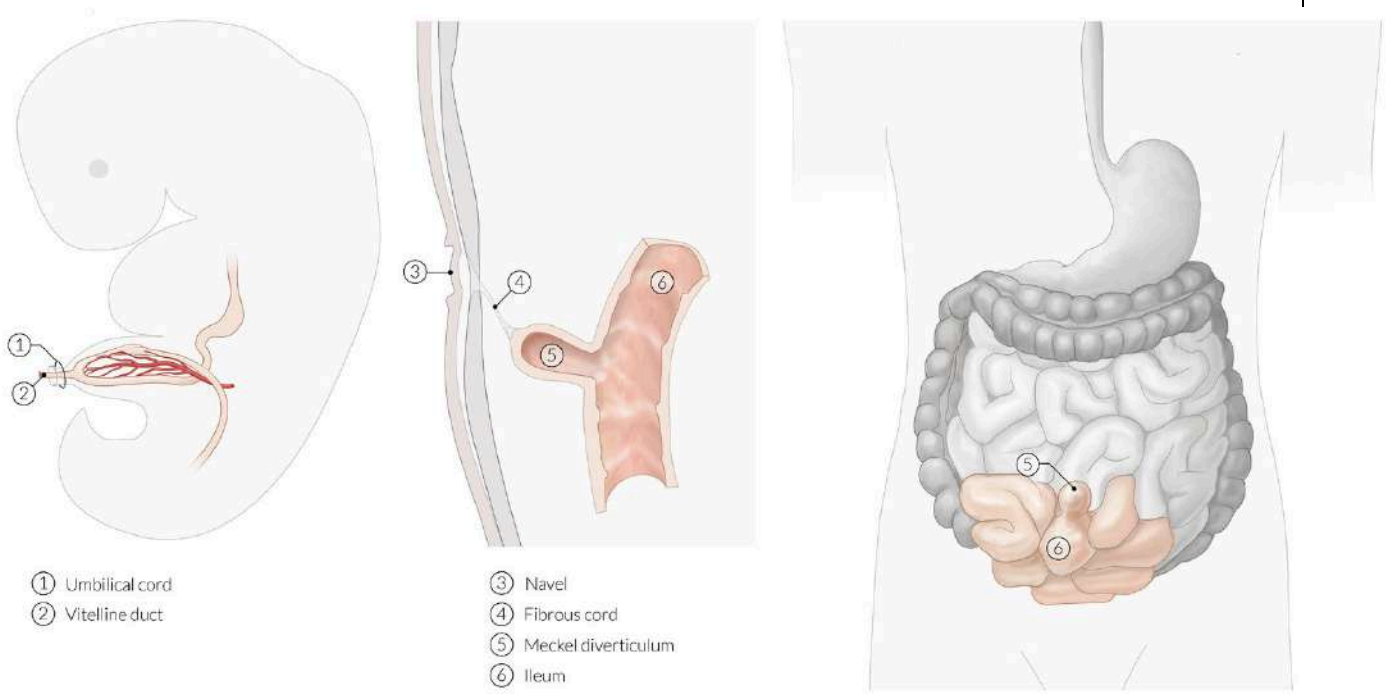
F - Bleeding from the gastrointestinal tract

Image



Explanation But

The rule of 2s in Meckel diverticulum: 2% of the population, 2 inches (5 cm) long, 2 feet (60 cm) from the ileocaecal valve, 2/3rd with ectopic mucosa, 2 types of ectopic tissue (gastric and pancreatic).

Explanation Why

Patients with Meckel diverticulum are usually asymptomatic. However, some patients can develop lower GI bleeding as a result of diverticulitis and/or intussusception (the diverticulum acts as a lead point for intussusception). In some patients, the diverticulum contains ectopic gastric tissue, which can also cause lower GI bleeding as a result of gastric acid induced ulceration of the ileal mucosa.

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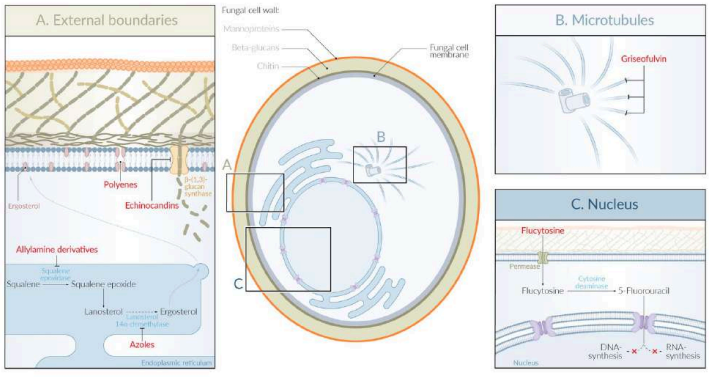
Question # 6

A 28-year-old woman with HIV comes to the physician because of an 8-day history of severe pain while swallowing. She has been hospitalized several times with opportunistic infections and has poor adherence to her antiretroviral drug regimen. Endoscopy shows extensive, white, plaque-like lesions in the proximal esophagus. Culture of a biopsy specimen grows *Candida albicans*. Treatment with intravenous anidulafungin is initiated. Which of the following is the primary mechanism of action of this drug?

	Answer	Image
A	Decreased DNA synthesis	
B	Inhibition of alpha-demethylase	
C	Binding to ergosterol	
D	Binding to tubulin	
E	Decreased glucan synthesis	
F	Inhibition of squalene epoxidase	

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Hint

Other drugs with a similar mechanism of action are caspofungin and micafungin.

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Correct Answer

A - Decreased DNA synthesis

Explanation Why

Decreased DNA synthesis is the mechanism of action of the antimetabolite antifungal drug flucytosine. Flucytosine can be used for systemic fungal infections when combined with amphotericin B, and is particularly useful for the treatment of cryptococcal meningitis. It is ineffective in the treatment of esophageal candidiasis.

B - Inhibition of alpha-demethylase

Explanation Why

Inhibition of 14-alpha-demethylase is the mechanism of action of the azole class (e.g., miconazole, voriconazole, and itraconazole) of antifungal drugs. The azole antifungal class has a wide spectrum of clinical use and are also considered first-line treatment for esophageal candidiasis. The medication administered to this patient has a different mechanism of action.

C - Binding to ergosterol

Explanation Why

Binding to ergosterol is the mechanism of action of the polyene class of antifungal drugs, which includes amphotericin B and nystatin. They have a very broad spectrum of efficacy but are not the first-line treatment for candida esophagitis.

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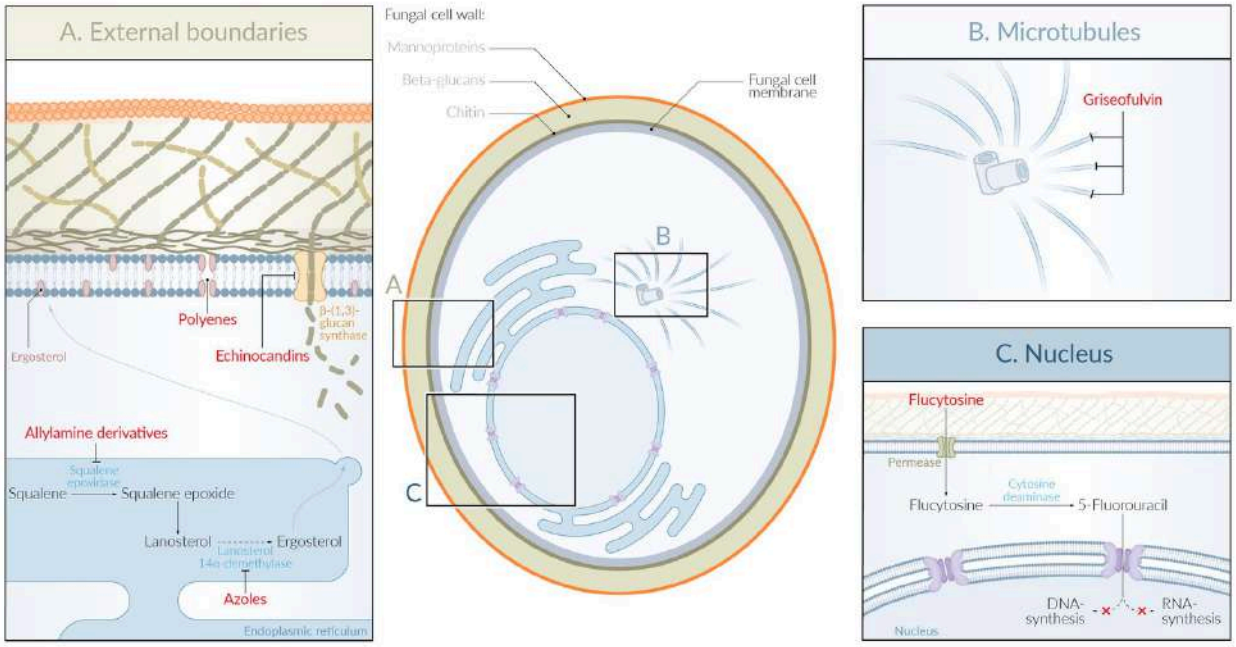
D - Binding to tubulin

Explanation Why

Binding to tubulin is the mechanism of action of griseofulvin, which is used to treat a variety of superficial fungal infections (e.g., tinea). It does not play a role in the treatment of esophageal candidiasis.

E - Decreased glucan synthesis

Image



Explanation Why

Echinocandin antifungal drugs (e.g., anidulafungin, caspofungin) block the synthesis of β-(1,3)-D-glucan, a component of the fungal cell wall. Echinocandin antifungals have a broad spectrum efficacy with minimal CSF penetration, and are used for management of both invasive aspergillosis and invasive candidiasis.

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F - Inhibition of squalene epoxidase

Explanation Why

Inhibition of squalene epoxidase is the mechanism of action of terbinafine. It is used as a treatment for dermatophyte skin infections (e.g., tinea, onychomycosis). Terbinafine has no role in the treatment of esophageal candidiasis.

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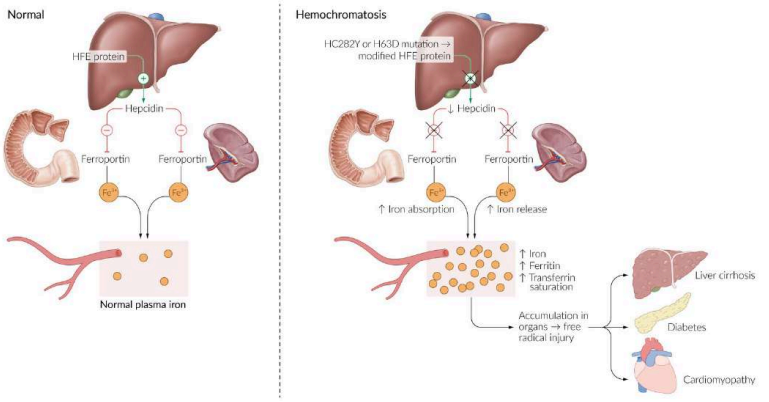
Question # 7

A 49-year-old man comes to the physician because of a 6-month history of increasing fatigue and reduced libido. He also complains of joint pain in both of his hands. His vital signs are within normal limits. Physical examination shows tanned skin and small testes. The second and third metacarpophalangeal joints of both hands are tender to palpation and range of motion is limited. The liver is palpated 2 to 3 cm below the right costal margin. Histopathologic examination of a liver biopsy specimen shows intracellular material that stains with Prussian blue. This patient is at greatest risk for developing which of the following complications?

	Answer	Image
A	Colorectal carcinoma	
B	Restrictive cardiomyopathy	
C	Rheumatoid arthritis	
D	Pancreatic adenocarcinoma	
E	Non-Hodgkin lymphoma	

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Hint

Skin hyperpigmentation, testicular atrophy, hepatomegaly, and siderosis with Prussian blue staining are all suggestive of hemochromatosis.

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Correct Answer

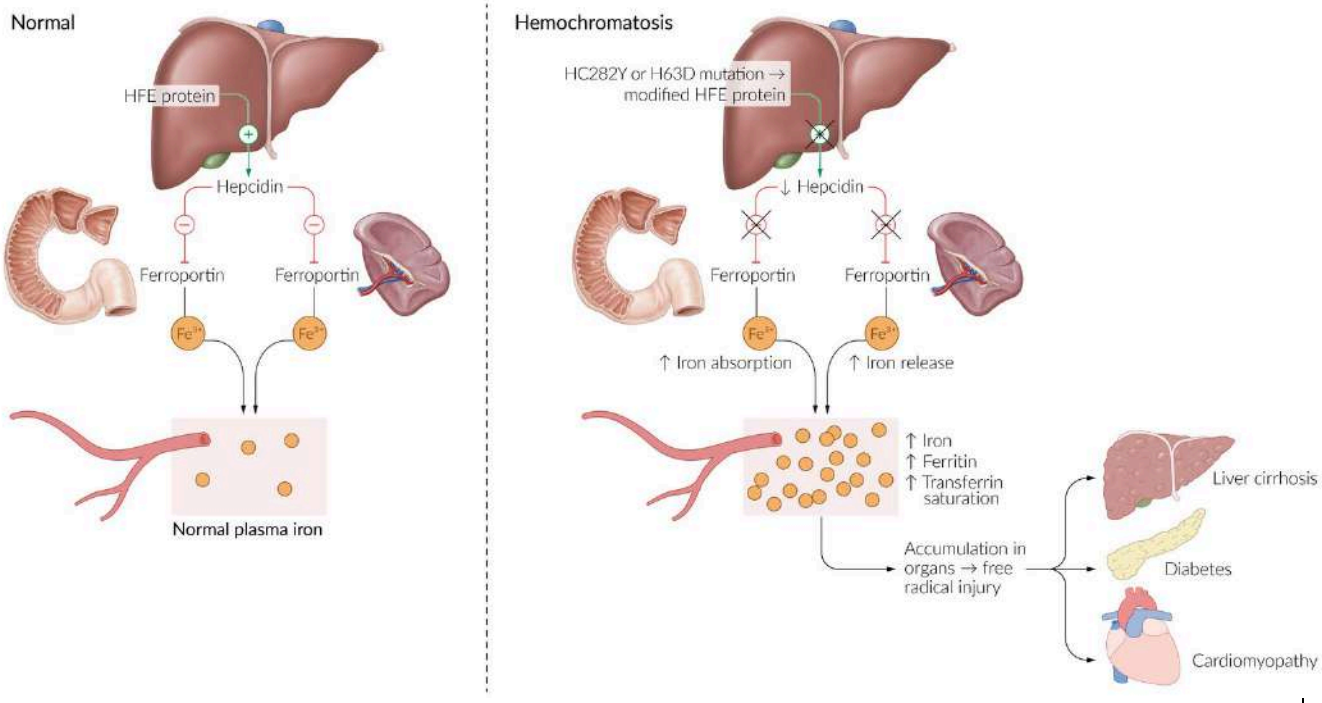
A - Colorectal carcinoma

Explanation Why

Many risk factors exist for colorectal carcinoma, including genetic syndromes (such as familial adenomatous polyposis and HNPCC), inflammatory bowel disease, tobacco use, and a low-fiber diet. Although some studies suggest an increased risk of colorectal cancer in patients with hemochromatosis, this association is not well established and other complications are more likely to occur.

B - Restrictive cardiomyopathy

Image



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Explanation But

Patients with hemochromatosis are also at a significantly higher risk of developing hepatocellular carcinoma (HCC) when compared to the general population. HCC is the most common cause of death in patients with hemochromatosis.

Explanation Why

In patients with untreated or advanced hemochromatosis, the deposition of iron in cardiac tissues and subsequent fibrosis can lead to either a restrictive cardiomyopathy (more typical) or dilated cardiomyopathy (less common, but often reversible).

C - Rheumatoid arthritis

Explanation Why

Known risk factors for rheumatoid arthritis include being female, genetic predisposition (HLA-DR4 has been implicated), and smoking. Hemochromatosis is not a risk factor for rheumatoid arthritis, but is associated with the development of calcium pyrophosphate deposition disease and irreversible arthropathy, especially affecting the MCP joints (as seen in this patient).

D - Pancreatic adenocarcinoma

Explanation Why

Risk factors for pancreatic adenocarcinoma include certain genetic syndromes (e.g., Peutz-Jeghers syndrome), tobacco use, chronic pancreatitis, and diabetes. There is no known link between hemochromatosis and pancreatic cancer.

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E - Non-Hodgkin lymphoma

Explanation Why

Risk factors for NHL include infections (e.g., EBV, HCV, *Helicobacter pylori*), autoimmune diseases (e.g., Hashimoto thyroiditis), and dermatomyositis. There is no known association between hemochromatosis and the development of NHL.

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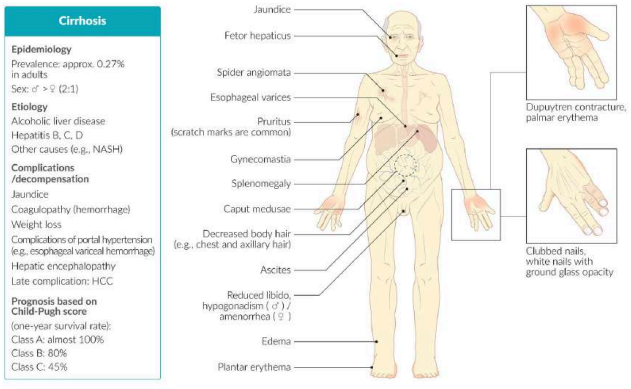
Question # 8

A 47-year-old man with alcoholic cirrhosis comes to the physician for a follow-up examination. Examination of the skin shows erythema over the thenar and hypothenar eminences of both hands. He also has numerous blanching lesions over the trunk and upper extremities that have a central red vessel with thin extensions radiating outwards. Which of the following is the most likely underlying cause of these findings?

	Answer	Image
A	Increased circulating ammonia	
B	Decreased circulating albumin	
C	Decreased circulating thrombopoietin	
D	Decreased circulating testosterone	
E	Increased circulating cortisol	
F	Increased circulating estrogen	

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Hint

This patient's skin findings are consistent with palmar erythema and spider angiomas, which are related to his cirrhosis.

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Correct Answer

A - Increased circulating ammonia

Explanation Why

Hepatic failure from cirrhosis results in inadequate elimination of metabolic products with subsequent accumulation of neurotoxic metabolites (e.g., ammonia). Elevated serum ammonia levels contribute to the development of hepatic encephalopathy. Elevated ammonia levels do not cause palmar erythema or spider angiomas.

B - Decreased circulating albumin

Explanation Why

Hypoalbuminemia due to impaired production of albumin can occur secondary to cirrhosis. The subsequently decreased oncotic pressure, together with increased venous pressures secondary to portal hypertension (a common finding in cirrhosis), promotes extravascular fluid shift into the interstitium and results in peripheral edema and ascites formation. Hypoalbuminemia, however, is not the underlying cause of palmar erythema and spider angiomas.

C - Decreased circulating thrombopoietin

Explanation Why

Impaired production of thrombopoietin secondary to cirrhosis, together with congestive splenomegaly with platelet sequestration due to portal hypertension (a common finding in cirrhosis), can cause thrombocytopenia. Decreased thrombopoietin does not cause palmar erythema or spider angiomas.

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D - Decreased circulating testosterone

Explanation Why

Cirrhosis can result in low testosterone levels and hypogonadism as liver dysfunction progresses. In men, this results in reduced libido, erectile dysfunction, infertility, and testicular atrophy. However, low testosterone levels are not the underlying cause of palmar erythema and spider angiomas.

E - Increased circulating cortisol

Explanation Why

Increased serum cortisol levels are characteristic of Cushing syndrome, which can cause various cutaneous manifestations, including thin, easily bruisable skin, purple abdominal striae, and flushing of the face. Cushing syndrome is not associated with palmar erythema or spider angiomas. Moreover, cirrhosis does not result in hypercortisolism.

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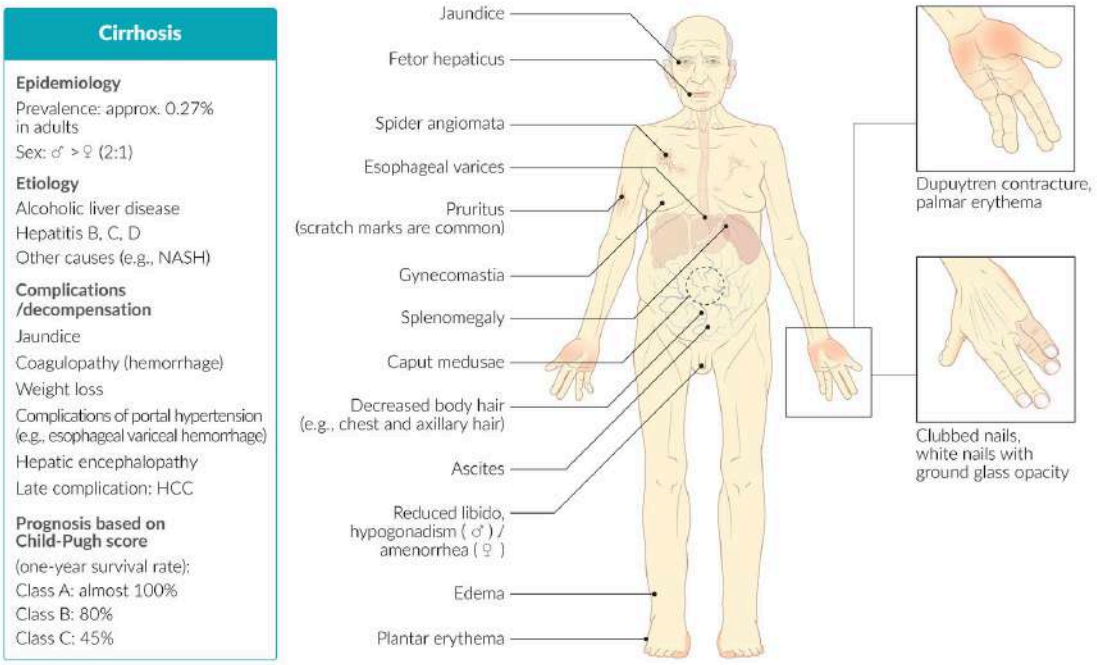
F - Increased circulating estrogen

Image



Explanation Why

Hyperestrogenism in patients with liver dysfunction occurs due to impaired hepatic metabolism of estrogen and androstenedione (which is then converted to estrogen by aromatase in adipose cells). Elevated estrogen levels stimulate the proliferation and dilation of capillaries, resulting in palmar erythema and spider angioma. In men, increased estrogen levels can also cause feminization, which may manifest as gynecomastia, decreased body hair (e.g., loss of chest, pubic, and/or axillary hair), and/or testicular atrophy.

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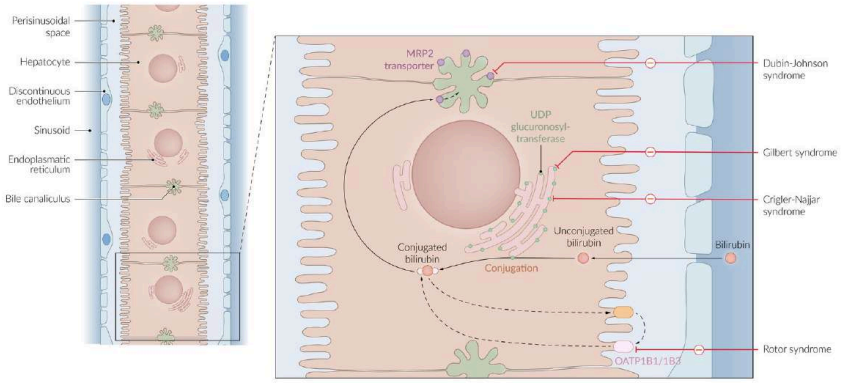
Question # 9

Two days after undergoing porcine aortic valve replacement surgery for aortic valve stenosis, a 62-year-old patient develops yellow discoloration of the sclera. His vital signs are within normal limits. Physical examination shows scleral icterus. Abdominal examination shows no abnormalities. Laboratory studies show:

Hematocrit	49%
Reticulocyte count	1.2%
Serum	
AST	15 U/L
ALT	18 U/L
Bilirubin, total	2.8 mg/dL
Direct	0.3 mg/dL
Lactate dehydrogenase	62 U/L

Which of the following is the most likely underlying mechanism of this patient's laboratory findings?

	Answer	Image
A	Impaired bilirubin conjugation	

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	Answer	Image
B	Mechanical erythrocyte damage	
C	Drug-induced toxicity	
D	Absent hepatic glucuronosyltransferase	
E	Impaired bilirubin excretion	

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Hint

Asymptomatic jaundice induced by physical stress (e.g., surgery) along with laboratory studies showing unconjugated hyperbilirubinemia, normal LDH, and normal liver enzyme levels is consistent with Gilbert syndrome.

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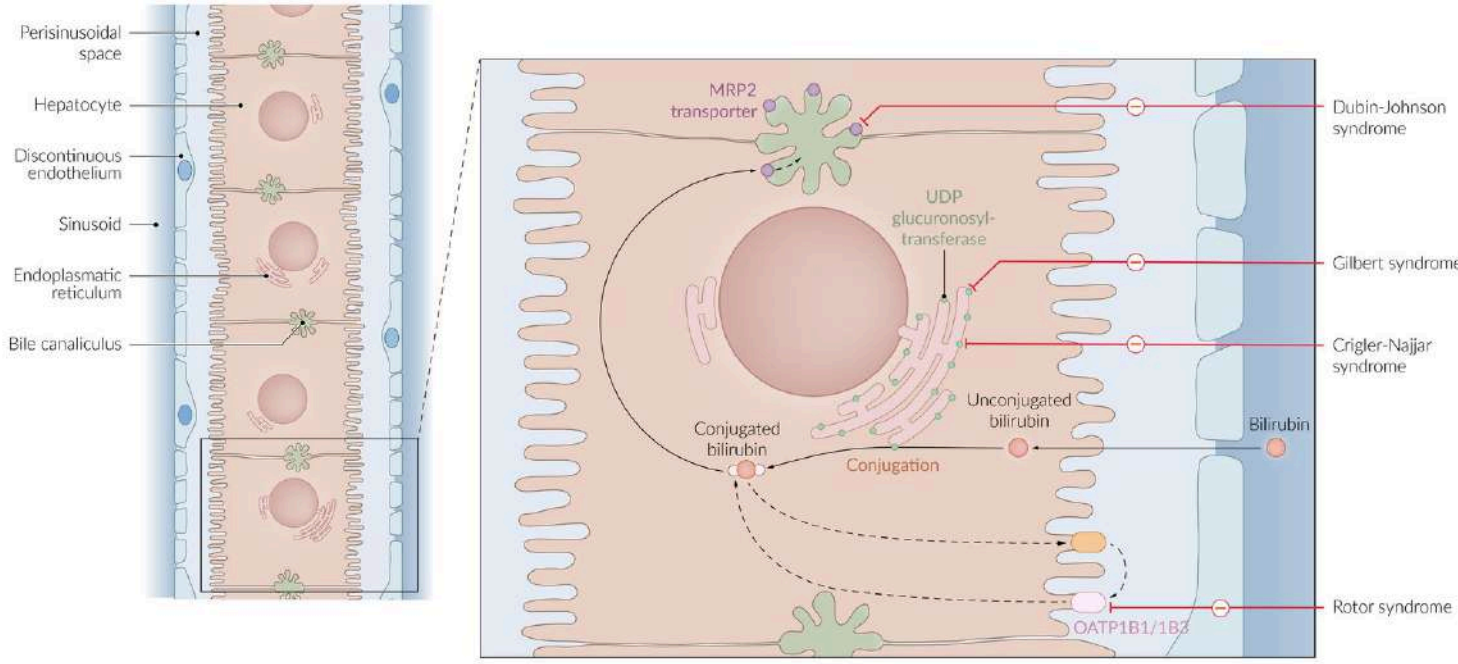
Correct Answer

A - Impaired bilirubin conjugation

Image



Explanation Why

A mutation in the promoter sequence of the *UGT1A1* gene causes decreased activity of UDP-glucuronosyltransferase, which is the underlying pathomechanism of Gilbert syndrome. Physical stress (trauma, surgery, exhaustion) triggers decreased conjugation of bilirubin, resulting in mild unconjugated hyperbilirubinemia and subsequent transient jaundice. Because hepatocytes are not damaged, liver enzyme levels are normal.

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B - Mechanical erythrocyte damage

Explanation Why

Mechanical damage to erythrocytes secondary to a prosthetic aortic valve can result in hemolysis with unconjugated hyperbilirubinemia. However, hemolytic anemia is marked by a decreased hematocrit as well as an elevated LDH and reticulocyte count. This patient's normal hematocrit, reticulocyte count, and LDH exclude this diagnosis. In addition, mechanical erythrocyte damage occurs more commonly with mechanical heart valves than with bioprosthetic valves.

C - Drug-induced toxicity

Explanation Why

Halogenated inhaled anesthetics (e.g., halothane) and amiodarone, which is often used for atrial fibrillation prophylaxis after cardiac surgeries, can cause liver toxicity. However, drug-induced liver toxicity causes hepatocyte damage, resulting in elevated liver enzymes (AST and ALT). This patient's AST and ALT levels are normal.

D - Absent hepatic glucuronosyltransferase

Explanation Why

The complete absence or marked loss of function of hepatic UDP-glucuronosyltransferase due to mutations in the coding sequence of the *UGT1A1* gene is characteristic of Crigler-Najjar syndrome (type 1). This condition causes severe unconjugated hyperbilirubinemia and manifests in infancy with neonatal jaundice and neurological symptoms caused by kernicterus; it is not the underlying cause of this 62-year-old patient's laboratory findings.

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E - Impaired bilirubin excretion

Explanation Why

Impaired hepatic bilirubin excretion is characteristic of Dubin-Johnson syndrome and Rotor syndrome. Both conditions are benign, hereditary hyperbilirubinemias, in which bilirubin is conjugated correctly but the hepatic excretion of bilirubin is impaired. Therefore, patients develop conjugated hyperbilirubinemia.

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Question # 10

A 47-year-old man comes to the physician because of abdominal pain and foul-smelling, watery diarrhea for several days. He has not had nausea, vomiting, or bloody stools. He has a history of alcohol use disorder and recently completed a 7-day course of clindamycin for pneumonia. He has not traveled out of the United States. Which of the following toxins is most likely to be involved in the pathogenesis of this patient's symptoms?

	Answer	Image
A	Shiga toxin	
B	Heat-stable toxin	
C	Cholera toxin	
D	Cereulide toxin	
E	Clostridioides difficile cytotoxin	
F	Alpha toxin	

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Hint

This man has watery diarrhea following recent antibiotic use. His presentation is consistent with *Clostridioides difficile* infection.

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Correct Answer

A - Shiga toxin

Explanation Why

Shiga toxin is produced by *Shigella* spp. and enterohemorrhagic E. coli O157:H7. This toxin inhibits the 60S subunit of ribosomes by cleaving adenine in ribosomal RNA. This causes enterocyte injury, which results in mucoid, bloody diarrhea, which is not present in this patient. This patient's recent antibiotic use is associated with a different cause of diarrhea.

B - Heat-stable toxin

Explanation Why

Heat-stable toxin is produced by enterotoxigenic E. coli (ETEC), a common pathogen implicated in traveler's diarrhea. This toxin stimulates guanylate cyclase, which in turn increases levels of cGMP, resulting in decreased reabsorption of sodium, chloride, and water from the intestinal lumen. A patient with no history of recent travel is unlikely to have diarrhea due to ETEC.

C - Cholera toxin

Explanation Why

The cholera toxin is produced by *Vibrio cholera*. This toxin stimulates adenylate cyclase, resulting in increased secretion of chloride and water into the intestinal lumen. Cholera is characterized by voluminous rice-water diarrhea and is most commonly associated with ingestion of contaminated water. Cholera is very rare in the US and there are no indications that this patient may have been exposed to contaminated water.

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D - Cereulide toxin

Explanation Why

The cereulide toxin (a preformed toxin) is produced by *Bacillus cereus*, which causes acute nausea and vomiting (1–5 hours after ingestion) and/or watery, nonbloody diarrhea (8–18 hours after ingestion). This toxin is typically found in reheated rice. However, this patient has no history of rice consumption or vomiting, and the time course of his illness is not consistent with *B. cereus* infection.

E - Clostridioides difficile cytotoxin

Explanation Why

Clostridioides difficile produces two toxins: toxin A (enterotoxin) and toxin B (cytotoxin). Both toxins depolymerize actin filaments and disrupt the cellular cytoskeleton, while toxin A also causes intestinal inflammation, leading to excessive fluid secretion. These traits cause pseudomembranous colitis and watery, foul-smelling diarrhea, as seen in this patient. Enzyme immunoassay of toxin A and B are commonly used as screening tests for C. difficile-associated diarrhea (CDAD).

F - Alpha toxin

Explanation Why

The alpha toxin is produced by *Clostridium perfringens*. This toxin is a phospholipase (lecithinase) that disrupts the cell membrane of enterocytes and causes Clostridium perfringens enterocolitis, which is characterized by abdominal pain and watery diarrhea. The diarrhea seen in Clostridium perfringens enterocolitis usually resolves within 24 hours and is unlikely in this patient.

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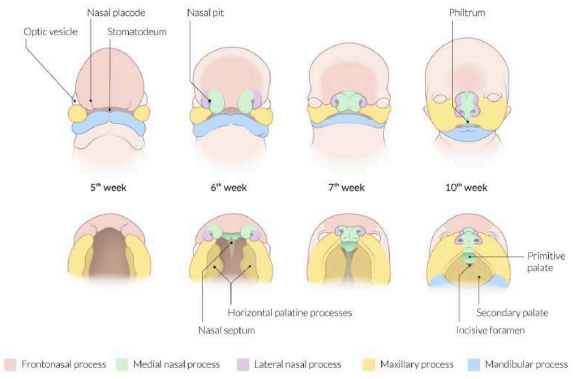
Question # 11

An investigator is studying the teratogenicity of cigarette smoking during pregnancy. He reviews several databases containing data about birth defects and prenatal drug exposures and finds that infants exposed to cigarette smoke in utero are approximately 2 times as likely to have a particular birth defect than unexposed infants. This defect results from abnormal development during the 6^{th} week of gestation, when the maxillary prominences grow medially and fuse first with the lateral and then the medial nasal prominence. The defect is most likely which of the following?

	Answer	Image
A	Cleft palate	
B	Cleft lip	
C	Choanal atresia	
D	Macrognathia	
E	Micrognathia	
F	Torus palatinus	

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Hint

The defect in question is a result of failure to fuse that is commonly seen in infants with Patau syndrome.

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Correct Answer

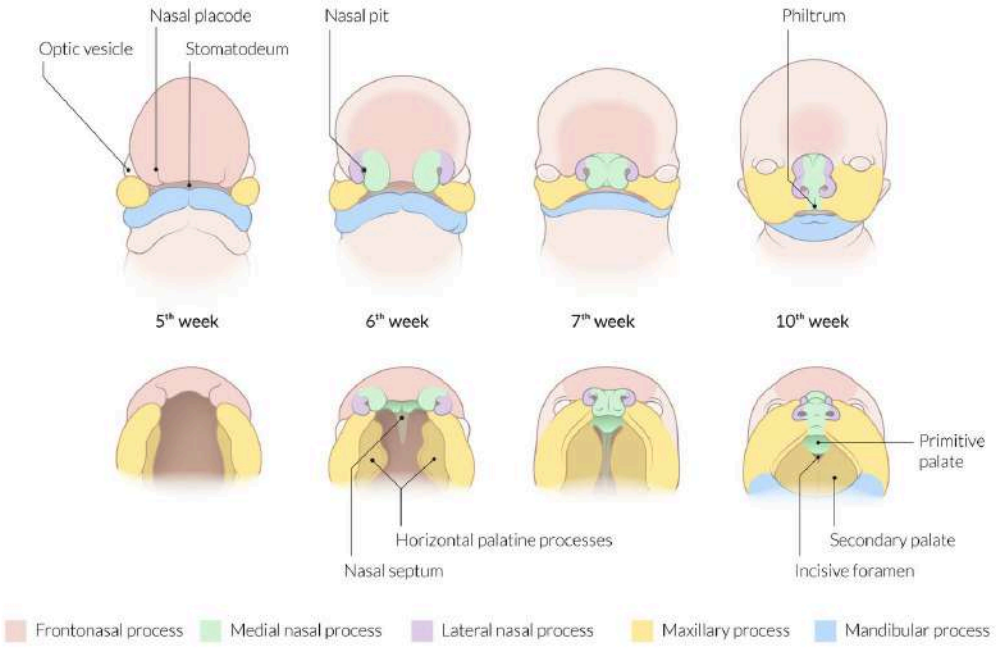
A - Cleft palate

Explanation Why

The secondary palate is formed when the lateral palatine shelves eventually fuse after moving from a horizontal to vertical orientation at about the 8th week of development. Failure of the shelves to either change in orientation (e.g., as in Pierre Robin syndrome), fuse together, or fully join the nasal septum leads to a cleft palate. While often coincidental with this patient's defect, a cleft palate develops later than the 6th week of gestation and does not involve the maxillary prominences.

B - Cleft lip

Image



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Explanation Why

Cleft lip is caused by failure of fusion of the maxillary prominence with the medial nasal prominence. Normally, children have two copies of GSTT1, a gene that is protective against the development of a cleft lip. However, embryos with only one copy of this gene (e.g., in some European and Asian ancestry) have a 20-fold increase in developing a cleft lip if exposed to cigarette smoke in utero.

C - Choanal atresia

Explanation Why

Congenital choanal atresia is due to a failure of the canalization of the nasal pits during the 5–6th week of fetal development. As the nasal sacs extend posteriorly to develop into the nares, a membrane forms between the nasal and oral epithelia. Canalization requires the rupture of this membrane; if it fails to do so, choanal atresia results. This can occur unilaterally, or less commonly bilaterally (33% of the time).

D - Macrognathia

Explanation Why

Macrognathia is a relatively rare condition in which the jaw develops normally but is much larger in proportion to the rest of the head. While there is a hereditary component, it is associated with neoplastic and metabolic conditions, such as Paget's disease and pituitary gigantism. There is no failure to fuse in the development of macrognathia.

E - Micrognathia

Explanation Why

An undersized jaw (micrognathia) due to mandibular hypoplasia can be found in many different

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conditions, including trisomy 18, fetal alcohol syndrome, and Pierre Robin syndrome. Although heavy maternal smoking may increase the risk of conditions related to some conditions that cause micrognathia (e.g., Pierre Robin syndrome), micrognathia is not associated with maxillary prominence fusion.

F - Torus palatinus

Explanation Why

Torus palatinus is a benign bony overgrowth that is typically located in the midline of the hard palate. Although it can occur congenitally in some cases, it is not caused by a failure of bones to fuse.

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Question # 12

A 47-year-old man with gastroesophageal reflux disease comes to the physician because of severe burning chest pain and belching after meals. He has limited his caffeine intake and has been avoiding food close to bedtime. Esophagogastroduodenoscopy shows erythema and erosions in the distal esophagus. Which of the following is the mechanism of action of the most appropriate drug for this patient?

	Answer	Image
A	Enhancement of the mucosal barrier	
B	Inhibition of D2 receptors	
C	Neutralization of gastric acid	
D	Inhibition of H2 receptors	
E	Inhibition of ATPase	

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Hint

This patient has symptoms consistent with severe GERD, and evidence of reflux-induced esophagitis. A proton pump inhibitor (PPI) would be the appropriate first-line drug therapy for this patient.

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Correct Answer

A - Enhancement of the mucosal barrier

Explanation Why

Enhancement of the mucosal barrier in the stomach and duodenum is the mechanism of action of sucralfate, which forms a protective barrier, acts as an acid buffer, and promotes HCO_3 production. It is commonly used in the treatment of peptic ulcer disease, but is not considered first-line for GERD.

B - Inhibition of D2 receptors

Explanation Why

Inhibition of D2 receptors in the stomach (e.g., metoclopramide) increases lower esophageal sphincter (LES) tone and increases gastric motility. While these agents can improve symptoms of GERD, they are not used for this purpose because of their adverse effects (e.g., parkinsonism).

C - Neutralization of gastric acid

Explanation Why

Neutralization of gastric acid is the mechanism of action of antacids such as calcium carbonate. These agents are commonly used for mild, intermittent heartburn, and/or GERD. However, this patient has severe symptoms and is unlikely to experience long-term improvement with antacids alone.

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D - Inhibition of H2 receptors

Explanation Why

H2 antihistamines, such as ranitidine, inhibit histamine-dependent gastric acid secretion via their antagonistic effect on H2 receptors in the gastric parietal cells. Although they may be used for mild GERD symptoms, a different agent is indicated for this patient with severe symptoms and esophagitis.

E - Inhibition of ATPase

Explanation Why

Proton pump inhibitors (PPIs) irreversibly inhibit H^+/K^+ ATPase in parietal cells of the stomach and thus reduce the ATP-dependent secretion of H^+ ions into the gastric lumen. They are considered first-line for patients with severe GERD.

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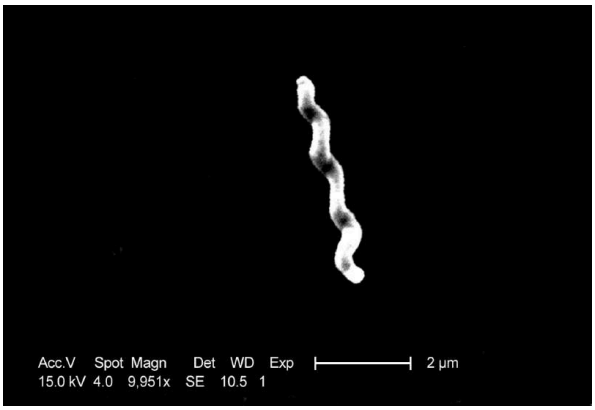
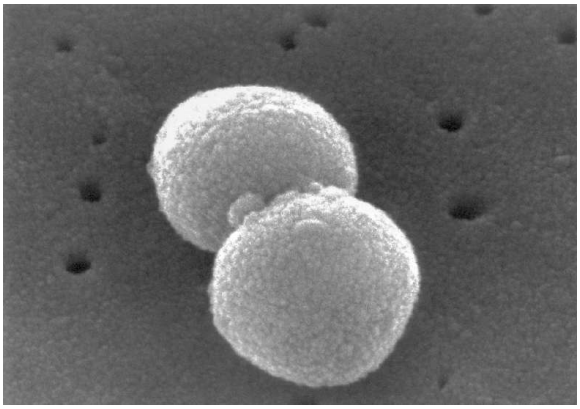
Question # 13

A 46-year-old woman from Ecuador is admitted to the hospital because of tarry-black stools and epigastric pain for 2 weeks. The epigastric pain is relieved after meals, but worsens after 1–2 hours. She has no history of serious illness and takes no medications. Physical examination shows no abnormalities. Fecal occult blood test is positive. Esophagogastroduodenoscopy shows a bleeding duodenal ulcer. Microscopic examination of a duodenal biopsy specimen is most likely to show which of the following?

	Answer	Image
A	Curved, flagellated gram-negative rods	
B	Gram-negative S-shaped rods with polar flagella	
C	Irregularly drumstick-shaped gram-positive rods	
D	Gram-positive lancet-shaped diplococci	

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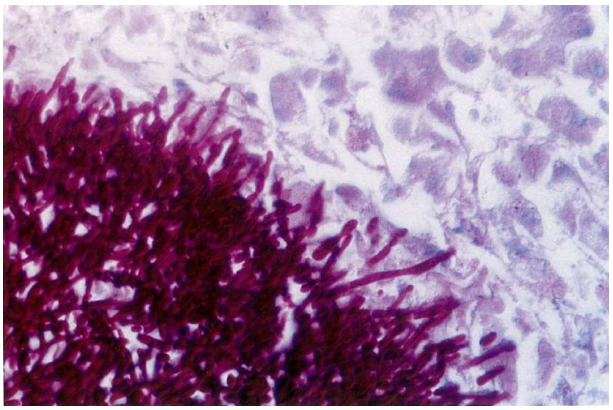
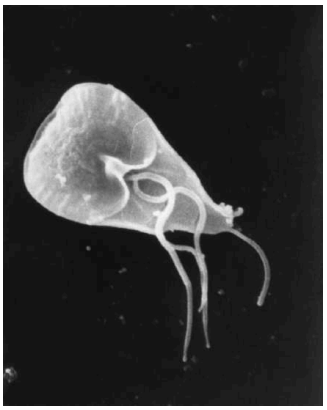
	Answer	Image
E	Dimorphic budding yeasts with pseudohyphae	
F	Teardrop-shaped multinucleated trophozoites	

Hint

This patient presents with a bleeding duodenal ulcer found on EGD. The most common cause of peptic ulcer disease is infection with *H. pylori*.

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Correct Answer

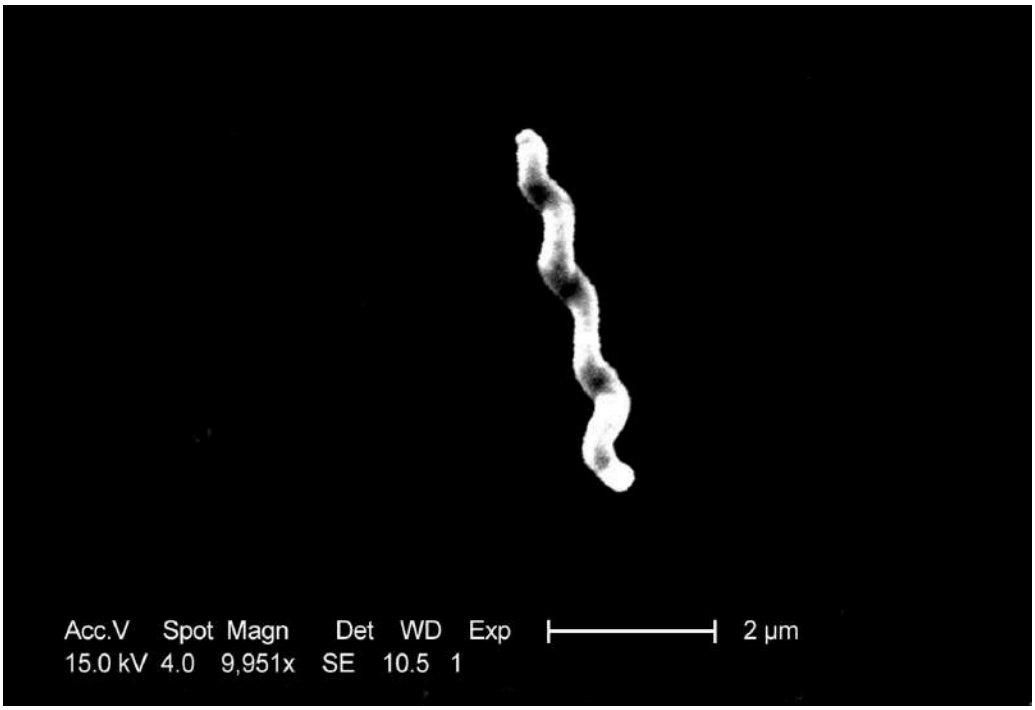
A - Curved, flagellated gram-negative rods

Explanation Why

H. pylori is a curved, flagellated gram-negative rod which mainly colonizes the antrum of the stomach. *H. pylori* is also catalase positive, oxidase positive, and urease positive.

B - Gram-negative S-shaped rods with polar flagella

Image



Explanation Why

Campylobacter jejuni is a S-shaped, gram-negative rod with polar flagella. It is the most common pathogen responsible for foodborne gastroenteritis in the US and causes bloody diarrhea. It may be antecedent to Guillain-Barré syndrome and reactive arthritis, but it has no association with PUD.

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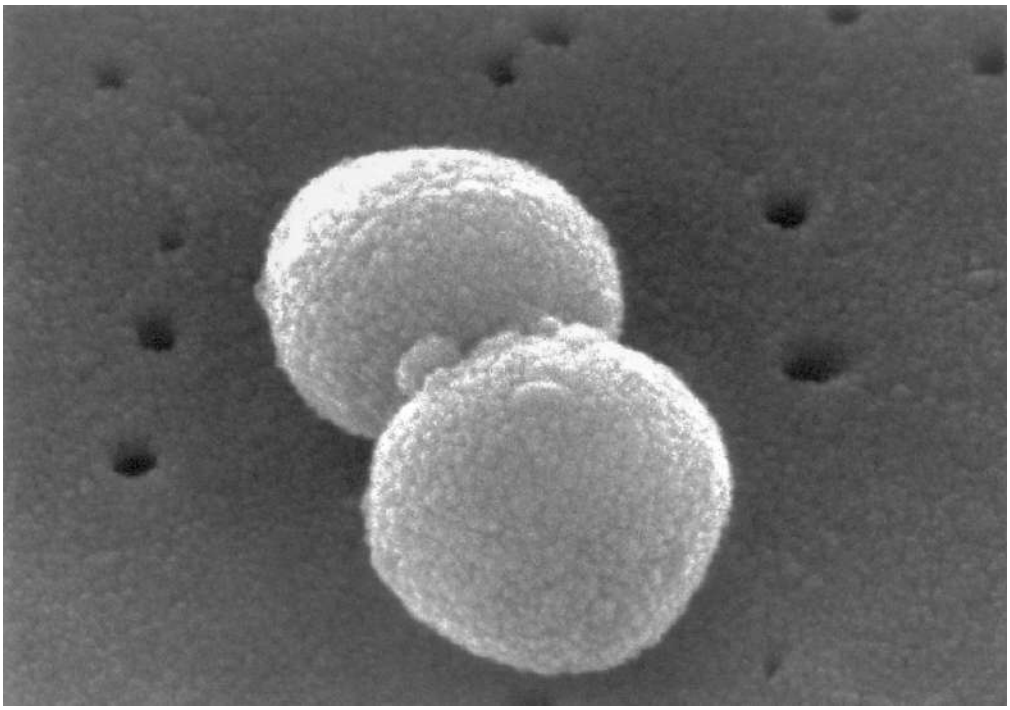
C - Irregularly drumstick-shaped gram-positive rods

Explanation Why

C. difficile is a drumstick-shaped, gram-positive rod that is part of the natural gut flora in 5% of adults. Although clostridium enterocolitis may lead to bloody diarrhea, the bacteria is not associated with PUD.

D - Gram-positive lancet-shaped diplococci

Image



Explanation Why

Gram-positive lancet-shaped diplococci describes the histological findings of *S. pneumoniae*, which may cause many conditions (e.g., pneumonia, meningitis, sinusitis) but not gastrointestinal ulcers.

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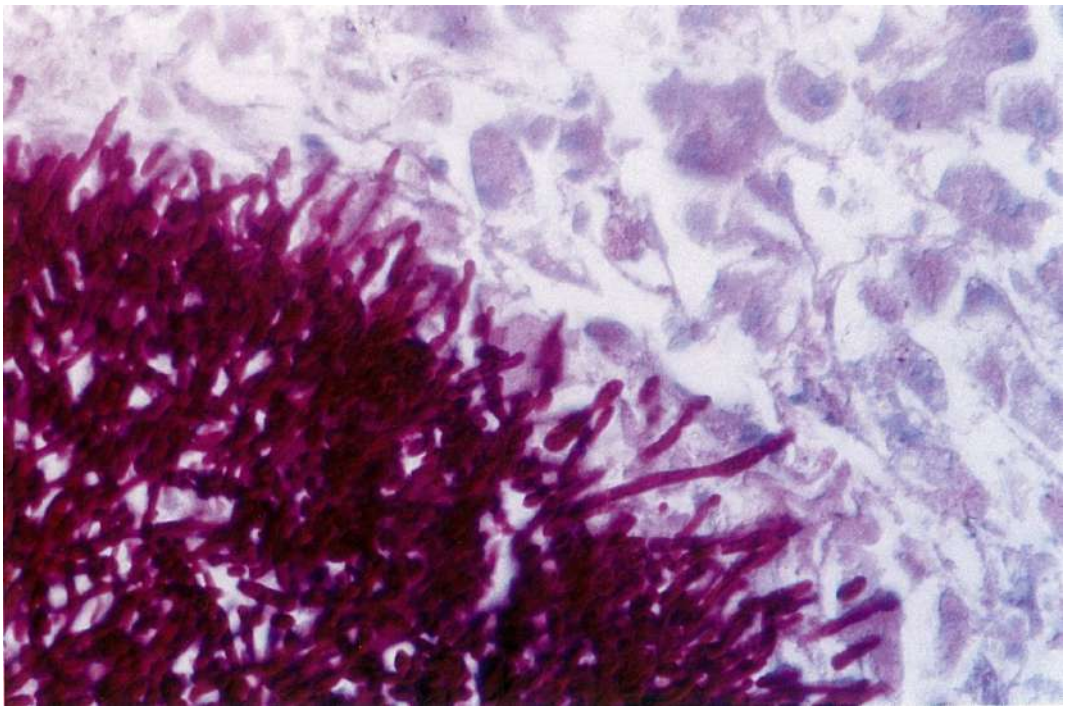
E - Dimorphic budding yeasts with pseudohyphae

Image



Explanation Why

Candida albicans is a dimorphic budding yeast forming hyphae and long pseudohyphae. *Candida albicans* can cause esophagitis in immunosuppressed patients (e.g., HIV, transplant patients, diabetes mellitus) that can also lead to tarry stools if bleeding occurs, but it is not a common cause of PUD.

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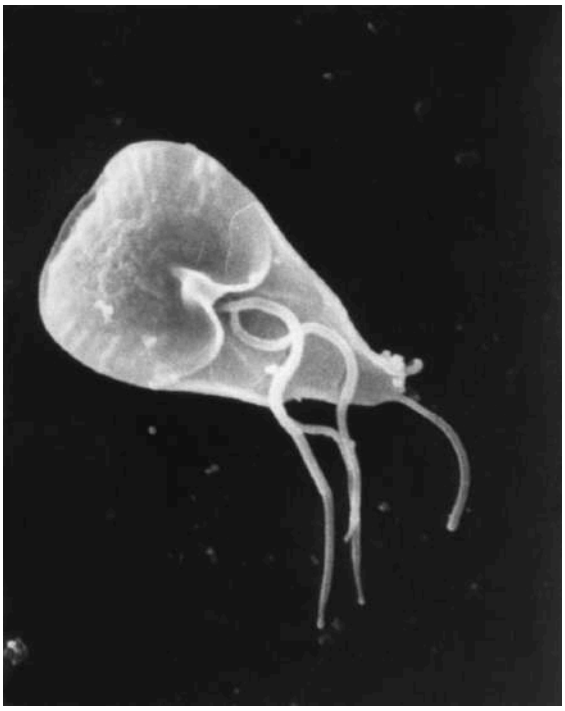
F - Teardrop-shaped multinucleated trophozoites

Image



Explanation Why

Giardiasis is a common parasitic infection caused by *Giardia lamblia*, which in their active form in the human body, appear as teardrop-shaped trophozoites. It presents with voluminous diarrhea characteristically consisting of frothy and greasy stools but is not associated with gastrointestinal bleeding or PUD.

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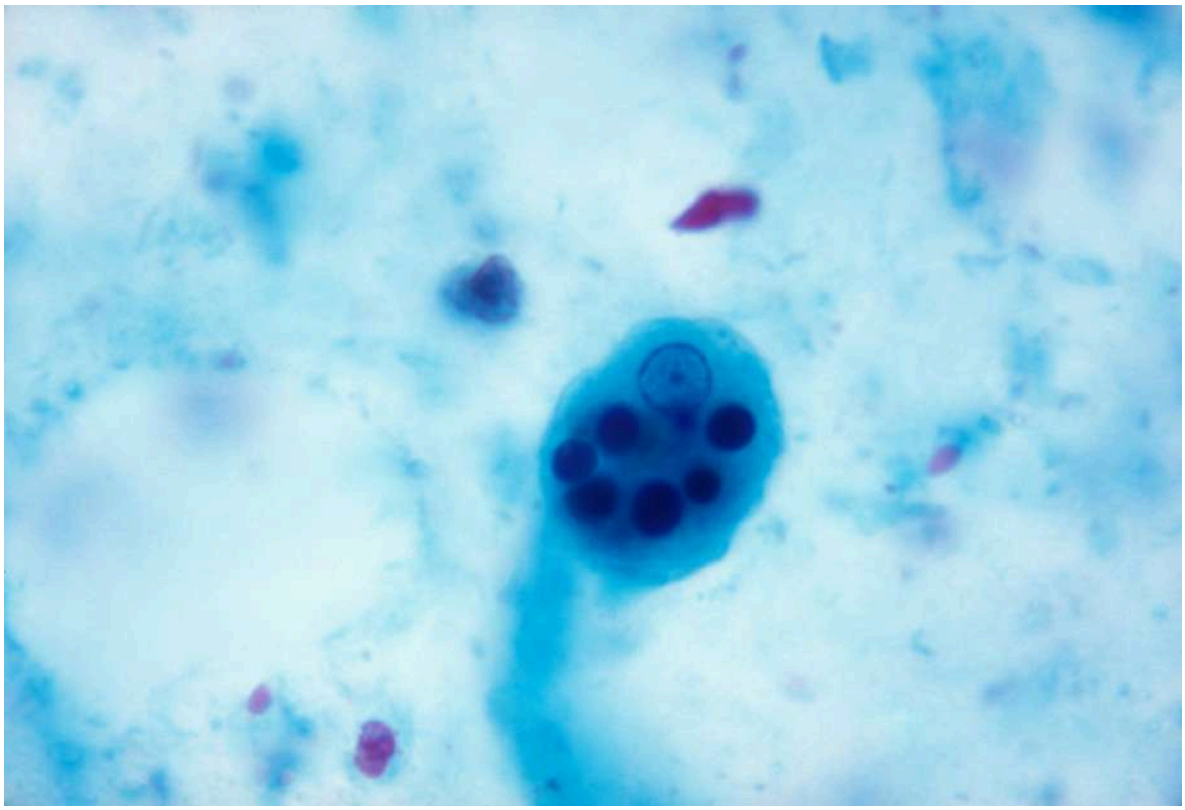
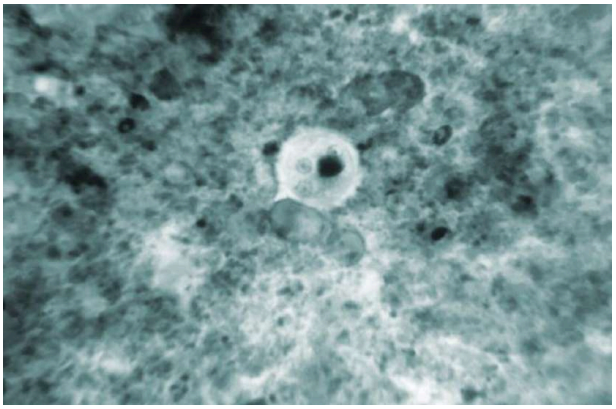
Question # 14

A 31-year-old man comes to the physician because of a 2-day history of abdominal pain and diarrhea. He reports that his stools are streaked with blood and mucus. He returned from a vacation in the Philippines 3 weeks ago. His vital signs are within normal limits. Abdominal examination shows hyperactive bowel sounds. A photomicrograph of a trichrome-stained wet mount of a stool specimen is shown. Which of the following organisms is the most likely cause of this patient's symptoms?



	Answer	Image
A	Entamoeba histolytica	

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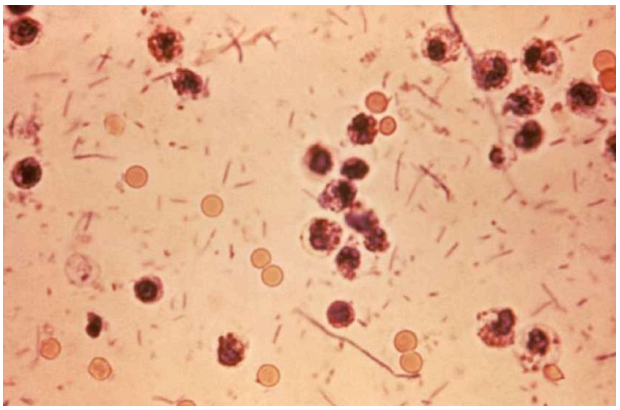
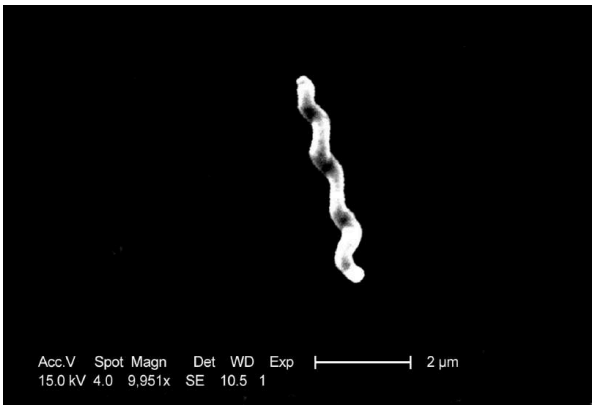
	Answer	Image
B	Giardia lamblia	
C	Shigella dysenteriae	
D	Campylobacter jejuni	

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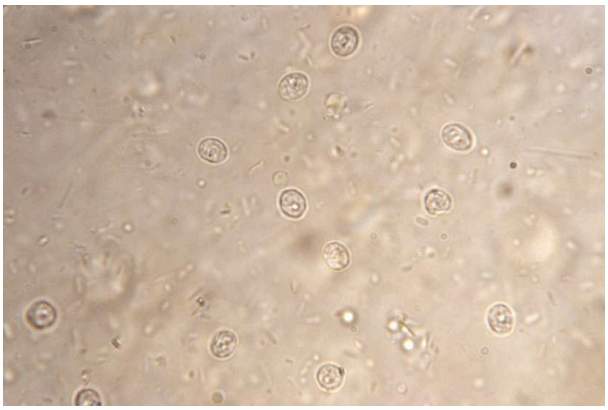
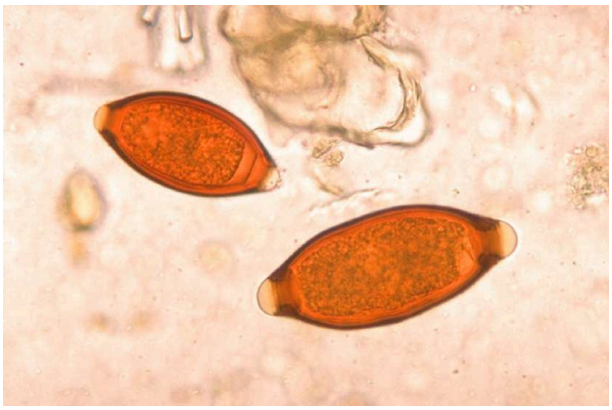
	Answer	Image
E	Cryptosporidium parvum	
F	Trichuris trichiura	

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Hint

The dark circular inclusions in the photomicrograph represent ingested erythrocytes within the trophozoite.

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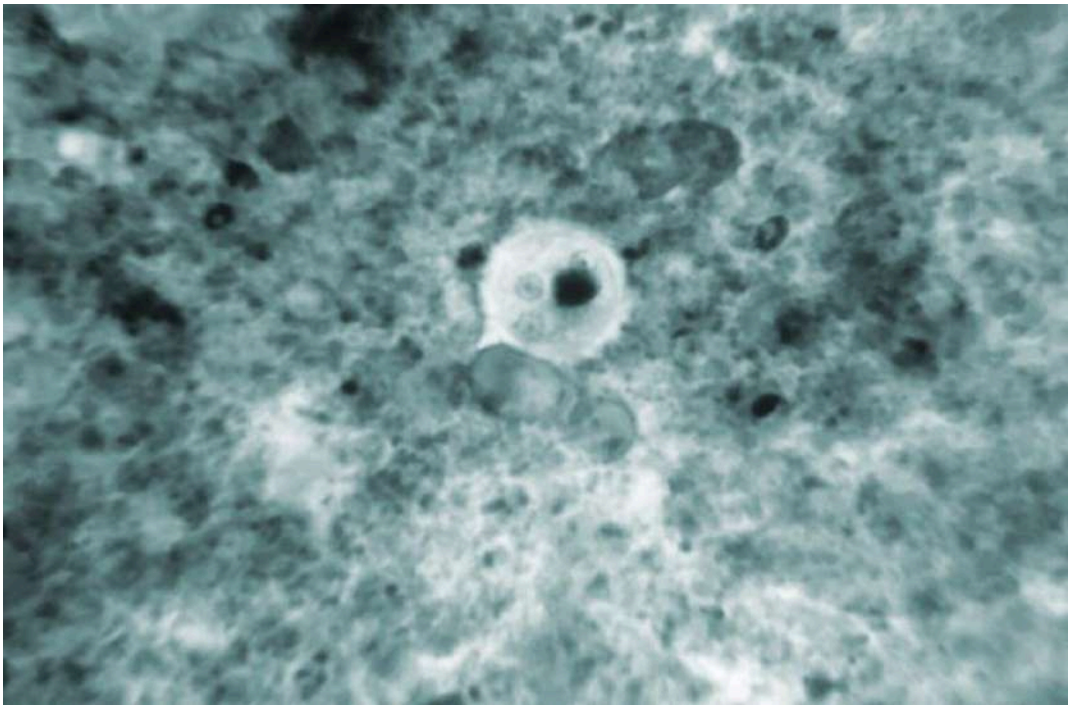
Correct Answer

A - Entamoeba histolytica

Image



Explanation Why

Entamoeba histolytica causes amebiasis, which is consistent with the clinical presentation of this patient (abdominal pain and bloody stool with mucus). Symptoms manifest after an incubation period of 1–4 weeks, which would correspond with this patient's vacation to an endemic area. It is diagnosed based on the presence of cysts or trophozoites containing phagocytosed erythrocytes in fresh stool, which are seen in the photomicrograph. Intestinal amebiasis is typically treated with metronidazole followed by paromomycin, a luminal agent that eradicates intestinal cysts.

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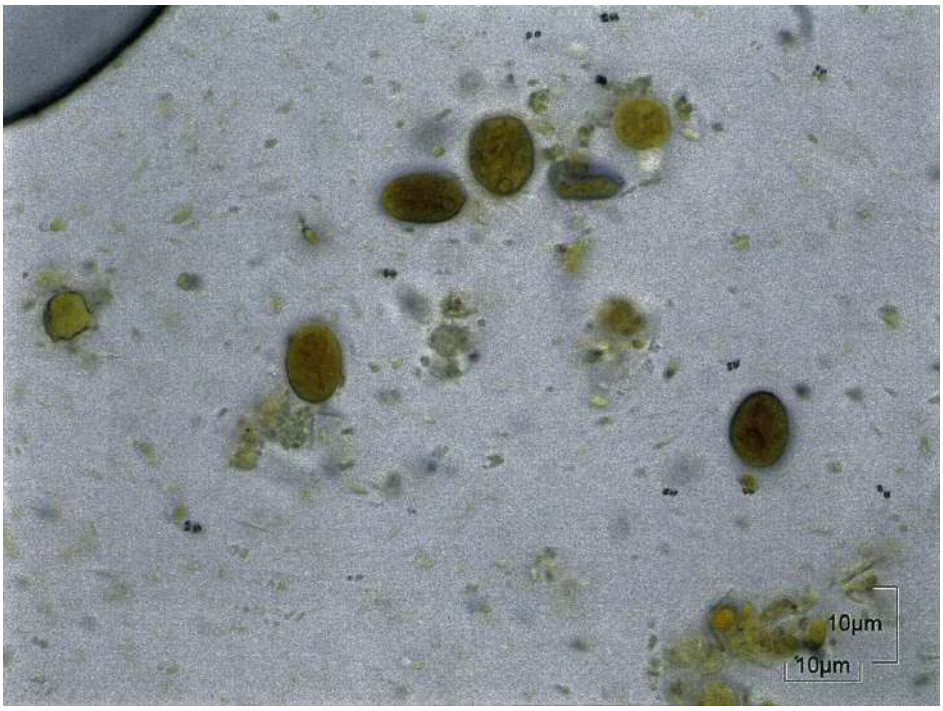
B - Giardia lamblia

Image



Explanation Why

Infection with *Giardia lamblia* can manifest with mucus in the stool, as seen in this patient. However, it does not cause bloody diarrhea, but rather voluminous, frothy steatorrhea. *Giardia* is identified on stool microscopy, where it takes the form of cysts with a two-layered cell wall, multiple nuclei and thread-like median bodies in the cytoplasm, none of which is present in this patient's specimen.

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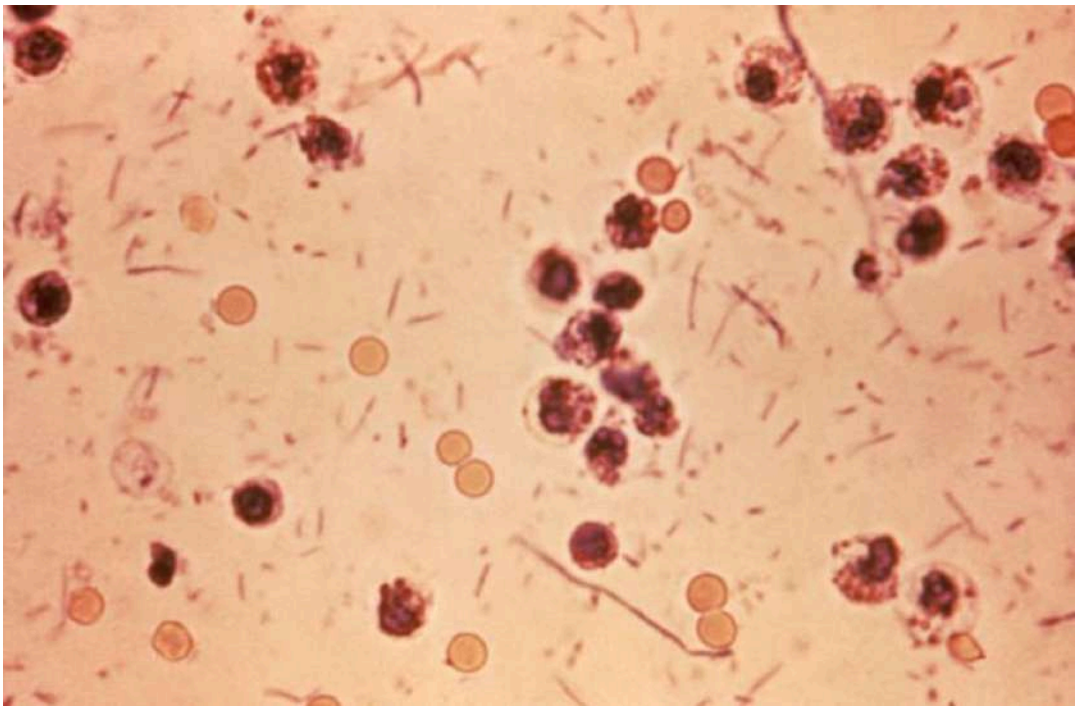
C - Shigella dysenteriae

Image



Explanation Why

Shigella dysenteriae infection manifests with inflammatory, bloody diarrhea and abdominal pain, as seen in this patient. However, Shigella are gram-negative bacilli. The presence of trophozoites in this wet stool mount suggests a different diagnosis.

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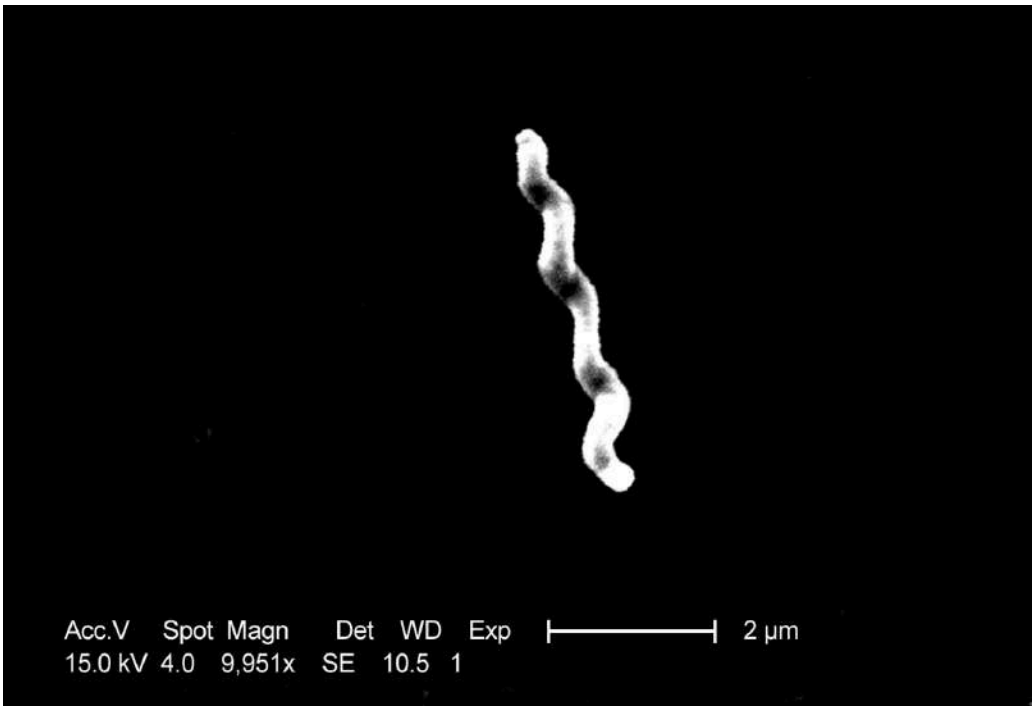
D - Campylobacter jejuni

Image



Explanation Why

Campylobacter jejuni infection manifests with inflammatory, bloody diarrhea and abdominal pain, as seen in this patient. However, the infection is diagnosed by stool culture at 42°C, which would grow gram-negative, oxidase-positive, comma-shaped bacilli. The presence of trophozoites in this wet stool wount suggests a different diagnosis.

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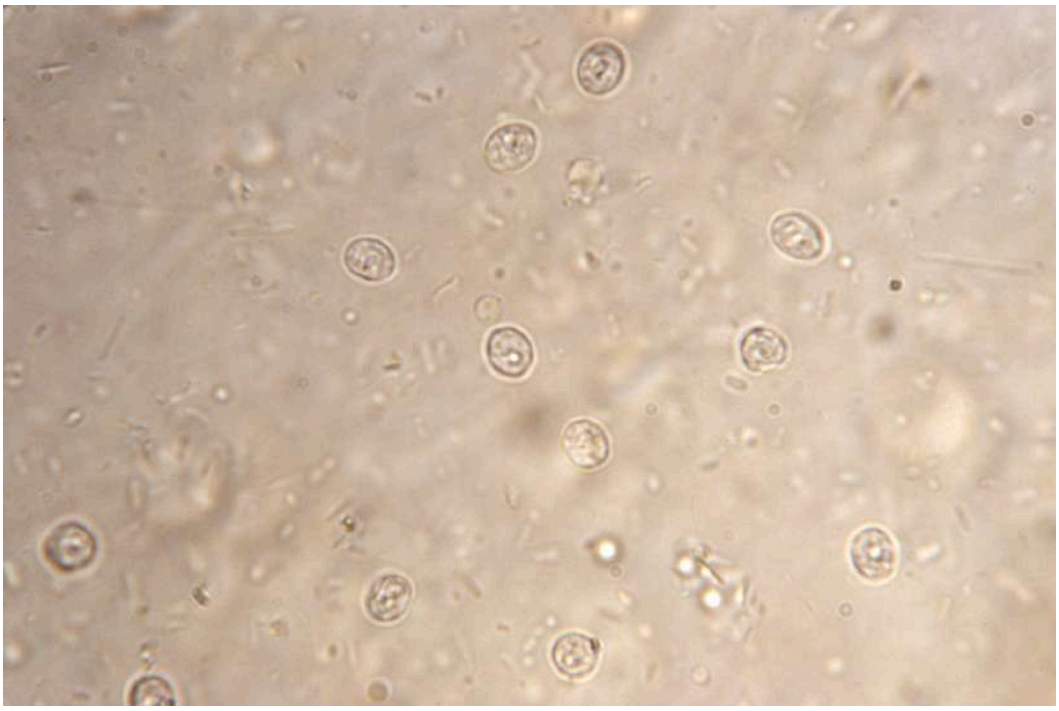
E - Cryptosporidium parvum

Image



Explanation Why

Cryptosporidium parvum causes chronic, watery, non-bloody diarrhea in immunocompromised patients. While it can cause mild, self-limited diarrhea in immunocompetent hosts, it would not cause bloody diarrhea, as seen in this patient. It appears on stool microscopy as round acid-fast oocysts, which are not present in this patient's specimen.

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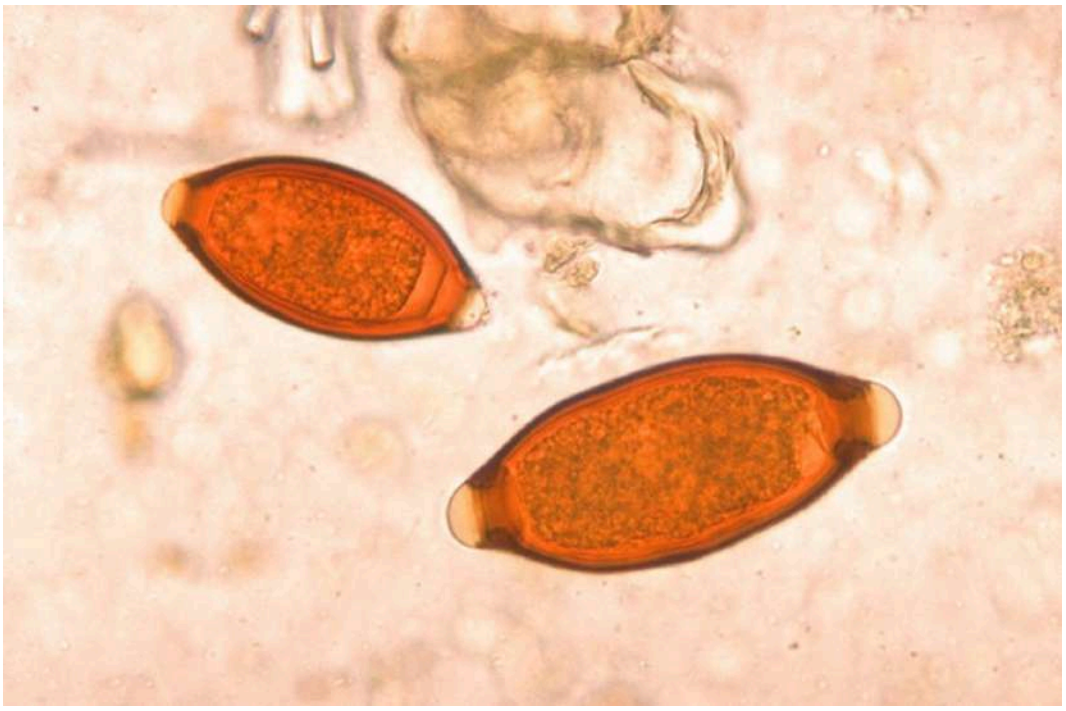
F - Trichuris trichiura

Image



Explanation Why

Infection with the parasite *Trichuris trichiura* (whipworm) is typically chronic and asymptomatic. Patients with a high worm burden can present with blood and mucus in the stool, as seen in this patient. However, *Trichuris trichiura* appears on stool microscopy as barrel-shaped eggs with bipolar protuberances. These findings are not present in this patient's specimen.

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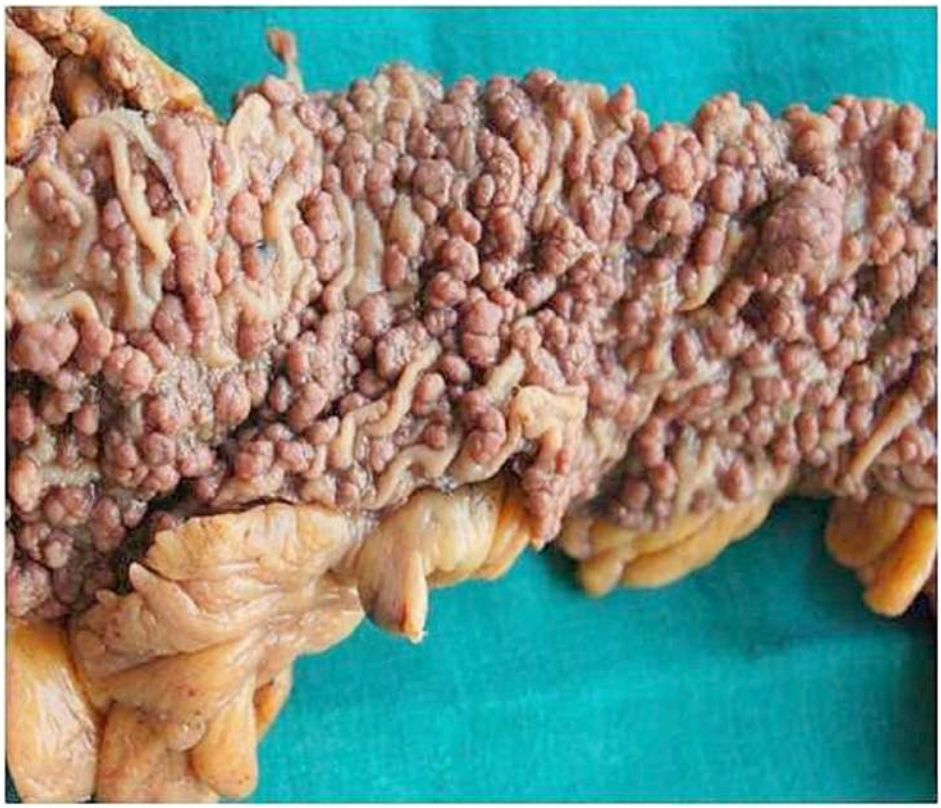
Question # 15

A previously healthy 42-year-old man comes to the emergency room with constipation and diffuse, worsening abdominal pain for 2 days. He has no history of major medical illness. His father died in a car accident at the age of 32 years, and his mother has type 2 diabetes mellitus but is otherwise healthy. A diagnosis of bowel obstruction is suspected and he is taken to the operating room for exploratory laparotomy. A partial resection of the colon is performed. The gross appearance of the patient's colonic tissue is shown. Microscopic examination shows tubular, tubulovillous, and villous adenomas. Assuming the patient's partner is not a carrier of the condition, which of the following is the likelihood that this patient’s children will develop this condition?



	Answer	Image
A	100%	
B	25%	

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	Answer	Image
C	75%	
D	50%	
E	0%	

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Hint

This patient has hundreds of colonic polyps with varying histology, consistent with a diagnosis of familial adenomatous polyposis (FAP).

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Correct Answer

A - 100%

Explanation Why

If the patient is a homozygous dominant (i.e. two dominant/diseased alleles), there is a 100% probability of passing down a dominant allele to his offspring. Almost all individuals with an autosomal dominant disease have only one affected parent and are thus genetically heterozygous. Even if this man developed a de novo mutation, the probability is exceptionally rare that he developed two de novo mutations in the same gene locus on both alleles, so he would be assumed to be heterozygous as well.

B - 25%

Explanation Why

When both parents are heterozygous for an autosomal recessive disease, the chance of disease inheritance is 25%. FAP is autosomal dominant, not autosomal recessive. Furthermore, there is one affected parent and no carriers in this scenario.

C - 75%

Explanation Why

When both parents are heterozygous for an autosomal dominant disease, the chance of disease inheritance is 75% (50% heterozygous and 25% homozygous dominant). FAP is an autosomal dominant disease, but only one parent is affected in this scenario.

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D - 50%

Explanation Why

Familial adenomatous polyposis (FAP) is caused by an autosomal dominant mutation in the APC tumor suppressor gene. It can be determined that this patient is heterozygous (i.e., one dominant/disease allele) because his mother is otherwise healthy. In addition, his partner has no FAP (i.e., two recessive/healthy alleles). Therefore, the patient's child has a 50% chance of inheriting one dominant allele and developing FAP.

E - 0%

Explanation But

In an exceedingly rare case of mosaicism, certain somatic cells will carry the de novo mutation for FAP while other cells, such as germ cells, will not. This scenario can lead to a 0% probability of disease in the offspring, but mosaicism should not be assumed unless otherwise stated.

Explanation Why

Some patients have no family history of FAP because they developed a de novo mutation. Regardless of past family history, once the mutation is established in an individual, FAP will be passed down to offspring in an autosomal dominant inheritance pattern.

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Question # 16

A 64-year-old woman with osteoarthritis is brought to the emergency room because of a 2-day history of nausea and vomiting. Over the past few weeks, she has been taking acetaminophen frequently for worsening knee pain. Examination shows scleral icterus and tender hepatomegaly. She appears confused. Serum alanine aminotransferase (ALT) level is 845 U/L, aspartate aminotransferase (AST) is 798 U/L, and alkaline phosphatase is 152 U/L. Which of the following is the most likely underlying mechanism of this patient's liver failure?

	Answer	Image
A	Glucuronide-conjugate formation	
B	Salicylic acid formation	
C	N-acetyl-p-benzoquinoneimine formation	
D	N-acetylcysteine formation	
E	Sulfate-conjugate formation	

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Hint

This patient presents with signs of acute liver failure due to acetaminophen toxicity.

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Correct Answer

A - Glucuronide-conjugate formation

Explanation Why

Glucuronidation and subsequent urinary excretion is one of the metabolic pathways for clearance of acetaminophen. Increased glucuronide formation would result in decreased hepatotoxic metabolite formation and decrease the risk of liver injury.

B - Salicylic acid formation

Explanation Why

Salicylic acid is a metabolite of aspirin (acetylsalicylic acid), not acetaminophen. Although aspirin toxicity could also cause liver failure, this patient was taking a different medication.

C - N-acetyl-p-benzoquinoneimine formation

Explanation Why

N-acetyl-p-benzoquinoneimine (NAPQI) is a toxic breakdown product of acetaminophen. At therapeutic doses, glutathione acts to inhibit toxic NAPQI. However, in cases of acetaminophen overdose, glutathione reserves are depleted and concentrations of NAPQI build up, ultimately leading to acute liver failure, as seen in this patient.

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D - N-acetylcysteine formation

Explanation Why

N-acetylcysteine is an antidote used in the management of acetaminophen-induced liver failure, rather than a cause of liver damage. It helps restore depleted glutathione levels, which enhances inactivation of toxic metabolites of acetaminophen.

E - Sulfate-conjugate formation

Explanation Why

Sulfation and subsequent urinary excretion is one of the metabolic pathways for clearance of acetaminophen. Increased sulfate formation would result in decreased hepatotoxic metabolite formation and decrease the risk of liver injury.

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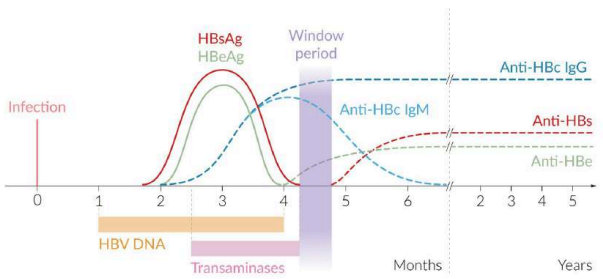
Question # 17

A previously healthy 25-year-old woman comes to the physician because of a one-week history of diffuse abdominal pain. Her temperature is 39.1°C (102.3°F). Physical examination shows numerous scars and excoriations along both arms, scleral icterus, and tender hepatomegaly. Serum studies show:

Alanine aminotransferase	927 U/L
Aspartate aminotransferase	796 U/L
Hepatitis B surface antigen	positive
Hepatitis B surface antibody	negative
Anti-hepatitis B core antibody	negative
Hepatitis C antibody	negative

Which of the following is the most likely outcome of this patient's infection?

	Answer	Image
A	Asymptomatic carrier state	
B	Hepatocellular carcinoma	
C	Transient infection	

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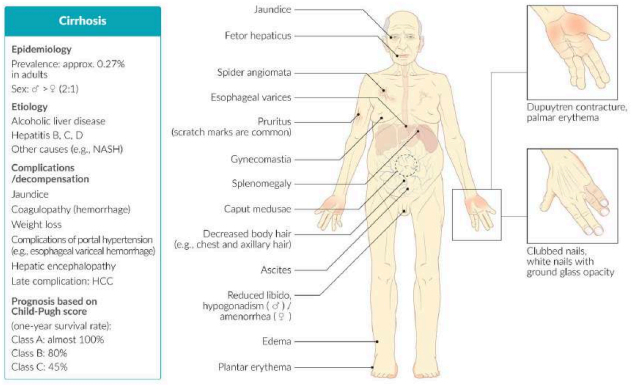
	Answer	Image
D	Fulminant hepatitis	
E	Liver cirrhosis	

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Hint

Tender hepatomegaly, jaundice, and fever are concerning for hepatitis. The positive hepatitis B surface antigen is consistent with acute hepatitis B infection.

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Correct Answer

A - Asymptomatic carrier state

Explanation But

Expected laboratory studies in a patient with inactive HBV carrier state would include positive HBsAg, anti-HBc, and anti-HBe antibodies, low serum HBV DNA, and normal transaminases.

Explanation Why

Risk factors for progression from acute HBV infection to chronic HBV infection include immunocompromised status, patients from certain geographical regions (e.g., China), and infants who acquired the virus perinatally. Of those patients who do develop chronic HBV infection, most of them are inactive, asymptomatic carriers of the virus. However, progression to chronic HBV infection is rare in adults with acute HBV infection, making this outcome unlikely.

B - Hepatocellular carcinoma

Explanation Why

The risk of hepatocellular carcinoma (HCC) is increased in patients with chronic HBV infection, but the risk of progression from acute HBV to chronic HBV is very low in adults. Therefore, it is very unlikely that this patient will develop HCC.

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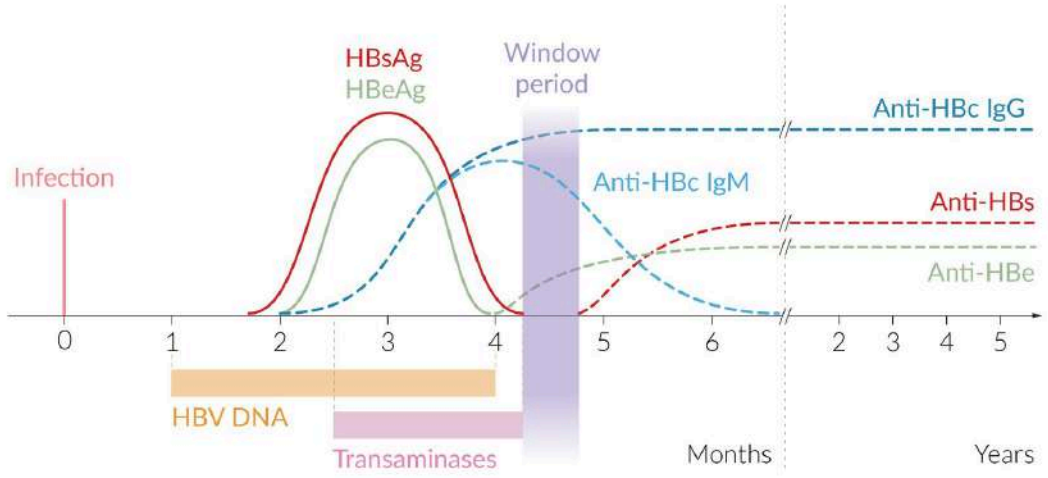
C - Transient infection

Image



Explanation Why

The vast majority of adults with acute HBV infection will clear their infection spontaneously with complete resolution of the infection, and only a minority will go on to develop chronic hepatitis B infection. Hepatitis B surface antigen is the first serum marker detected during the earliest phase of acute hepatitis B infection. Approximately 1–3 months after infection, anti-HBc and anti-HBs antibodies can be detected.

D - Fulminant hepatitis

Explanation Why

Fulminant hepatitis can occur as a complication of acute HBV infection but is incredibly rare, representing < 0.5% of cases of acute HBV infection. A different outcome is more likely.

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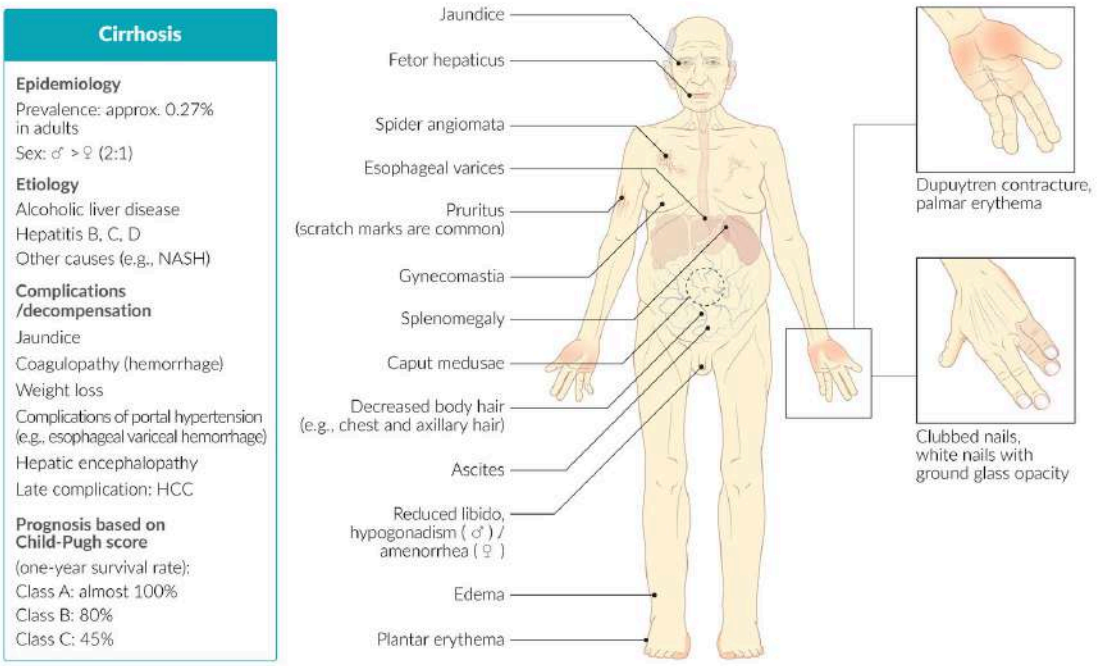
E - Liver cirrhosis

Image



Explanation But

Expected laboratory studies in a patient with active chronic HBV infection would include positive HBsAg, HBeAg, and anti-HBc, elevated serum HBV DNA, and normal or elevated transaminases.

Explanation Why

Approximately 20% of patients with active chronic HBV infection will progress to develop liver cirrhosis. However, the risk of progression from acute HBV to chronic HBV is very low and a different outcome is more likely.

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Question # 18

A 57-year-old man comes to the physician because of progressively worsening epigastric pain and 6.8-kg (15-lb) weight loss for the past 2 months. Two weeks ago, he noticed painful, red blotches on the medial aspect of his right calf. He has smoked one pack of cigarettes daily for the last 35 years. He appears thin. Physical examination shows tender, erythematous nodules on the right ankle and left antecubital fossa. Endoscopy shows a large mass in the antrum of the stomach. A biopsy specimen of the gastric mass shows disorganized, mucin-secreting cells with surrounding fibrosis. These cells most likely originated from which of the following structures?

	Answer	Image
A	Lymphoid tissue in the terminal ileum	
B	Mature hepatocytes in the liver	
C	Exocrine ducts in the body of the pancreas	
D	Squamous epithelium in the proximal esophagus	
E	Glandular epithelium in the sigmoid colon	

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Hint

This patient's cancer is associated with an increased CA 19-9 and is typically diagnosed at a late stage because it does not cause symptoms until it has metastasized.

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Correct Answer

A - Lymphoid tissue in the terminal ileum

Explanation Why

Lymphoid tissue in the terminal ileum is consistent with the origin of metastatic MALT lymphoma. Although this patient's age and vague symptoms support this diagnosis, MALT lymphoma is unlikely for two reasons: histopathologic examination of nongastric MALToma shows dense collections of lymphoid cells (rather than secretory cells), and the condition is associated with chronic autoimmune diseases, which this patient does not have.

B - Mature hepatocytes in the liver

Explanation Why

Mature hepatocytes in the liver are consistent with the origin of hepatocellular carcinoma, which is unlikely in this patient, as he has no risk factors for this condition (e.g., cirrhosis, chronic HBV infection, chronic HCV infection). In addition, though HCC itself is often asymptomatic until it is very advanced, it is extremely rare for patients not to have symptoms of underlying cirrhosis and/or hepatitis. Moreover, histopathologic examination of HCC shows cells arranged in trabeculae and can have other features of liver tissue, such as bile inclusions.

C - Exocrine ducts in the body of the pancreas

Explanation But

The tender, erythematous nodules on this patient's right ankle and left antecubital fossa are suggestive of Trousseau syndrome.

Explanation Why

The most likely diagnosis in this patient is pancreatic adenocarcinoma, the most common type of

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pancreatic cancer. The glandular mucin-secreting cells are typical of pancreatic adenocarcinoma, which is derived from exocrine cells of the pancreas. The pancreatic head is the most common site for adenocarcinoma, but cancers that originate there often manifest with pruritus and painless jaundice secondary to obstruction of the common bile duct. Since this patient lacks these symptoms, his cancer more likely originates in the body or tail of the pancreas. No matter where the cancer starts, pancreatic adenocarcinoma does not typically manifest until after it has metastasized, as seen in this patient.

D - Squamous epithelium in the proximal esophagus

Explanation Why

Squamous epithelium in the proximal esophagus is consistent with the origin of esophageal cancer. Although this patient's age and smoking status support this diagnosis, esophageal squamous cell carcinoma is unlikely for two reasons: histopathologic examination shows clusters of squamous cells with keratinization (rather than secretory cells), and this condition typically manifests with progressive dysphagia and retrosternal pain, which this patient does not have.

E - Glandular epithelium in the sigmoid colon

Explanation Why

Glandular epithelium in the sigmoid colon is consistent with the origin of colorectal cancer. Although this patient's age and smoking status support this diagnosis, it is unlikely for two reasons: adenocarcinoma of the colon typically manifests with iron deficiency anemia, hematochezia, and/or changes in bowel habits depending on the cancer location, which this patient does not have. In addition, histopathologic examination of adenocarcinoma of the colon typically shows heaped-up epithelia with nuclear hypochromia, elongation, and stratification.

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Question # 19

A 53-year-old man comes to the physician because of a 2-week history of fatigue, generalized itching, and yellowing of the eyes and skin. He underwent a liver transplantation because of acute liver failure following α-amanitin poisoning 1 year ago. Physical examination shows scleral icterus and abdominal distention with shifting dullness. A liver biopsy specimen shows decreased hepatic duct density. Further histological examination of the liver biopsy specimen is most likely to show which of the following findings?

	Answer	Image
A	Graft vessel vasculitis	
B	Neoplastic cells containing bile	
C	Fibrinoid necrosis	
D	Interstitial fibrosis	
E	Viral inclusions	

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Hint

This patient with a history of liver transplantation is now exhibiting features of liver failure (jaundice, pruritus, fatigue, ascites). Biopsy shows ductopenia, which indicates vanishing bile duct syndrome.

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Correct Answer

A - Graft vessel vasculitis

Explanation Why

Acute rejection occurs within 6 months of transplantation and is due to antibody formation against donor MHCs. It is characterized histologically by vasculitic changes of the graft vessels and an interstitial lymphocytic infiltrate. The timing of the patient's symptoms is inconsistent with acute rejection, as is the biopsy finding of ductopenia.

B - Neoplastic cells containing bile

Explanation Why

Hepatocellular carcinoma may manifest with liver failure, as seen in this patient. However, the incidence of HCC in transplant recipients is only increased in those who were previously diagnosed with HCC, or in those who have recurrent viral hepatitis. Furthermore, HCC is not associated with ductopenia, as seen on this patient's liver biopsy.

C - Fibrinoid necrosis

Explanation Why

Hyperacute rejection occurs within 48 hours of organ transplantation and is due to the reaction of pre-existing antibodies against donor antigens, leading to complement activation and widespread thrombosis and necrosis. It is characterized histologically by fibrinoid necrosis, vessel thrombosis, and tissue ischemia. The timing of the patient's symptoms and ductopenia on biopsy is inconsistent with hyperacute rejection.

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D - Interstitial fibrosis

Explanation Why

Signs and symptoms of liver failure one year after liver transplantation suggests chronic graft rejection, which occurs due to reactions at both the cellular and humoral level in response to donor peptides. The ensuing inflammation leads to interstitial fibrosis, atrophy of the parenchyma, vascular smooth muscle proliferation, and ductopenia (as seen on this patient's biopsy).

E - Viral inclusions

Explanation Why

Cytomegalovirus infection is an important cause of transplant failure in the first 6 months, due to iatrogenic immunosuppression to prevent transplant rejection and subsequent seroconversion (e.g., if the patient was initially seronegative but received a graft from a seropositive donor) or reactivation of the virus. CMV infection typically manifests with fever, malaise, and hepatitis, similarly to acute transplant rejection. A liver biopsy would show viral inclusions, a mononuclear cell infiltrate, and microabscesses. This patient's timeline of hepatic failure one year after transplant makes a different cause and associated finding more likely.

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Question # 20

A 62-year-old man with gastroesophageal reflux disease and osteoarthritis is brought to the emergency department because of a 1-hour history of severe, stabbing epigastric pain. For the last 6 months, he has had progressively worsening right knee pain, for which he takes ibuprofen several times a day. He has smoked half a pack of cigarettes daily for 25 years. The lungs are clear to auscultation. An ECG shows sinus tachycardia without ST-segment elevations or depressions. This patient is most likely to have referred pain in which of the following locations?

	Answer	Image
A	Right scapula	
B	Left shoulder	
C	Umbilicus	
D	Left jaw	
E	Right groin	

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Hint

This man has multiple risk factors for peptic ulcer disease, including smoking, NSAID use, and gastroesophageal reflux disease. The sudden onset of pain is concerning for a perforated peptic ulcer.

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Correct Answer

A - Right scapula

Explanation Why

Cholecystitis, which manifests with RUQ pain, nausea, and vomiting, can cause right scapular pain due to gallbladder-mediated irritation of the right phrenic nerve. This patient's risk factors and symptoms are more consistent with a perforated peptic ulcer, which is associated with referred pain to a different region of the body.

B - Left shoulder

Explanation Why

This patient's history of smoking and chronic NSAID use put him at increased risk of developing peptic ulcers. Perforated gastric ulcers can manifest with the sudden onset of severe abdominal pain, as seen in this patient, and referred pain to the left shoulder due to irritation of the left hemidiaphragm. Both the phrenic nerve (C3-5), which innervates the diaphragm, and the supraclavicular nerves (C3-4), which innervate the shoulder, share sensory fibers from the C3-4 nerve roots.

C - Umbilicus

Explanation Why

Periumbilical pain is seen in conditions that cause irritation of the T10 dermatome, such as in the early stages of appendicitis. This patient's risk factors and symptoms are more consistent with a perforated peptic ulcer, which is associated with referred pain in a different region of the body.

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D - Left jaw

Explanation Why

Referred pain to the jaw can occur in a myocardial infarction and is caused by irritation of nerves of the cervical plexus, which innervate the neck and the jaw. Although this patient's smoking history is a risk factor for coronary artery disease, his normal ECG makes this diagnosis less likely.

E - Right groin

Explanation Why

Referred pain to the groin can occur in conditions that cause irritation to the L1 dermatome, including nephrolithiasis, hip arthritis, and testicular pathology. This patients risk factors and symptoms are more consistent with a perforated peptic ulcer, which is associated with referred pain to a different region of the body.

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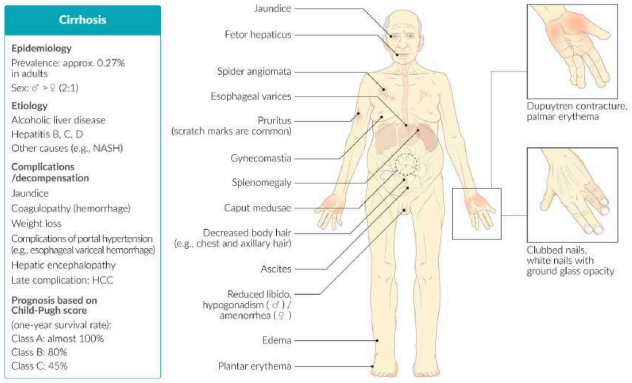
Question # 21

A 36-year-old man is brought to the emergency department by his girlfriend because of increasing confusion for the past 6 hours. He drinks large amounts of alcohol daily and occasionally uses illicit drugs. He is lethargic and oriented only to person. Physical examination shows jaundice, hepatomegaly, and scattered petechiae over the trunk and back. Neurologic examination shows normal, reactive pupils and a flapping tremor when the wrists are extended. A drug with which of the following mechanism of action would be most appropriate for this patient's condition?

	Answer	Image
A	Inhibition of μ-opioid receptors	
B	Inhibition of D2 receptors	
C	Excretion of NH_4	
D	Excretion of free iron	
E	Activation of GABA receptors	
F	Production of NH_3	

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	Answer	Image
G	Production of glutathione	

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Hint

This patient has signs of liver failure (jaundice, petechiae, hepatomegaly) and a history of excessive drinking, which suggests alcoholic cirrhosis. Neurological features like confusion and flapping tremors in this setting indicate hepatic encephalopathy.

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Correct Answer

A - Inhibition of μ-opioid receptors

Explanation Why

Medications that inhibit μ-opioid receptors, e.g., naloxone, can aid in the treatment of opioid overdose. Although opioid overdose can cause lethargy, the increasing confusion and flapping tremor in a patient with features of chronic liver disease suggest hepatic encephalopathy, which requires an alternative treatment.

B - Inhibition of D2 receptors

Explanation Why

Many antipsychotics, e.g., haloperidol, work by inhibiting D2 receptors. These medications may be used for patients with severe agitation from hepatic encephalopathy. However, they would not address the underlying cause of this patient's condition.

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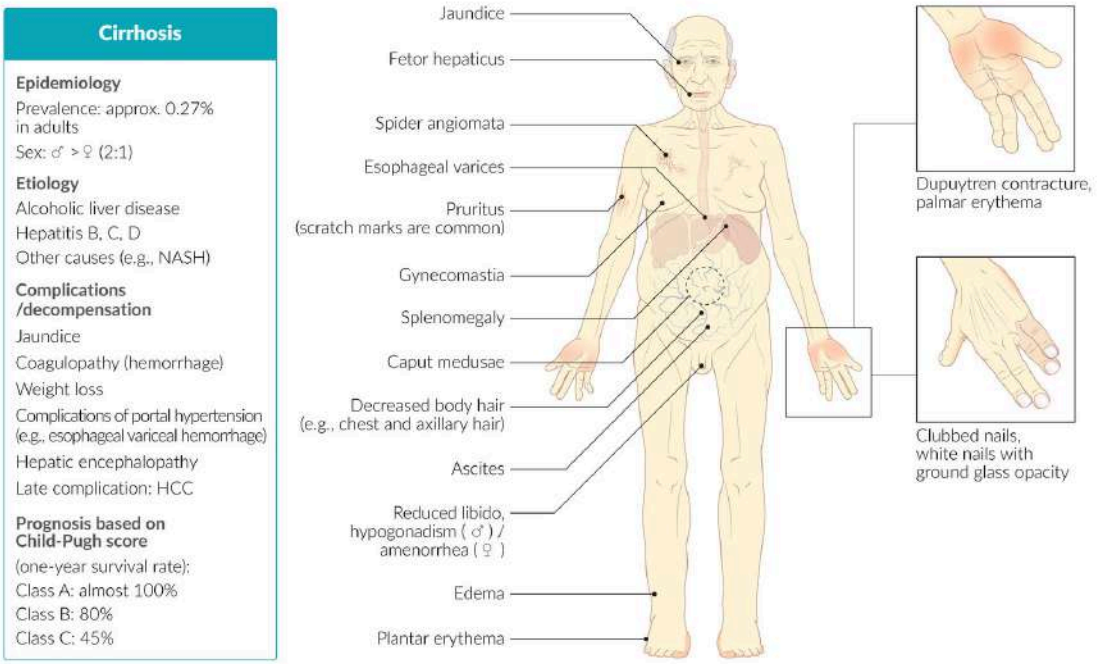
C - Excretion of NH_4

Image



Explanation But

'Disturbances of consciousness, ranging from mild confusion to coma'

Explanation Why

Hepatic encephalopathy is caused by the accumulation of toxic metabolites (predominantly ammonia) in the systemic circulation due to liver failure. Lactulose administered orally (or rectally) is converted to lactic acid in the intestine, leading to acidification in the gut and promoting the conversion of ammonia (NH_3) to ammonium (NH_4^+). Ammonium is not absorbed in the intestine and is instead excreted in feces, reducing the overall systemic load of ammonia.

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D - Excretion of free iron

Explanation Why

Medications like deferoxamine, which chelate iron and lead to its excretion, can be used to treat hemochromatosis. Although hemochromatosis can cause cirrhosis and liver disease, this patient is presenting with hepatic encephalopathy, which requires an alternative treatment.

E - Activation of GABA receptors

Explanation Why

Activation of GABA receptors by medications like benzodiazepines can be used to sedate agitated patients. However, in patients with hepatic encephalopathy and liver disease, administration of benzodiazepines can quickly result in oversedation and should therefore generally be avoided. Medications that treat the underlying cause of encephalopathy should be favored.

F - Production of NH_3

Explanation Why

As hepatic encephalopathy is caused by accumulation of toxic metabolites like ammonia (NH_3), increased production of NH_3 would exacerbate rather than improve the condition. Medications like rifaximin or neomycin can decrease production of NH_3 by killing NH_3-producing bacteria in the gut and are potential treatment options for hepatic encephalopathy.

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G - Production of glutathione

Explanation Why

Increased glutathione production is the mechanism of N-acetylcysteine, a medication that can be used to help protect the liver from oxidative injury from acetaminophen overdose. Although this patient has signs of liver failure – including jaundice, hepatomegaly, and petechiae – increased confusion and a flapping tremor suggest hepatic encephalopathy, which requires an alternative treatment.

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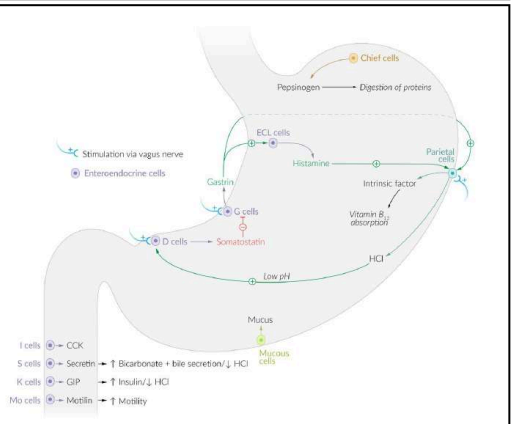
Question # 22

A 44-year-old woman with hypothyroidism comes to the physician because of a 1-month history of tingling in her feet and poor balance. Her only medication is levothyroxine. Physical examination shows conjunctival pallor and an ataxic gait. Proprioception and sense of vibration are decreased in her toes bilaterally. Laboratory studies show macrocytic anemia and normal thyroid hormone levels. Histological evaluation of tissue samples obtained by esophagogastroduodenoscopy reveals atrophic changes of the gastric body and fundus with normal antral mucosa. Which of the following structures is most likely being targeted by antibodies in this patient?

	Answer	Image
A	Islet cell cytoplasm	
B	Deamidated gliadin peptide	
C	Parietal cells	
D	Smooth muscle	
E	Erythrocytes	

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Hint

Anemia, gait ataxia, and neurological symptoms (e.g., paresthesias, sensory deficits, hyperreflexia) are signs of vitamin B_{12} deficiency. This patient's symptoms and EGD findings suggest a diagnosis of pernicious anemia and atrophic gastritis, which is often associated with other autoimmune diseases (particularly vitiligo and Hashimoto thyroiditis).

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Correct Answer

A - Islet cell cytoplasm

Explanation But

Type 1DM is also associated with other autoimmune conditions such as Hashimoto thyroiditis and/or vitiligo.

Explanation Why

Type 1 diabetes mellitus is characterized by the presence of autoantibodies against pancreatic islet cells (e.g., anti-islet cell, anti-glutamic acid decarboxylase). Patients with this condition have an insulin deficiency and may develop peripheral neuropathy due to poor glycemic control. However, the anemia and atrophic gastritis described here are not common features of type 1 DM.

B - Deamidated gliadin peptide

Explanation Why

IgG antibodies against deamidated gliadin peptides are characteristic of celiac disease, which can also cause anemia due to iron malabsorption. Laboratory studies would show microcytic anemia rather than the macrocytic anemia seen in this patient. Additionally, neurologic deficits and atrophic gastritis are not consistent with celiac disease.

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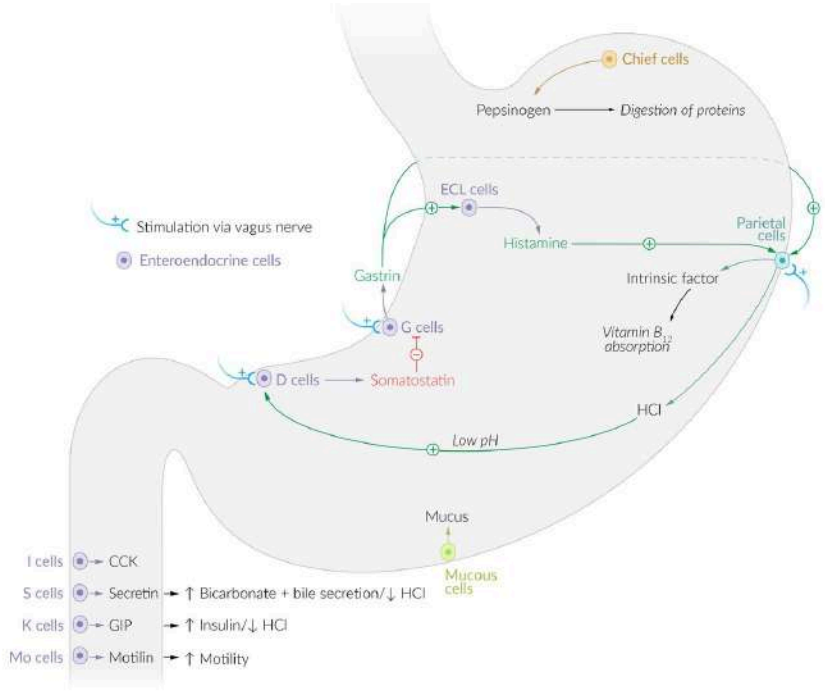
C - Parietal cells

Image



Explanation Why

Pernicious anemia is a common cause of vitamin B12 deficiency and is associated with both antiparietal cell antibodies and anti-intrinsic factor antibodies. Antibody-mediated destruction of parietal cells leads to decreased intrinsic factor production, resulting in impaired vitamin B12 absorption in the terminal ileum, and subsequent vitamin B12 deficiency, as seen in this patient. Vitamin B12 deficiency classically manifests with macrocytic anemia, peripheral neuropathy, and symptoms of subacute combined degeneration of spinal cord.

D - Smooth muscle

Explanation Why

Anti-smooth muscle antibodies are typically seen in patients with autoimmune hepatitis, which is

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commonly associated with other autoimmune conditions. Symptomatic patients with this condition may present with jaundice, hepatosplenomegaly, and pruritus. Anemia, neurologic deficits, and atrophic gastritis are not common features of autoimmune hepatitis.

E - Erythrocytes

Explanation Why

Antibodies against RBCs are seen in autoimmune hemolytic anemia (AIHA). The condition typically manifests with anemia and symptoms of hemolysis (e.g., jaundice). Neurologic deficits, macrocytic anemia, and atrophic gastritis are not common features of hemolytic anemia.

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Question # 23

A 37-year-old woman comes to the physician because of a 6-month history of weight loss, bloating, and diarrhea. She does not smoke or drink alcohol. Her vital signs are within normal limits. She is 173 cm (5 ft 8 in) tall and weighs 54 kg (120 lb); BMI is 18 kg/m^2. Physical examination shows bilateral white spots on the temporal half of the conjunctiva, dry skin, and a hard neck mass in the anterior midline that does not move with swallowing. Urinalysis after a D-xylose meal shows an increase in renal D-xylose excretion. Which of the following is most likely to have prevented this patient's weight loss?

	Answer	Image
A	Gluten-free diet	
B	Pancreatic enzyme replacement	
C	Tetracycline therapy	
D	Mesalamine therapy	
E	Lactose-free diet	

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Hint

This patient has xeroderma and keratin deposits on the conjunctivae (Bitot's spots), which are features suggestive of vitamin A deficiency.

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Correct Answer

A - Gluten-free diet

Explanation Why

A gluten-free diet is the treatment of celiac disease, an autoimmune disorder involving hypersensitivity to gliadin in gluten. Celiac disease can also present with weight loss, diarrhea, bloating, and cutaneous manifestations, as in this patient. However, instead of xeroderma, skin manifestations include papules and vesicles on the extensor surfaces (dermatitis herpetiformis). The D-xylose test would also have shown decreased xylose excretion due to malabsorption. Celiac disease would also not explain this patient's hard anterior neck mass.

B - Pancreatic enzyme replacement

Explanation Why

This patient's hard, immobile neck mass in the anterior midline is suggestive of Riedel's thyroiditis, which is associated with other IgG4-related systemic diseases. Her xeroderma and Bitot's spots indicate a vitamin A deficiency, and her weight loss, diarrhea, and increased D-xylose excretion indicate exocrine pancreatic insufficiency, most likely due to an autoimmune pancreatitis. Pancreatic enzyme replacement would be the preventative treatment.

C - Tetracycline therapy

Explanation Why

A therapy regimen of tetracycline in combination with folic acid would be a treatment of tropical sprue. This condition can cause diarrhea and a deficiency of fat-soluble vitamins like vitamin A. However, it is unlikely to manifest with an anterior neck mass or a normal result on the D-xylose test since it would be associated with intestinal malabsorption. Tropical sprue would also more likely present following travel to the tropics.

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D - Mesalamine therapy

Explanation Why

Mesalamine therapy is a treatment for ulcerative colitis, which can cause chronic diarrhea, bloating, and weight loss, as in this patient. However, it does not manifest with an anterior neck mass or normal findings on the D-xylose test since it is associated with intestinal malabsorption. Instead of Bitot's spots, expected ophthalmologic findings would be uveitis or episcleritis.

E - Lactose-free diet

Explanation Why

A lactose-free diet would prevent symptoms in the condition of lactose intolerance, a deficiency of the lactase enzyme. Lactose intolerance manifests with diarrhea and a normal result of the D-xylose test, as in this patient. However, the symptoms only follow the consumption of dairy products. The condition is also not be associated with either an anterior neck mass or a deficiency of fat-soluble vitamins like vitamin A.

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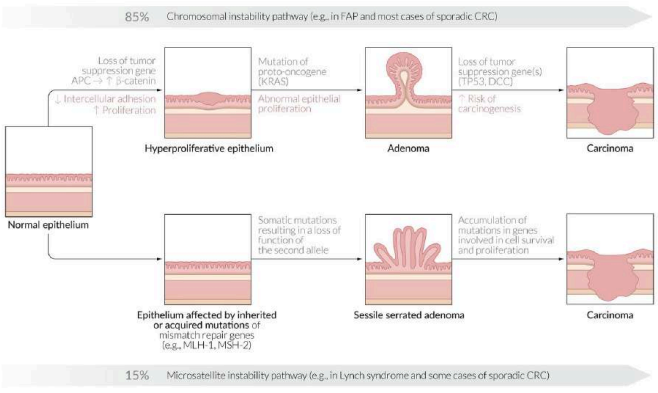
Question # 24

A 62-year-old man comes to the physician because of progressive fatigue and dyspnea on exertion for 3 months. During this time, he has also had increased straining during defecation and a 10-kg (22-lb) weight loss. He has no personal or family history of serious medical illness. Physical examination shows conjunctival pallor. Laboratory studies show microcytic anemia. Test of the stool for occult blood is positive. Colonoscopy shows an exophytic mass in the ascending colon. Pathologic examination of the mass shows a well-differentiated adenocarcinoma. A gain-of-function mutation in which of the following genes is most likely involved in the pathogenesis of this patient's condition?

	Answer	Image
A	DCC	
B	TP53	
C	MLH1	
D	APC	
E	KRAS	

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Hint

This patient has iron deficiency anemia (progressive fatigue, dyspnea, conjunctival pallor, microcytic anemia, positive stool occult blood) secondary to a well-differentiated, sporadic, right-sided colorectal carcinoma. Most sporadic cases of colorectal carcinoma progress from adenoma to carcinoma due to chromosomal instability.

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Correct Answer

A - DCC

Explanation Why

A loss-of-function mutation (not a gain-of-function mutation) in the tumor suppressor gene Deleted in Colon Cancer (*DCC*) is a late event in the chromosomal instability pathway (i.e., the adenoma-carcinoma sequence) and promotes malignant transformation of an adenoma to a carcinoma.

B - TP53

Explanation Why

A loss-of-function mutation (not a gain-of-function mutation) in the tumor suppressor gene *TP53* is a late event in the chromosomal instability pathway (i.e., the adenoma-carcinoma sequence) and promotes malignant transformation of an adenoma to a carcinoma. Normally, *TP53* is activated in response to DNA damage and ultimately inhibits G1-S progression and allows DNA repair to occur. *TP53* can also activate apoptosis if DNA damage is irreparable. Mutations in *TP53*, therefore, result in unregulated progression through the cell cycle and accumulation of genetic errors. Loss-of-function mutations in *TP53* are associated with most human cancers and Li-Fraumeni syndrome.

C - MLH1

Explanation Why

The microsatellite instability pathway is characterized by a loss-of-function mutation (not a gain-of-function mutation) or epigenetic silencing (i.e., promoter hypermethylation) of mismatch repair genes, including *MLH1*, and can result in the development of colorectal carcinoma. This mechanism underlies Lynch syndrome. However, it is an uncommon cause of sporadic cases of colorectal carcinoma.

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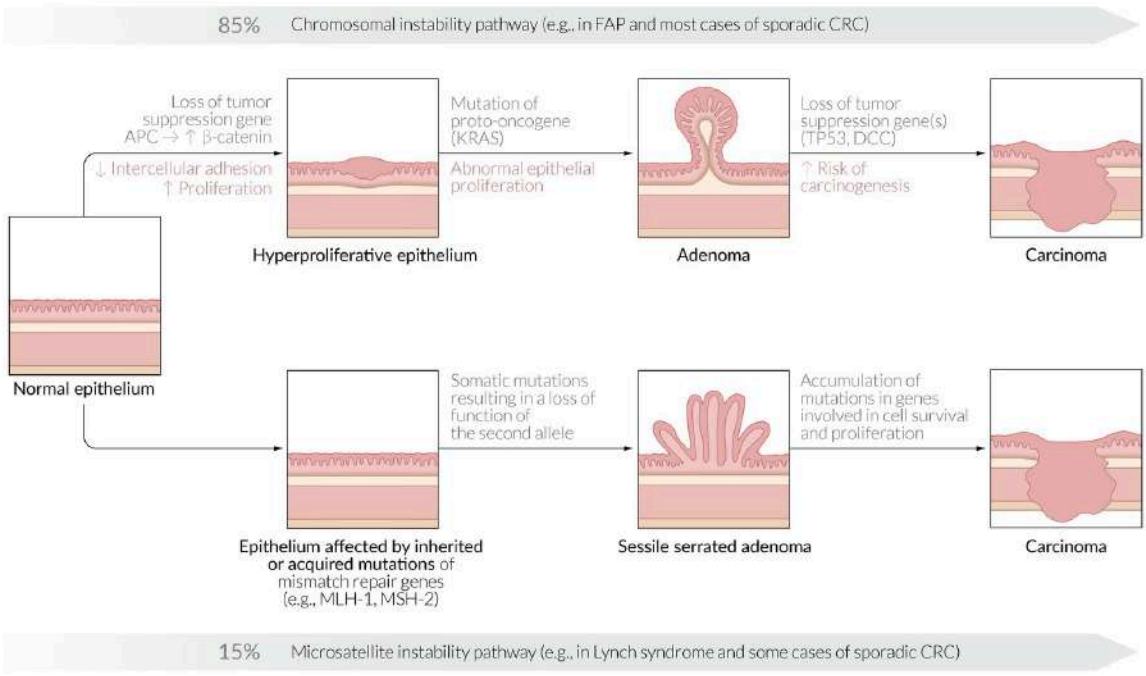
D - APC

Explanation Why

A loss-of-function mutation (not a gain-of-function mutation) of the tumor suppressor gene *APC* is the initiating event in the chromosomal instability pathway (i.e., the adenoma-carcinoma sequence). This loss-of-function mutation results in decreased intercellular adhesion and increased epithelial proliferation in the colon. Loss-of-function mutations in *APC* also underlie familial adenomatous polyposis, an inherited syndrome that predisposes to colorectal cancer formation.

E - KRAS

Image



Explanation But

Gain-of-function mutations in *KRAS* are also associated with lung cancer and pancreatic cancer.

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Explanation Why

Most sporadic cases of colorectal carcinoma arise from the chromosomal instability pathway (i.e., the adenoma-carcinoma sequence). In this pathway, a loss-of-function mutation of the tumor suppressor gene *APC* results in decreased intercellular adhesion and increased epithelial proliferation. Next, a gain-of-function mutation in the *KRAS* proto-oncogene results in unregulated cellular signaling and cellular proliferation, which predisposes to adenoma formation. Finally, loss-of-function mutations of additional tumor suppressor genes (e.g., *TP53*, *DCC*) results in malignant transformation of an adenoma to a carcinoma.

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Question # 25

An investigator is studying gastric secretions in human volunteers. Measurements of gastric activity are recorded after electrical stimulation of the vagus nerve. Which of the following sets of changes is most likely to occur after vagus nerve stimulation?

	Somatostatin secretion	Gastrin secretion	Gastric pH
A	↑	↑	↓
B	↓	↑	↓
C	↑	↑	↑
D	↓	↓	↓
E	↑	↓	↑

	Answer	Image
A	A	
B	B	
C	C	
D	D	
E	E	

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Hint

The vagus nerve is part of the parasympathetic nervous system. Vagal stimulation promotes digestive processes by stimulating G cells.

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Correct Answer

A - A

Explanation Why

High gastrin levels and low gastric pH would be suggestive of gastrinoma (Zollinger-Ellison syndrome). Low gastric pH secondary to increased acid production would stimulate D cells to produce somatostatin. However, vagal stimulation would not be consistent with this combination of findings.

B - B

Explanation Why

Stimulation of the vagus nerve activates gastric G cells via gastrin-releasing peptide (GRP). G cells produce and release gastrin, which stimulates parietal cells directly and through histamine release from enterochromaffin-like cells. Vagus nerve stimulation also leads to ACh-mediated direct activation of parietal cells and inhibition of somatostatin-producing D cells. The resulting activation of proton pumps in parietal cells increases acid production, which lowers gastric pH.

C - C

Explanation Why

Somatostatin inhibits the activity of G cells and parietal cells, resulting in decreased gastric acid production, which results in high gastric pH. However, somatostatin also inhibits gastrin secretion, so this combination is not physiologically possible. The increased somatostatin seen with this option is not consistent with vagal nerve stimulation.

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D - D

Explanation Why

Somatostatin inhibits the activity of G cells and parietal cells. Vagal stimulation causes a decrease in somatostatin levels and subsequent increase in gastric acid production, which results in low gastric pH. However, increased gastrin release from G cells would also be expected.

E - E

Explanation Why

High somatostatin levels in conjunction with low gastrin levels and increased pH are seen in fasting state metabolism. Somatostatin release inhibits gastric acid production and decreases gastrin release.

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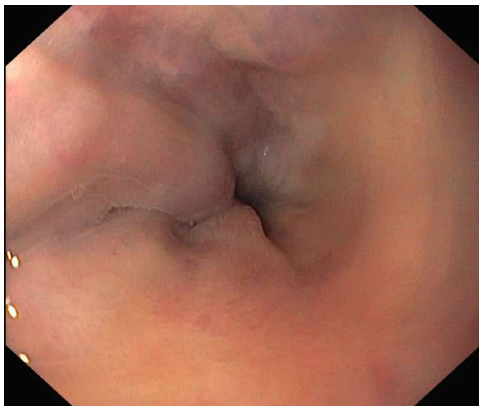
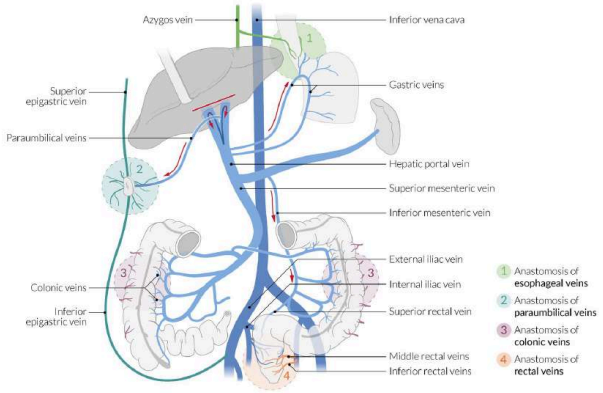
Question # 26

A 65-year-old man comes to the physician because of progressive abdominal distension and swelling of his legs for 4 months. He has a history of ulcerative colitis. Physical examination shows jaundice. Abdominal examination shows shifting dullness and dilated veins in the periumbilical region. This patient's abdominal findings are most likely caused by increased blood flow in which of the following vessels?

	Answer	Image
A	Left gastric vein	
B	Hepatic vein	
C	Splenic vein	
D	Superior epigastric vein	

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	Answer	Image
E	Superior mesenteric vein	
F	Superior rectal vein	

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Hint

Ascites (shifting dullness), edema, jaundice, and dilated veins in the periumbilical region suggest cirrhosis. His history of ulcerative colitis makes primary sclerosing cholangitis a likely cause. The dilated periumbilical veins (caput medusae) are formed by portosystemic shunts.

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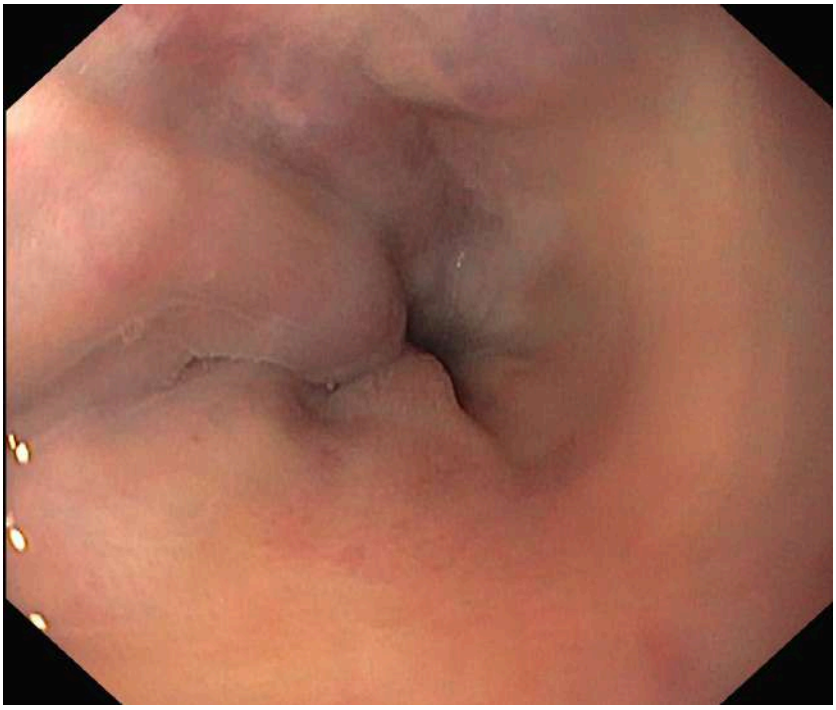
Correct Answer

A - Left gastric vein

Image



Explanation Why

Increased flow in the left gastric vein is not responsible for this patient's abdominal findings. The left gastric vein is a site of a portosystemic shunt, connecting the left gastric vein (portal circulation) and the esophageal veins (systemic circulation via the azygous vein), causing esophageal varices.

B - Hepatic vein

Explanation Why

Increased flow in the hepatic vein is not responsible for this patient's abdominal findings. In portal hypertension, hepatic vein flow would be decreased as hepatic inflow via the portal vein is markedly

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reduced.

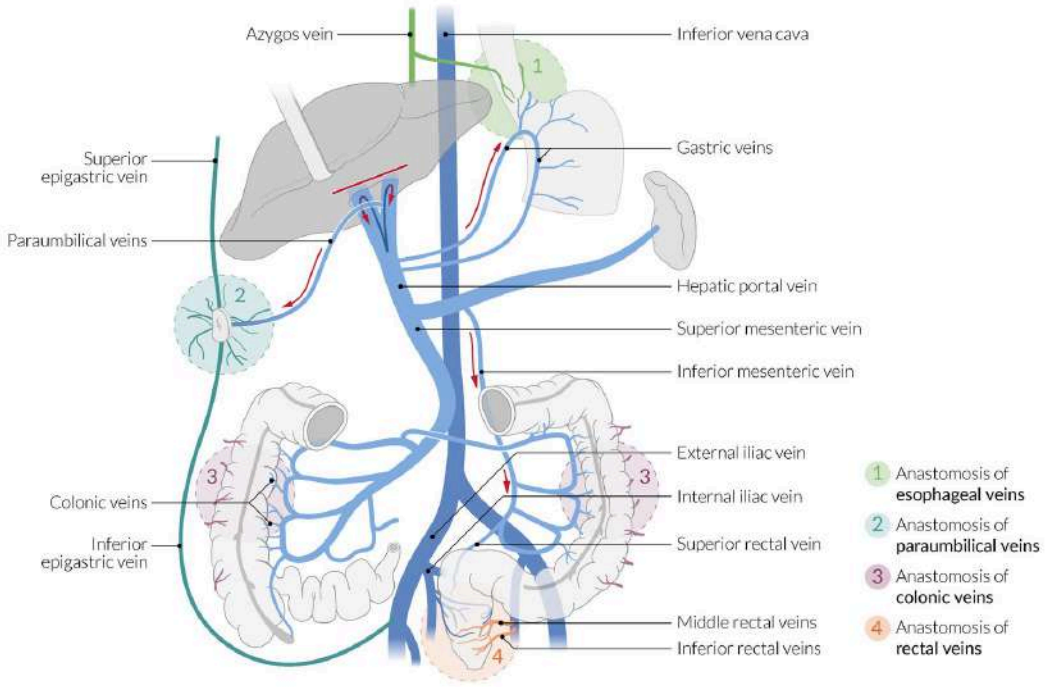
C - Splenic vein

Explanation Why

Increased flow in the splenic vein is not responsible for this patient's abdominal findings. In portal hypertension, the splenic vein decompresses via the renal and lumbar veins into systemic circulation, causing spleno-renal and spleno-lumbar shunts.

D - Superior epigastric vein

Image



Explanation But

In patients with cirrhosis, ascites is partly caused by the increased hydrostatic pressures present in portal hypertension. Impaired hepatic protein synthesis (especially albumin) also leads to a reduced

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intravascular oncotic pressure that exacerbates ascites. Additionally, splanchnic vasodilation in patients with cirrhosis results in underfilling of the systemic arterial system, which activates the RAAS. Activation of RAAS leads to Na^+ and water retention, which aggravates ascites and peripheral edema.

Explanation Why

The veins of the abdominal wall (e.g., inferior epigastric vein, superior epigastric vein) drain into the systemic circulation inferiorly via the iliofemoral system and superiorly via the veins of the thoracic wall and axilla. The umbilical vein drains venous blood from the paraumbilical veins into the portal system but it is normally a low-flow vein. Portal hypertension is associated with an impedance to flow in the hepatic portal venous system. This results in a retrograde flow of blood from the portal via the umbilical vein into the epigastric veins so that blood can be shunted into systemic circulation (portocaval anastomoses). This shunting of blood causes the paraumbilical abdominal wall veins to dilate, resulting in caput medusae. Other manifestations of portocaval shunting include esophageal varices (shunting between the left gastric vein and esophageal veins) and rectal varices (shunting between the superior rectal vein and middle or inferior rectal veins).

E - Superior mesenteric vein

Explanation Why

Increased flow in the superior mesenteric vein (SMV) is not responsible for this patient's abdominal findings. In portal hypertension, collateral vessels from the SMV and inferior mesenteric veins dilate and ultimately drain into the inferior vena cava via the pelvic veins and veins of Retzius (retroperitoneal shunts).

F - Superior rectal vein

Explanation Why

Increased flow in the superior rectal vein is not responsible for this patient's abdominal findings. Normally, the superior rectal vein drains into the inferior mesenteric vein, which drains into the portal vein. In portal hypertension, porto-systemic anastomoses between the superior rectal vein (portal circulation) and the inferior and middle rectal veins (systemic circulation) dilate, causing rectal varices.

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Question # 27

A 75-year-old man comes to the physician because of a 3-month history of upper abdominal pain, nausea, and sensation of early satiety. He has also had a 9.4-kg (20.7-lb) weight loss over the past 4 months. He has osteoarthritis. He drinks two beers every night with dinner. His only medication is ibuprofen. Esophagogastroduodenoscopy shows an ulcerated mass in the lesser curvature of the stomach. A biopsy specimen obtained during endoscopy shows irregular-shaped tubules with intraluminal mucus and debris. Which of the following is the most likely predisposing factor for this patient's condition?

	Answer	Image
A	Inflammatory bowel disease	
B	NSAID use	
C	Low-fiber diet	
D	Low body weight	
E	Dietary nitrates	
F	Blood type O	

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Hint

This patient with dyspepsia, early satiety, and weight loss, most likely has gastric cancer. The biopsy findings indicate a tubular adenocarcinoma, an intestinal type of gastric cancer.

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Correct Answer

A - Inflammatory bowel disease

Explanation Why

Inflammatory bowel diseases (e.g., Crohn disease, ulcerative colitis) are not commonly associated with an increased risk of intestinal-type gastric cancer. They are, however, a significant risk factor for colorectal cancers.

B - NSAID use

Explanation Why

Regular use of NSAIDs (e.g., ibuprofen) has been associated with a decreased, not increased, risk of intestinal-type gastric cancer. NSAIDs are thought to have an inhibitory effect on carcinogenesis because of their antiproliferative and anti-inflammatory action.

C - Low-fiber diet

Explanation Why

A low-fiber diet is not commonly associated with an increased risk of intestinal-type gastric cancer. It is, however, a risk factor for colorectal cancers.

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D - Low body weight

Explanation Why

Low body weight is not associated with a higher incidence of intestinal-type gastric cancer. Conversely, obesity is a major risk factor for several types of cancers, including gastric cancer.

E - Dietary nitrates

Explanation Why

Nitrates can be found in smoked, dried, and preserved food. Increased consumption of dietary nitrates is associated with an increased risk of intestinal-type gastric cancer. Other risk factors include tobacco use, chronic gastritis, and infection with *H. pylori*.

F - Blood type O

Explanation Why

Blood type O is not associated with a higher incidence of intestinal-type gastric cancer. However, the risk of gastric cancer and *H. pylori* infection has been shown to be higher in individuals with blood type A.

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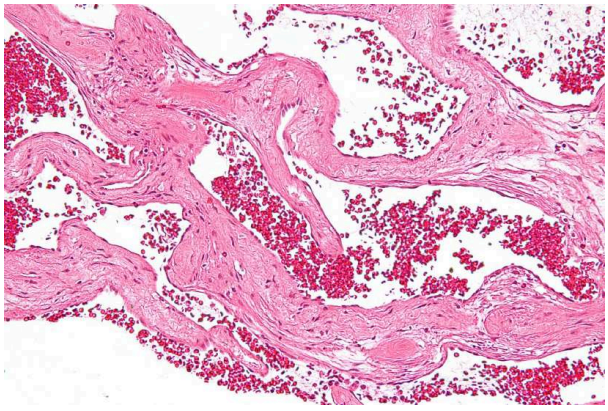
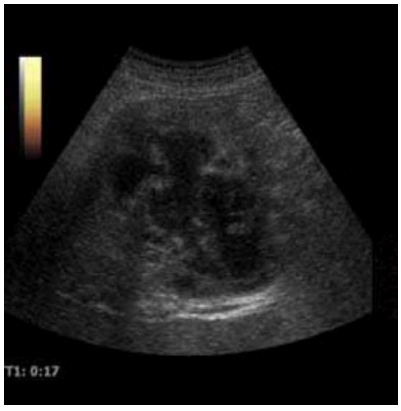
Question # 28

A 45-year-old woman comes to the physician because of a 3-month history of mild right upper abdominal pain. She has not had any fevers, chills, or weight loss. There is no personal or family history of serious illness. Medications include transdermal estrogen, which she recently started taking for symptoms related to menopause. Abdominal examination shows no abnormalities. Ultrasonography of the liver shows a well-demarcated, homogeneous, hyperechoic mass surrounded by normal liver tissue. A biopsy of the lesion would put this patient at greatest risk for which of the following complications?

	Answer	Image
A	Intraperitoneal hemorrhage	
B	Biliary peritonitis	
C	Bacteremia	
D	Metastatic spread	

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	Answer	Image
E	Anaphylactic shock	

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Hint

The ultrasound findings in this patient are consistent with cavernous hemangioma, the most common type benign liver tumor.

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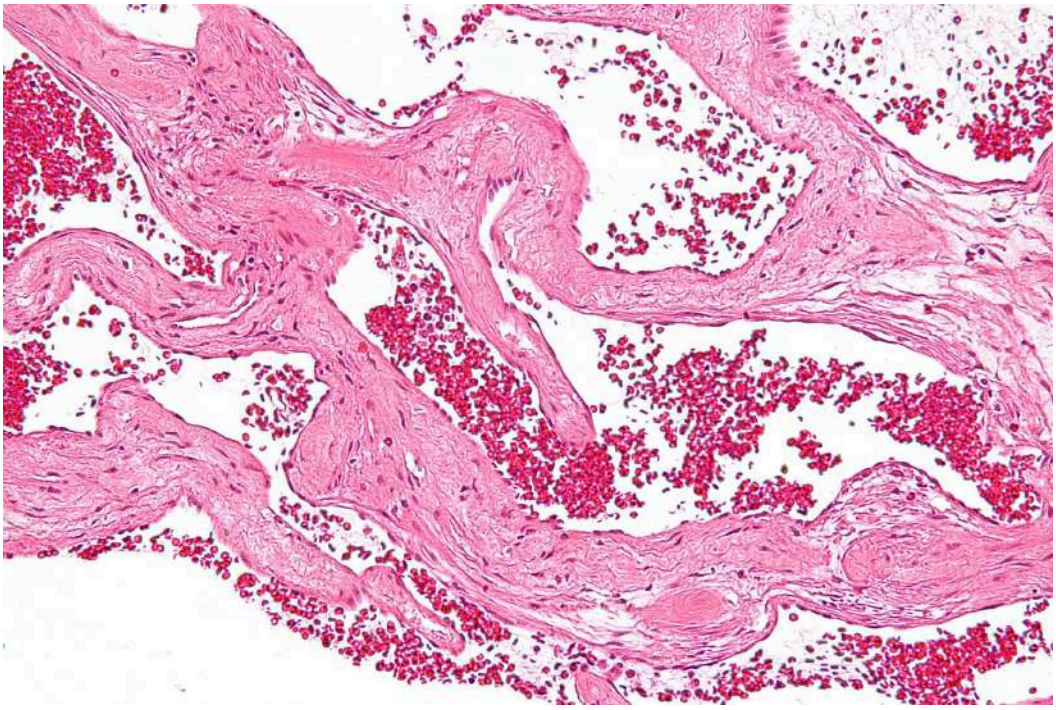
Correct Answer

A - Intraperitoneal hemorrhage

Image



Explanation Why

Hepatic hemangioma is a benign tumor composed of cavernous vascular spaces of variable size that are lined by flat endothelial cells. They are most common in women between the ages of 30-50 years old and may become enlarged during hormonal therapy. Most hepatic hemangiomas are asymptomatic and diagnosed incidentally on imaging, appearing hyperechogenic (due to increased vascularity), well-demarcated, and homogeneous. Being a highly vascular tumor, biopsy represents a high risk of severe hemorrhage and is not recommended unless the diagnosis is uncertain.

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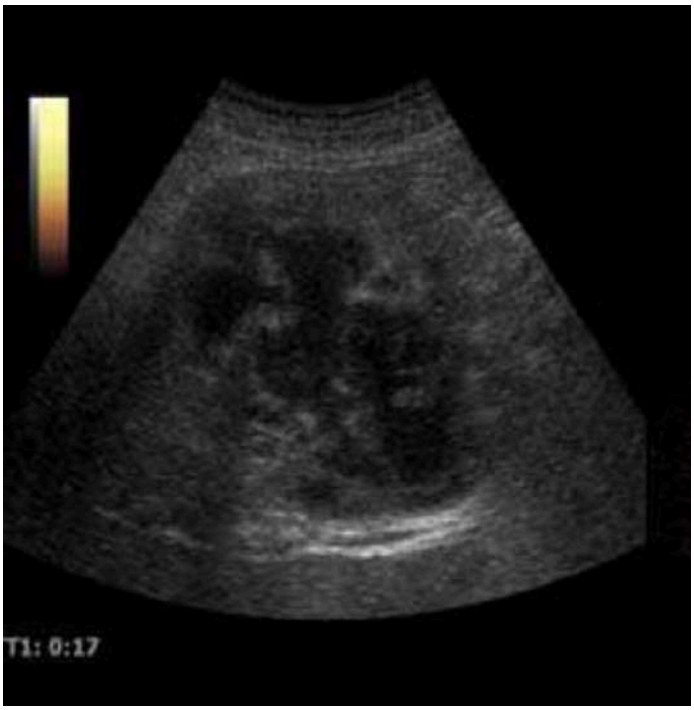
B - Biliary peritonitis

Explanation Why

Biliary peritonitis occurs when bile leaks out of the gallbladder or bile ducts and can occur due to inadvertent penetration of the biliary tract during a liver biopsy. Although this is a possible complication of liver biopsy for any condition, it is extremely rare and thus does not present the complication with the greatest risk for this patient.

C - Bacteremia

Image



Explanation Why

Biopsy of an intrahepatic abscess (pyogenic liver abscess or amebic liver abscess) risks spreading the infectious focus into the abdominal cavity and bloodstream and should only be performed when laboratory studies and imaging are inconclusive. Although RUQ pain is a common manifestation of

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liver abscess, most patients also present with fever or other systemic complaints. Ultrasonography of a liver abscess would show poorly demarcated, fluid-filled, hypoechoic lesion(s) within the hepatic parenchyma with surrounding edema and hyperemia, rather than the findings seen here.

D - Metastatic spread

Explanation Why

Biopsy of a malignant hepatic lesion (e.g., hepatocellular carcinoma) can seed tumor cells throughout the track of the biopsy needle, risking metastatic spread. Although HCC may manifest with nonspecific RUQ pain, as seen in this patient, ultrasonography would typically show an ill-defined mass with irregular borders and variable echogenicity with areas of necrosis and calcification. Furthermore, HCC would be unlikely in this healthy woman without any significant past medical history.

E - Anaphylactic shock

Explanation Why

Biopsy of a hepatic hydatid cyst can result in anaphylaxis due to the release of the highly antigenic hydatid fluid. In an unruptured cyst, the echinococcal antigens evade the host's immune system; sudden exposure to hydatid fluid triggers a hyperacute immune reaction. Hepatic hydatid cyst can manifest as non-specific abdominal pain, as seen in this patient, but ultrasonography would typically show a unilocular, anechoic, well-defined cyst with hyperdense internal septa (spoke-wheel pattern), usually with daughter cysts floating within. Furthermore, this patient does not have any stated risk factors for Echinococcal infection (e.g., ingestion of contaminated food, travel to endemic region).

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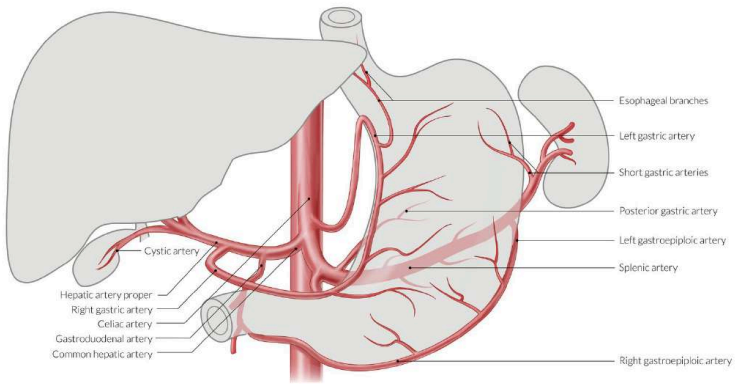
Question # 29

A 68-year-old man with atrial fibrillation comes to the emergency department with acute-onset severe upper abdominal pain. He takes no medications. He is severely hypotensive. Despite maximal resuscitation efforts, he dies. Autopsy shows necrosis of the proximal portion of the greater curvature of the stomach caused by an embolic occlusion of an artery. The embolus most likely passed through which of the following vessels?

	Answer	Image
A	Superior mesenteric artery	
B	Inferior mesenteric artery	
C	Gastroduodenal artery	
D	Right gastric artery	
E	Right gastroepiploic artery	
F	Splenic artery	

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	Answer	Image
G	Left gastric artery	

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Hint

The area of the stomach described in the autopsy report is supplied by the left gastroepiploic artery.

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Correct Answer

A - Superior mesenteric artery

Explanation Why

The superior mesenteric artery supplies the midgut (i.e., from the distal duodenum to the proximal two-thirds of the transverse colon). It does not supply the stomach.

B - Inferior mesenteric artery

Explanation Why

The inferior mesenteric artery supplies the hindgut (i.e., from the distal third of the transverse colon to the anal canal). It does not supply the stomach.

C - Gastroduodenal artery

Explanation Why

The gastroduodenal artery usually arises from the common hepatic artery and divides into the right gastroepiploic artery and the superior pancreaticoduodenal artery. These vessels supply the pylorus, the proximal duodenum, and the pancreatic head, not the proximal portion of the greater curvature of the stomach

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D - Right gastric artery

Explanation Why

The right gastric artery is a branch of the hepatic artery proper and supplies the distal portion of the lesser curvature of the stomach, not the proximal portion of the greater curvature of the stomach.

E - Right gastroepiploic artery

Explanation Why

The right gastroepiploic artery supplies the distal portion of the greater curvature of the stomach, not the proximal portion.

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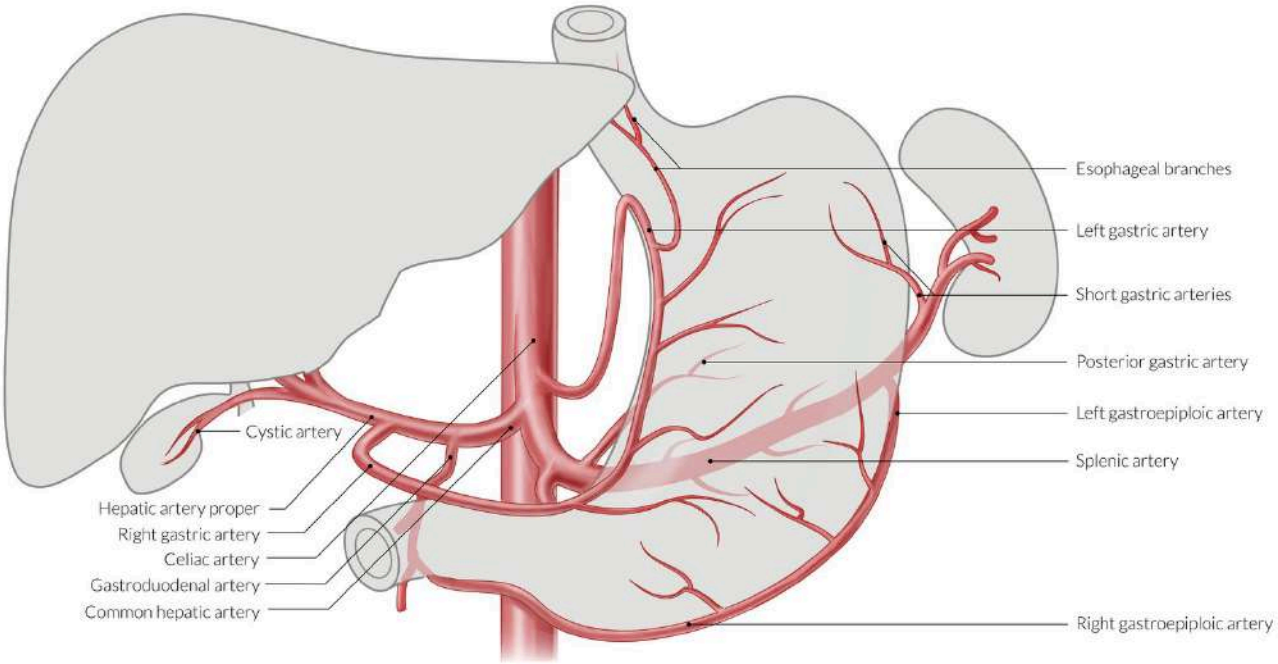
F - Splenic artery

Image



Explanation Why

The proximal portion of the greater curvature (GC) of the stomach is supplied by the short gastric arteries (at the fundus) and the left gastroepiploic artery (proximal GC), both of which arise from the splenic artery. The embolus in question must have passed through the splenic artery to cause necrosis of the proximal GC.

G - Left gastric artery

Explanation Why

The left gastric artery supplies the gastroesophageal junction and the proximal portion of the lesser curvature of the stomach, not the proximal portion of the greater curvature of the stomach.

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Question # 30

A 65-year-old woman comes to the physician because of progressive weight loss for 3 months. Physical examination shows jaundice and a nontender, palpable gallbladder. A CT scan of the abdomen shows an ill-defined mass in the pancreatic head. She is scheduled for surgery to resect the pancreatic head, distal stomach, duodenum, early jejunum, gallbladder, and common bile duct and anastomose the jejunum to the remaining stomach, pancreas, and bile duct. Following surgery, this patient is at the greatest long-term risk for which of the following?

	Answer	Image
A	Hypercoagulable state	
B	Microcytic anemia	
C	Calcium oxalate kidney stones	
D	Wide-based gait	
E	Increased bile production	

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Hint

What substances are absorbed from the lumen of the gastrointestinal tract into the bloodstream in the duodenum only?

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Correct Answer

A - Hypercoagulable state

Explanation Why

A hypercoagulable state may either result from inherited gene mutations or insufficient inhibitors of the coagulation cascade, both of which this patient does not have. However, Whipple procedure involves resection of the first part of the jejunum, which is responsible for the absorption of vitamin K. This may actually contribute to the development of a coagulopathy due to a deficiency of vitamin K-dependent clotting factors.

B - Microcytic anemia

Explanation Why

Patients without a duodenum are prone to developing iron deficiency as iron is solely absorbed in this part of the GI tract. Iron deficiency, in turn, leads to microcytic, hypochromic anemia, which is why this patient may require intravenous iron supplementation.

C - Calcium oxalate kidney stones

Explanation Why

Calcium absorption is mediated through active transport and passive diffusion with the greatest amount being absorbed in the duodenum. When this patient's duodenum is removed, she will have diminished intestinal calcium uptake, which leads to increased reabsorption of calcium in the kidney to maintain normal serum levels. As a result, urinary calcium is low, which decreases the likelihood of calcium oxalate stone formation.

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D - Wide-based gait

Explanation Why

The finding of wide-based gait is commonly associated with long-standing vitamin B12 deficiency, which leads to diminished proprioception in the lower extremities. Common causes of B12 deficiency include pernicious anemia, malnutrition, or gastrectomy. A Whipple procedure, as described in this case, would not alter vitamin B12 absorption as this vitamin is absorbed in the terminal ileum. Moreover, intrinsic factor (IF) function would also remain unaffected despite this patient's distal gastrectomy, because IF is produced by the parietal cells of the stomach (located in the gastric cardia and fundus).

E - Increased bile production

Explanation Why

Bile acids play a pivotal role in the metabolism of lipids and fat-soluble vitamins as well as cholesterol excretion. Bile excretion into the duodenum is stimulated by food intake, which is followed by reabsorption of up to 95% of bile acids in the ileum, not the duodenum. This cycle is known as enterohepatic circulation. Thus, bile synthesis remains unaffected by pancreaticoduodenectomy.

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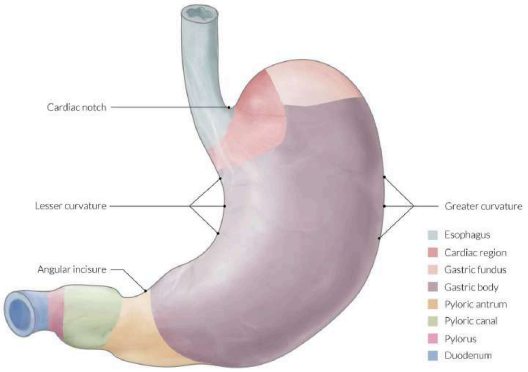
Question # 31

An otherwise healthy 56-year-old man comes to the physician for a 2-year history of recurrent upper abdominal pain and fullness that worsens after meals. Urea breath test is positive. An endoscopy shows diffuse mucosal atrophy and patchy erythema, but no ulcer. A biopsy from which of the following areas is most likely to yield an accurate diagnosis?

	Answer	Image
A	Gastric fundus	
B	Distal esophagus	
C	Gastric antrum	
D	Duodenal bulb	
E	Gastric pylorus	

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Hint

This patient with recurrent upper abdominal pain and fullness after meals (dyspepsia), positive urea breath test, and upper endoscopy findings of diffuse mucosal atrophy and patchy erythema, likely has atrophic gastritis caused by *Helicobacter pylori*.

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Correct Answer

A - Gastric fundus

Explanation Why

H. pylori-induced atrophic gastritis can cause mucosal changes in the fundus, making it an important location to biopsy when *H. pylori* gastritis is suspected but the heaviest infection with *H. pylori* is usually seen in another location. The gastric fundus and body are primarily affected in autoimmune atrophic gastritis, which can present similarly but the urea breath test would be negative and other features suggestive of autoimmune disease (e.g., pernicious anemia, vitiligo, autoimmune thyroiditis) would usually be present.

B - Distal esophagus

Explanation But

Autoimmune atrophic gastritis is a risk factor for the development of squamous cell carcinoma of the esophagus and may require further monitoring. However, squamous cell carcinoma of the esophagus usually affects the proximal, not distal esophagus.

Explanation Why

Distal esophageal biopsies are indicated in patients with treatment-resistant reflux esophagitis to rule out Barrett esophagus and dysplastic changes. This patient's findings, which indicate atrophic gastritis due to *H. pylori* infection, do not necessitate esophageal biopsy because *H. pylori* infection is not associated with an increased risk of esophageal carcinoma.

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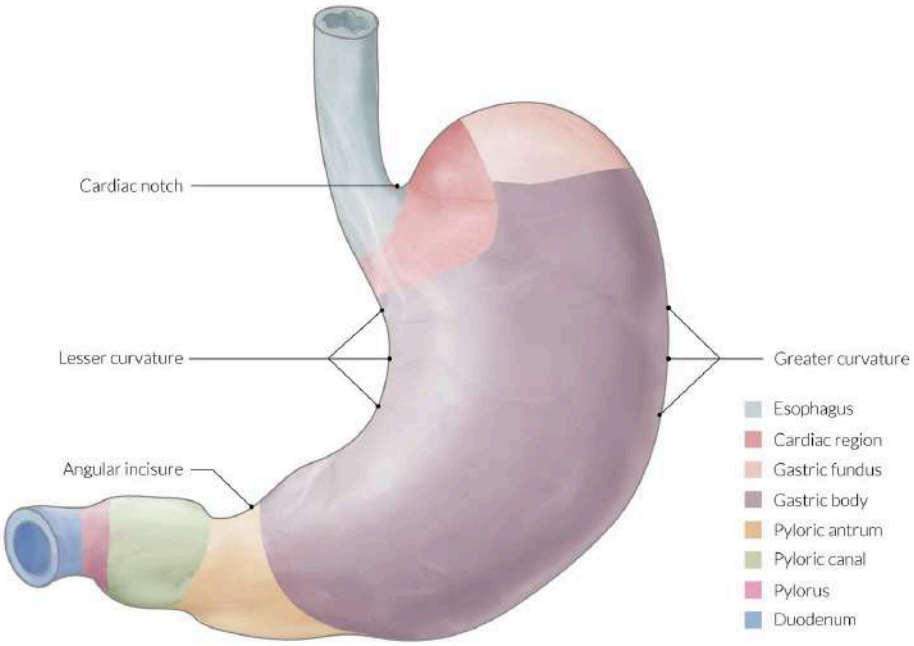
C - Gastric antrum

Image



Explanation But

Persistent dyspepsia in a patient over 55 years of age mandates evaluation with an upper endoscopy, even in the absence of alarm symptoms (dysphagia, unintentional weight loss, hematemesis, or melena), to rule out malignant lesions.

Explanation Why

Chronic atrophic gastritis due to *H. pylori* infection begins in the gastric antrum (pyloric antrum) and then spreads to other regions such as the fundus and body. Biopsies from the gastric antrum are therefore most likely to yield an accurate diagnosis because atrophic changes and *H. pylori* infection load is greatest at this site. Gastric MALToma is a potential complication of *H. pylori* infection. In contrast to *H. pylori*-induced atrophic gastritis, the gastric fundus and body are primarily affected in autoimmune atrophic gastritis, which can present similarly but the urea breath test would be negative and other features suggestive of autoimmune disease (e.g., pernicious anemia, vitiligo, autoimmune thyroiditis) would usually be present. Patients with atrophic gastritis have decreased gastric acid secretion (hypochlorhydria) with a secondary increase in gastrin levels.

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D - Duodenal bulb

Explanation Why

The duodenal bulb is a common location for duodenal ulcers, which are often associated with *H. pylori* infection. However, upper endoscopy findings in this patient show diffuse gastric mucosal atrophy and inflammation without an ulcer, which is consistent with chronic atrophic gastritis rather than peptic ulcer disease. A different site has the heaviest *H. pylori* infection load in patients with chronic atrophic gastritis.

E - Gastric pylorus

Explanation Why

The pylorus is not a common site for atrophic gastritis or for colonization by *H. pylori*. Pyloric biopsies would be indicated in patients with a pyloric mass causing gastric outlet obstruction. Although this man has early satiety, he lacks other symptoms consistent with gastric outlet obstruction, such as postprandial, nonbilious vomiting, progressive gastric dilation, and weight loss.

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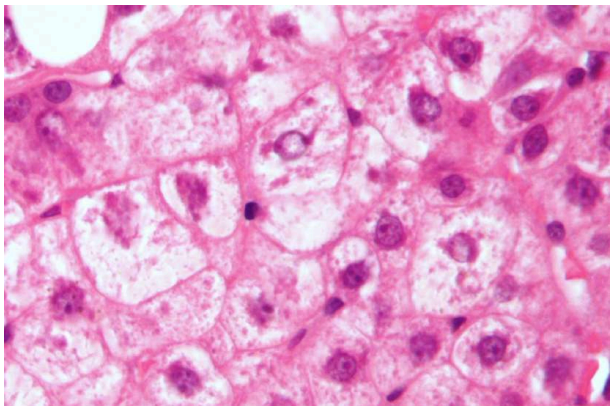
Question # 32

A 38-year-old man is admitted to the hospital because of fever, yellowing of the skin, and nausea for 1 day. He recently returned from a backpacking trip to Brazil and Paraguay, during which he had a 3-day episode of high fever that resolved spontaneously. Physical examination shows jaundice, epigastric tenderness, and petechiae over his trunk. Five hours after admission, he develops dark brown emesis and anuria. Despite appropriate lifesaving measures, he dies. Postmortem liver biopsy shows eosinophilic degeneration of hepatocytes with condensed nuclear chromatin. This patient's hepatocytes were most likely undergoing which of the following processes?

	Answer	Image
A	Necrosis	
B	Regeneration	
C	Apoptosis	
D	Proliferation	

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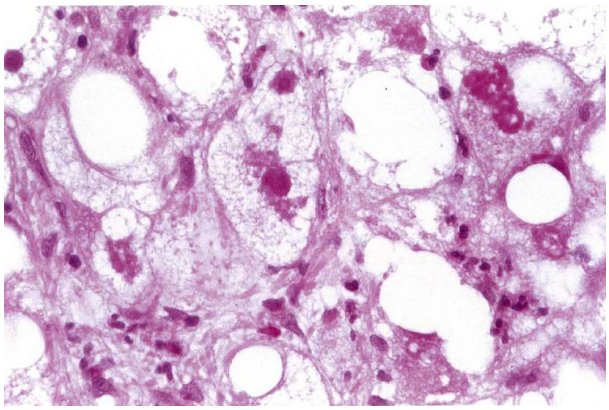
	Answer	Image
E	Steatosis	

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Hint

This patient passed the three clinical stages of yellow fever (infection, remission, intoxication), which is endemic in tropical regions of South America. Liver biopsy shows Councilman bodies, which are typical for yellow fever.

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Correct Answer

A - Necrosis

Explanation Why

Necrosis is the most common mechanism of hepatocellular death in cases of hypoxic or ischemic injury and is characterized by unprogrammed cell death with inflammation. Necrotic hepatocytes appear swollen with prominent membrane blebs and are surrounded by numerous macrophages, unlike the findings that are seen here.

B - Regeneration

Explanation Why

Regenerating hepatocytes may occur in response to cellular injury and would appear as mitotic replication surrounded by areas of cell death. This is not consistent with the biopsy findings in this patient.

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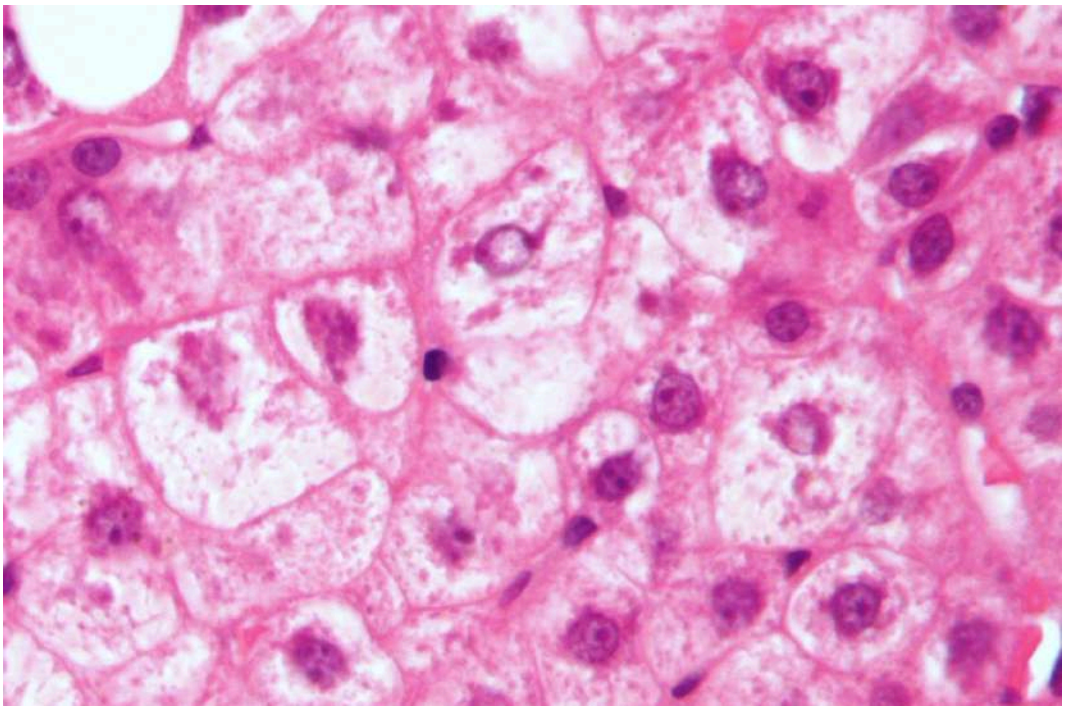
C - Apoptosis

Image



Explanation Why

Apoptosis is the process through which hepatocytes respond to certain hepatotoxic insults such as acute viral hepatitis or yellow fever (as seen here). On liver biopsy, apoptotic hepatocytes appear shrunken and deeply eosinophilic with condensed chromatin (pyknosis) and a fragmented nucleus (karyorrhexis).

D - Proliferation

Explanation Why

Proliferation refers to the rapid division and increase in the number of cells. The proliferation of hepatocytes would be seen with hepatic neoplasms (e.g., hepatocellular carcinoma), but would not be expected with yellow fever liver injury. This patient's liver biopsy findings are not consistent with

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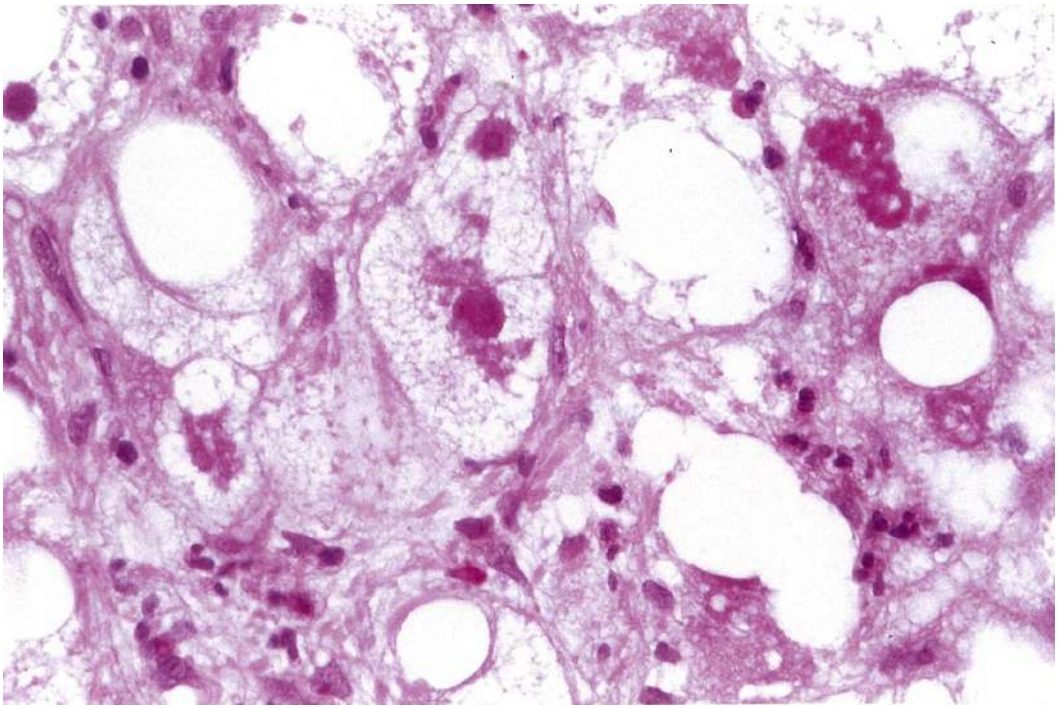
proliferation.

E - Steatosis

Image



Explanation But

Non-alcoholic fatty liver disease is associated with obesity, hyperlipidemia, and insulin resistance and is the most common cause of liver disease worldwide.

Explanation Why

Hepatic steatosis refers to the accumulation of triglycerides and other fats in hepatocytes. Steatosis appears as hepatocytes engorged with fatty droplets and is not consistent with the findings in this patient's biopsy.

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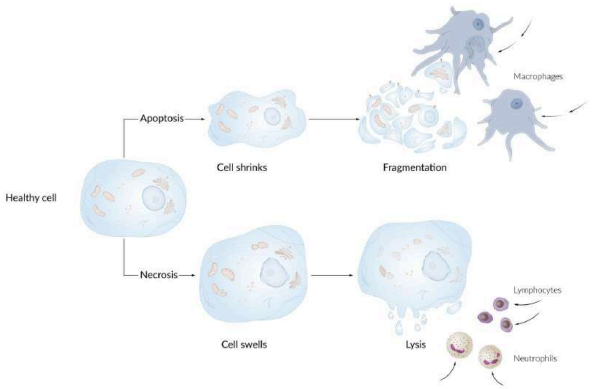
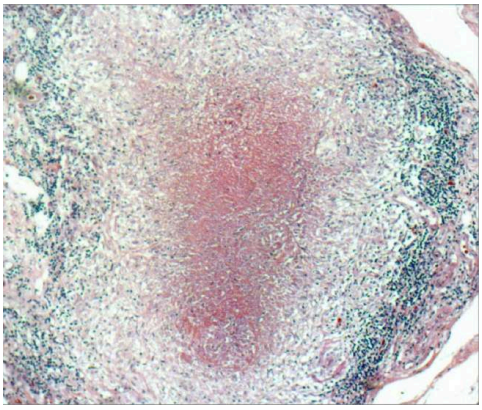
Question # 33

A 31-year-old woman is brought to the emergency department with fever, right upper quadrant pain, and myalgia. Her boyfriend says she recently returned from a trip to Southeast Asia. She appears ill and is lethargic. Her temperature is 39°C (102.2°F). Physical examination shows jaundice and tender hepatomegaly. Laboratory studies show the presence of anti-hepatitis A IgM antibodies. A liver biopsy performed at this time would most likely show which of the following histopathological findings?

	Answer	Image
A	Hepatocytes with shrunken, eosinophilic cytoplasm and pyknotic nuclei	
B	Acellular debris surrounded by lymphocytes and macrophages	

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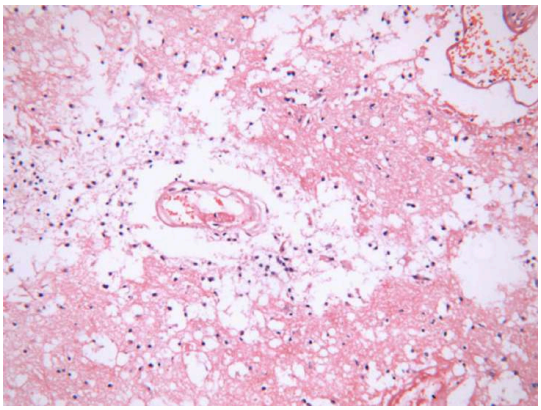
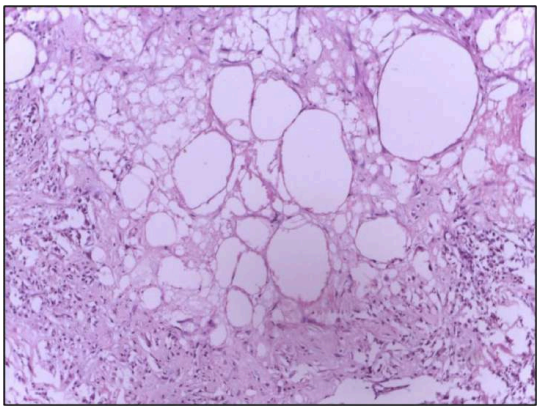
	Answer	Image
C	Cystic spaces with scattered areas of cellular debris	
D	Basophilic adipocyte remnants, filled with calcifications	
E	Engorged hepatocytes with red blood cell infiltration	

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Hint

This patient has acute hepatitis A and biopsy is likely to show findings consistent with apoptosis.

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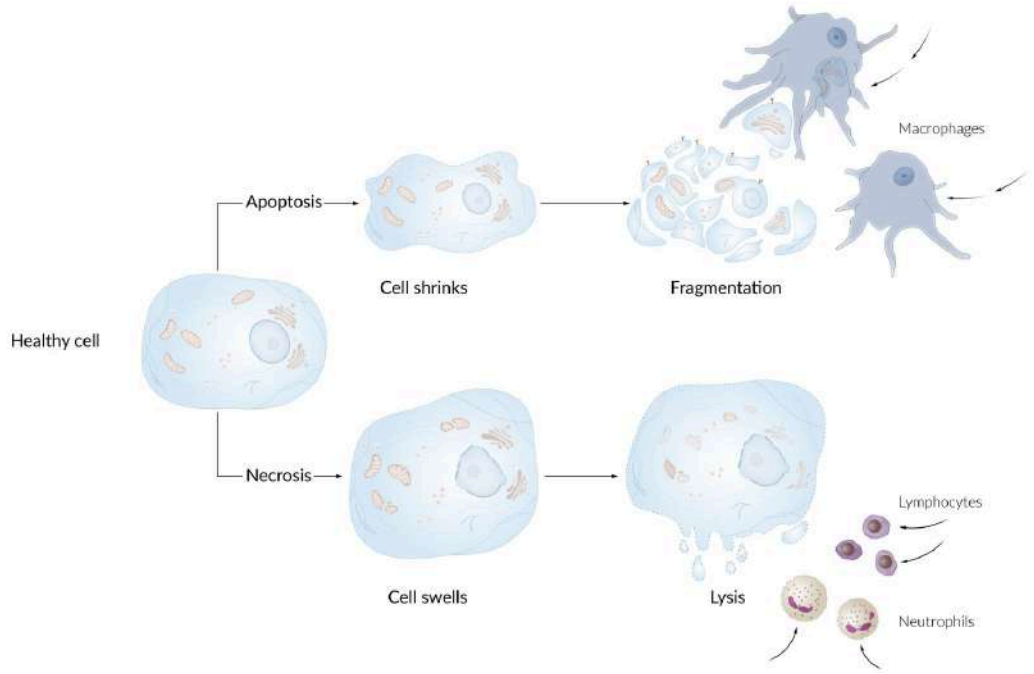
Correct Answer

A - Hepatocytes with shrunken, eosinophilic cytoplasm and pyknotic nuclei

Image



Explanation Why

Hepatocytes with shrunken, eosinophilic cytoplasm and pyknotic nuclei are the histopathological characteristics of Councilman bodies. Councilman bodies are remnants of apoptotic hepatocytes and can be found in patients with acute hepatitis A. Apoptosis of virus-infected cells, such as HAV-infected hepatocytes, is induced by the release of granzyme B and perforin from cytotoxic T cells (the extrinsic pathway of apoptosis). Other histopathological signs in patients with hepatitis A include ballooning degeneration (swelling of hepatocytes) and bridging necrosis (confluent necrosis spanning adjacent lobules).

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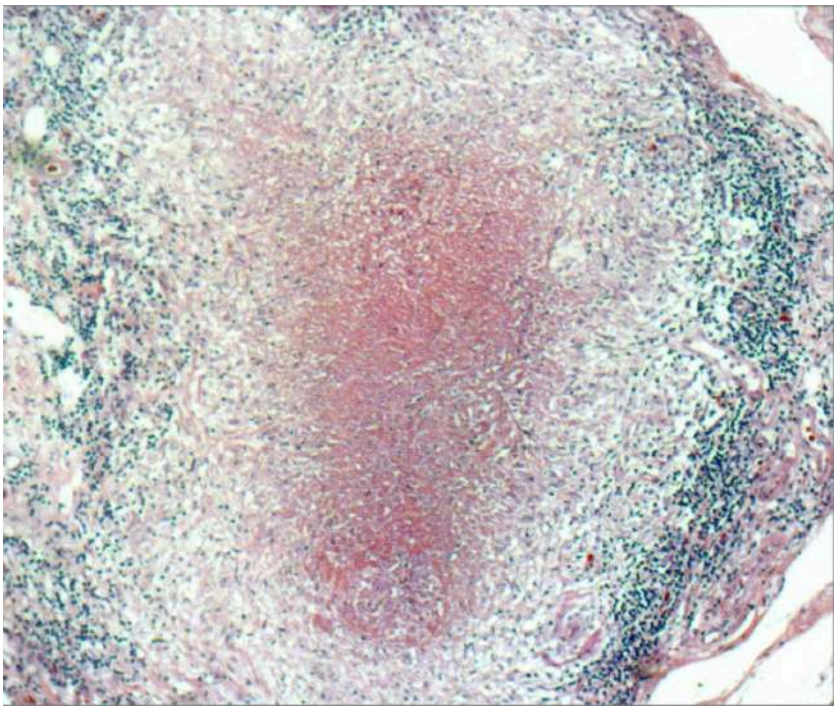
B - Acellular debris surrounded by lymphocytes and macrophages

Image



Explanation Why

Acellular debris with encapsulating inflammatory cells, including lymphocytes and macrophages, is characteristic of caseous necrosis. This process is typically seen in tuberculosis, histoplasmosis, cryptococcosis, and coccidioidomycosis, each of which could cause focal necrosis in the liver. However, hepatitis A is not associated with the formation of caseous necrosis.

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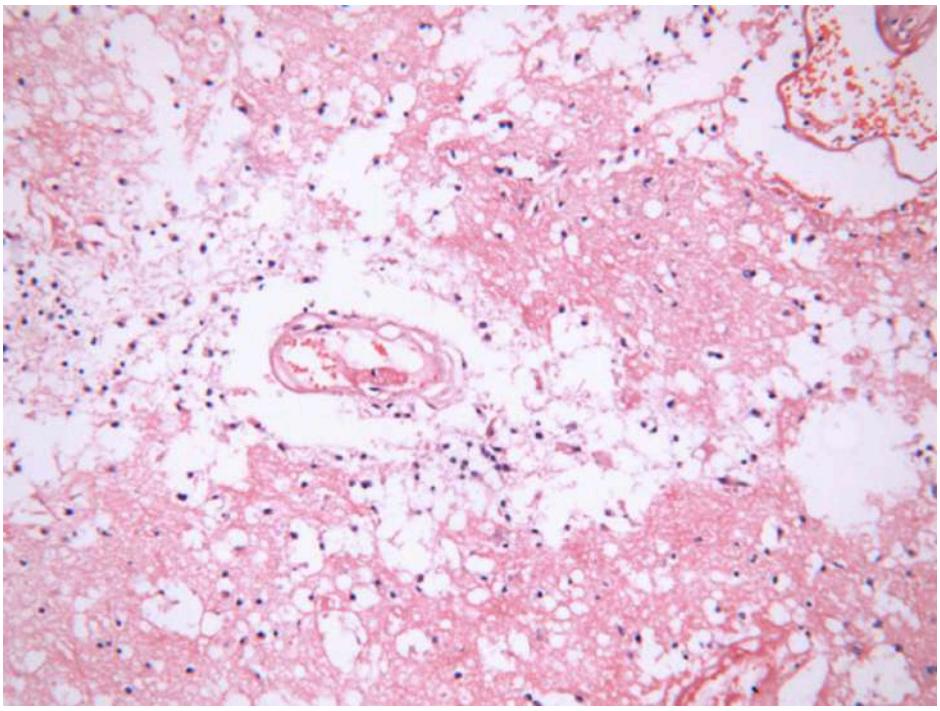
C - Cystic spaces with scattered areas of cellular debris

Image



Explanation Why

The presence of cystic space and cellular debris is characteristic of liquefactive necrosis. Liquefaction is due to the release of neutrophilic enzymes that degrade tissue into a liquid, viscous mass. Liquefactive necrosis is commonly seen in bacterial abscesses and brain infarcts. However, it rarely occurs in the liver and in conjunction with a viral infection such as hepatitis A.

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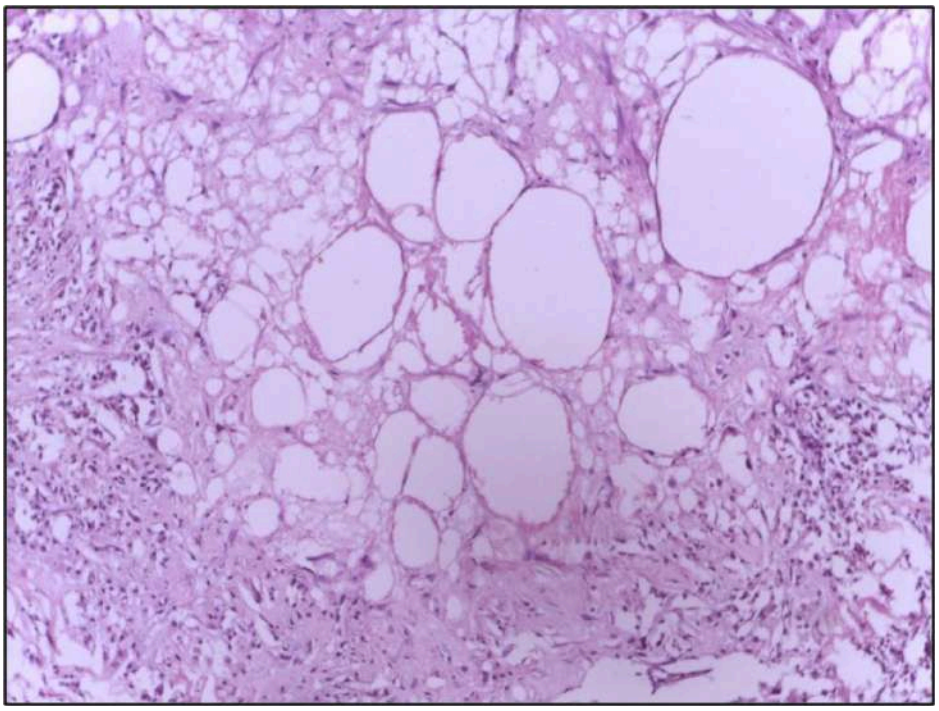
D - Basophilic adipocyte remnants, filled with calcifications

Image



Explanation Why

Remnants of basophilic adipocytes with calcification are characteristic of fat necrosis. Fat necrosis occurs due to the release of lipases that degrade triglycerides, causing saponification. This process is seen in the acute inflammation or trauma of tissue with a high concentration of adipocytes (e.g., pancreas, breast).

E - Engorged hepatocytes with red blood cell infiltration

Explanation Why

Engorged hepatocytes with RBC infiltration can be seen in hemorrhagic infarcts (red infarcts) of the liver. Hemorrhagic infarcts occur in organs with dual blood supply (e.g., lung, GI tract, testes, and liver), secondary to occlusion of vessels and subsequent extravasation of RBCs into the ischemic

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tissue. This finding would not be explained by a viral infection such as hepatitis A.

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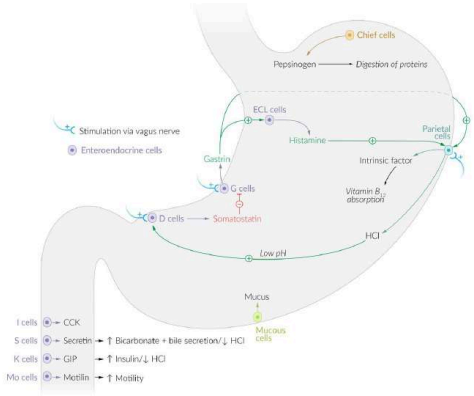
Question # 34

A 59-year-old woman comes to the physician because of a 1-year history of nausea and chronic abdominal pain that is worse after eating. She has Hashimoto thyroiditis. She does not smoke or drink alcohol. A biopsy specimen of the corpus of the stomach shows destruction of the upper glandular layer of the gastric mucosa and G-cell hyperplasia. This patient is at greatest risk for which of the following conditions?

	Answer	Image
A	Gastric adenocarcinoma	
B	Duodenal perforation	
C	Curling ulcer	
D	Aplastic anemia	
E	Gastric MALT lymphoma	

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Hint

The patient has chronic indigestion and gastric biopsy has revealed corporal parietal cell destruction (upper glandular layer). In a patient with a history of autoimmune disease (Hashimoto thyroiditis), this constellation of findings is consistent with autoimmune atrophic gastritis.

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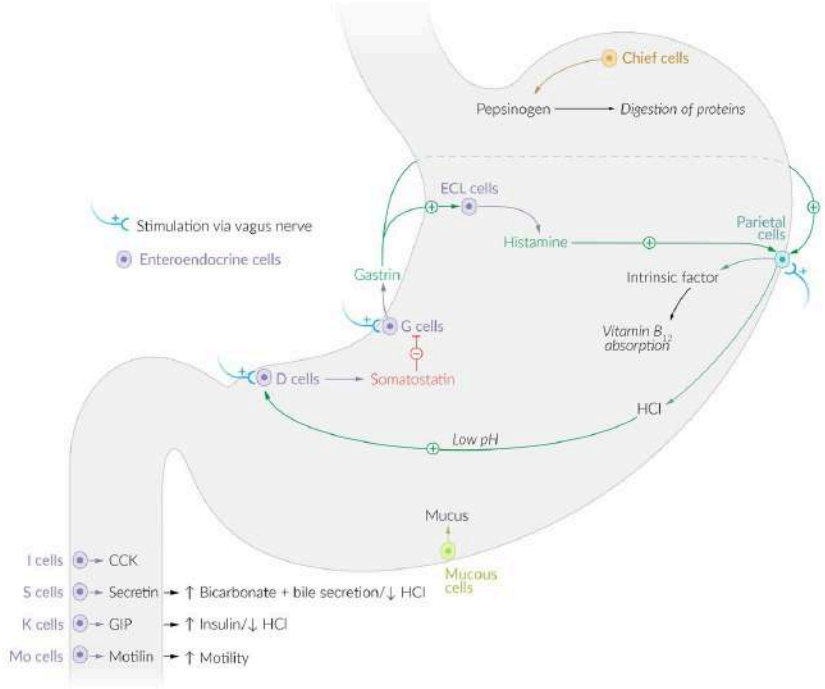
Correct Answer

A - Gastric adenocarcinoma

Image



Explanation Why

Autoimmune atrophic gastritis is a type of chronic gastritis (type A gastritis) that can lead to intestinal metaplasia, which increases the risk of gastric adenocarcinoma. Patients with autoimmune atrophic gastritis are also at increased risk for carcinoid tumor because of the presence of autoantibodies against parietal cells, which normally produce gastric acid. The resulting achlorhydria stimulates the release of gastrin and antral G-cell hyperplasia, resulting in hypergastrinemia. Hypergastrinemia, in turn, is associated with enterochromaffin-like cell hyperplasia, which may progress to gastric carcinoid tumor.

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B - Duodenal perforation

Explanation Why

Duodenal perforation is a complication of environmental atrophic gastritis, which is due to increased production of gastric acids in *H. pylori* infection and resulting mucosal inflammation and thinning. The autoimmune destruction of parietal cells in autoimmune atrophic gastritis results in achlorhydria, which is not associated with an increased risk of duodenal perforation.

C - Curling ulcer

Explanation Why

A Curling ulcer is a stress ulcer that occurs in patients with recent severe burn injuries and could manifest with nausea and abdominal pain, which are seen in this patient. However, symptoms would be acute rather than chronic. Curling ulcers also have a tendency to perforate, which would result in severe pain and peritonitis due to perforation. Lastly, in the case of a Curling ulcer, there would be damage extending through the muscularis mucosa, which is not consistent with this patient's biopsy findings.

D - Aplastic anemia

Explanation Why

Aplastic anemia is a type of normocytic anemia that is caused by bone marrow failure. Autoimmune atrophic gastritis is characterized by the presence of autoantibodies against parietal cells, which usually produce intrinsic factor. A deficiency of intrinsic factor can result in vitamin B_{12} malabsorption in the terminal ileum, causing macrocytic pernicious anemia.

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E - Gastric MALT lymphoma

Explanation Why

The risk of gastric MALT lymphoma, a B-cell lymphoma, is increased in patients with environmental atrophic gastritis that is secondary to *H. pylori* infection. However, gastric MALT lymphoma is not associated with autoimmune atrophic gastritis.

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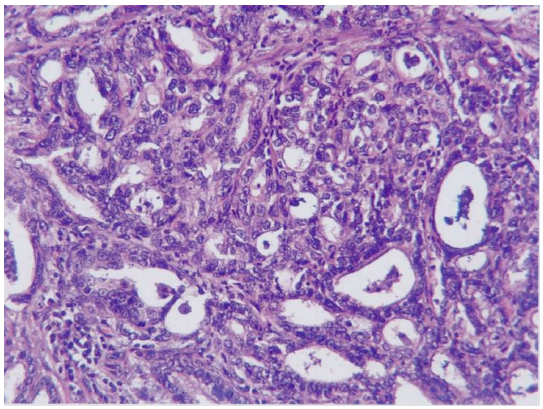
Question # 35

A 61-year-old man comes to the physician because of a 6-month history of epigastric pain and a 9-kg (20-lb) weight loss. He feels full and bloated even after eating small portions of food. His hemoglobin concentration is 9.5 g/dL with a mean corpuscular volume of 78 μm^3. Test of the stool for occult blood is positive. Esophagogastroduodenoscopy shows a 2-cm raised lesion with central ulceration on the lesser curvature of the stomach. Histologic examination of a gastric biopsy specimen from the lesion is most likely to show which of the following?

	Answer	Image
A	Neutrophilic infiltration with pit abscesses	
B	Foveolar and smooth muscle hyperplasia	
C	Gland-forming columnar cells	
D	Lymphocytic aggregates with noncaseating granulomas	

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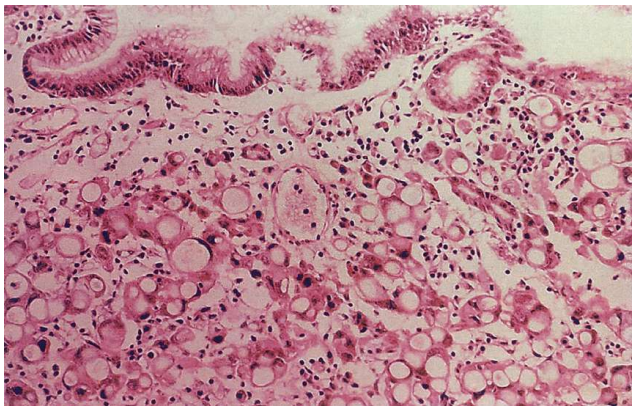
	Answer	Image
E	Mucin-filled round cells	

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Hint

Epigastric pain, weight loss, early satiety, and microcytic anemia in a patient with a suspicious lesion in the lesser curvature of the stomach should raise suspicion for gastric cancer. Adenocarcinoma is by far the most common type of gastric cancer.

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Correct Answer

A - Neutrophilic infiltration with pit abscesses

Explanation Why

Neutrophilic infiltration with pit abscesses is seen in *H. pylori*-positive gastritis, which can also cause epigastric pain and is an important risk factor for gastric adenocarcinoma. However, the EGD findings in this patient are not consistent with gastritis.

B - Foveolar and smooth muscle hyperplasia

Explanation Why

Foveolar cell and smooth muscle cell hyperplasia would be consistent with chemical gastropathy, which is also characterized histologically by edema of the lamina propria. While chemical gastropathy may result in epigastric pain similar to what is seen in this patient, the degree of weight loss and the presence of a suspicious ulceration in this patient makes this diagnosis highly unlikely. Moreover, this patient has no history of risk factors for this condition, such as chronic NSAID, alcohol, or tobacco use.

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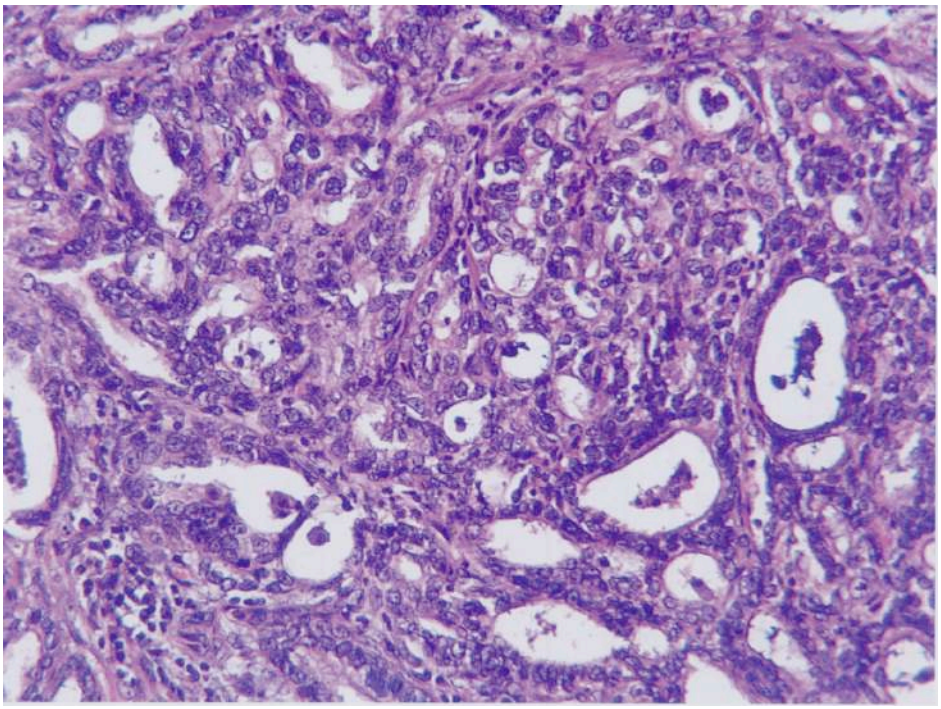
C - Gland-forming columnar cells

Image



Explanation Why

Gland-forming columnar cells are seen in adenocarcinoma, which is the most common type of gastric cancer (accounting for approx. 90% of cases). The endoscopic finding of a suspicious ulcer confined to the lesser curvature is consistent with intestinal (type I) gastric adenocarcinoma, which is characterized by aggressive local spread and typically metastasizes to the liver and regional lymph nodes. Risk factors include chronic *H. pylori* infection, smoking, and chronic gastritis.

D - Lymphocytic aggregates with noncaseating granulomas

Explanation Why

Noncaseating granulomas with lymphocytic aggregates are characteristic of Crohn disease, which can present with weight loss and epigastric pain similar to this patient. However, Crohn disease

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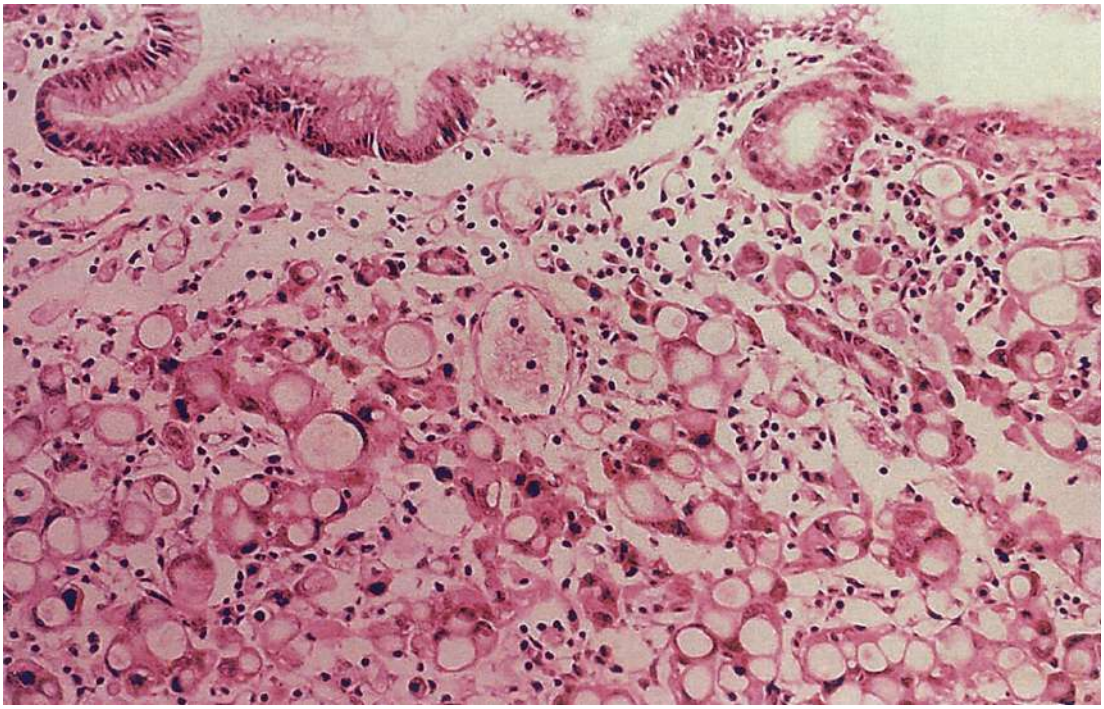
typically presents with chronic diarrhea and this patient lacks any characteristic extraintestinal manifestations (e.g., sacroiliitis, pyoderma gangrenosum, erythema nodosum). His endoscopy findings are more consistent with gastric adenocarcinoma, which would appear differently on histologic examination.

E - Mucin-filled round cells

Image



Explanation Why

Mucin-filled round cells with a peripherally dislocated nucleus are known as signet ring cells, which would suggest signet ring cell carcinoma. A patient with this type of cancer could also present with weight loss, epigastric pain, and bloody stool. However, endoscopic examination would typically reveal diffuse involvement of the stomach wall and possibly linitis plastica, rather than a single ulceration confined to the lesser curvature.

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Question # 36

A 67-year-old man comes to the physician because of a 4-month history of fatigue and weight loss. Physical examination shows jaundice. The liver is palpated 3 cm below the right costal margin. Serum studies show an elevated alpha-fetoprotein and a prolonged prothrombin time. Genetic analysis of a liver biopsy specimen shows a G:C to T:A transversion in codon 249 of the gene coding for the TP53 protein in affected cells. Which of the following risk factors is most specific to the patient's condition?

	Answer	Image
A	Alcoholism	
B	Hepatitis C infection	
C	Dietary aflatoxin exposure	
D	Schistosomiasis	
E	Anabolic steroid use	
F	Hemochromatosis	

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Hint

Fatigue, weight loss, jaundice, and hepatomegaly with elevated alpha-fetoprotein and impaired coagulation (elevated INR), are consistent with hepatocellular carcinoma (HCC). The G:C → T:A transversion is present in HCC with a specific etiology.

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Correct Answer

A - Alcoholism

Explanation Why

Chronic alcoholism causes significant liver damage and is a common cause of liver cirrhosis, which is associated with roughly 80% of cases of hepatocellular carcinoma. However, if hepatocellular carcinoma develops due to cirrhosis, there is no specific mutation of the TP53 gene.

B - Hepatitis C infection

Explanation Why

Chronic hepatitis C infection is a substantial risk factor for the development of hepatocellular carcinoma (HCC). The majority of HCC cases can be attributed to chronic hepatitis B or C infection through a series of viral and non-viral pathophysiological steps. Nevertheless, the G:C → T:A transversion in the genetic analysis of this patient's liver biopsy is highly indicative of HCC of another etiology.

C - Dietary aflatoxin exposure

Explanation Why

Signs of hepatocellular carcinoma and G:C → T:A transversion in codon 249 should raise suspicion for a history of aflatoxin B_1 ingestion. Aflatoxin is produced by some strains of the mold *Aspergillus*. A metabolite of aflatoxin B1 interferes with proper DNA transcription of TP53 gene through an inactivating mutation, resulting in the base transversions seen in this case. This mutation can be found in up to 60% of individuals with HCC in areas with high levels of exposure to aflatoxin B1.

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D - Schistosomiasis

Explanation Why

Patients who have contracted *Schistosoma mansoni* are at increased risk of developing hepatocellular carcinoma because *Schistosoma* potentiates dysplastic changes induced by viral hepatitis or carcinogenic substances like diethylnitrosamine. However, this disease is not associated with a specific transversion in the TP53 gene.

E - Anabolic steroid use

Explanation Why

A history of anabolic steroids use is associated with hepatic adenoma, which does not necessarily resolve after discontinuation of the drug. Adenomas may undergo malignant transformation in a limited number of patients, but they are not associated with a specific transversion of the TP53 gene.

F - Hemochromatosis

Explanation Why

Hemochromatosis predisposes patients to hepatocellular carcinoma. However, hemochromatosis is associated with an autosomal recessive mutation in the HFE gene on chromosome 6. The two most common types of mutations responsible for hemochromatosis are the substitution of cysteine with tyrosine due to a G → A genetic transition at codon 282 or substitution of histidine with aspartate due to a C → G transversion at codon 63. A different condition is responsible for the mutation in this patient.

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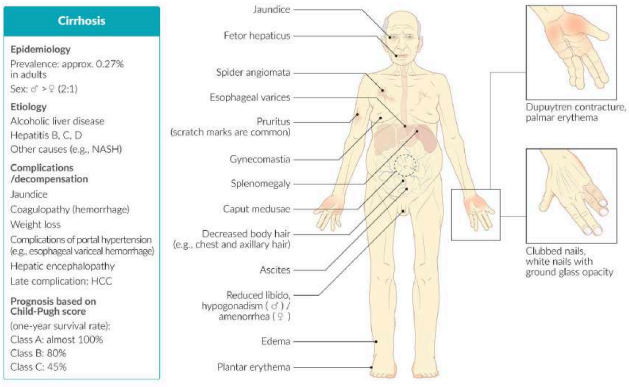
Question # 37

A 59-year-old man comes to the emergency department because of progressive abdominal swelling and shortness of breath for 1 week. He drinks 12 to 13 alcoholic beverages daily. He appears emaciated. Examination shows pallor, jaundice, hepatomegaly, gynecomastia, and a protuberant abdomen with a fluid wave and shifting dullness. Periodic monitoring of which of the following markers is most appropriate for this patient?

	Answer	Image
A	Chromogranin A	
B	Calcitonin	
C	Lactate dehydrogenase	
D	Desmin	
E	S-100 protein	
F	Alpha-fetoprotein	

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	Answer	Image
G	Cancer antigen 125	
H	Cancer antigen 15-3	
I	Carcinoembryonic antigen	
J	Cancer antigen 19-9	
K	Beta-human chorionic gonadotropin	

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Hint

This patient most likely has alcoholic liver cirrhosis (pallor, jaundice, hepatomegaly, gynecomastia, ascites, history of alcohol use disorder) and is at an increased risk of developing hepatocellular carcinoma.

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Correct Answer

A - Chromogranin A

Explanation Why

Chromogranin A is a serum tumor marker associated with tumors of neuroendocrine origin (e.g., carcinoid tumors, small cell lung carcinoma). Chromogranin A can be used to help in the diagnosis of neuroendocrine tumors, assess treatment efficacy, response to therapy, and tumor recurrence after surgical resection. This patient is not at increased risk for neuroendocrine tumors.

B - Calcitonin

Explanation Why

Calcitonin is a serum tumor marker that can be used to screen for medullary thyroid carcinoma. However, this patient lacks risk factors of medullary thyroid carcinoma (e.g., family history of MEN 2A or MEN 2B).

C - Lactate dehydrogenase

Explanation Why

Lactate dehydrogenase is a non-specific serum tumor marker associated with testicular germ cell tumors, ovarian tumors (dysgerminoma), lymphomas, and Ewing sarcoma. LDH can be used to assess tumor stage, treatment efficacy, and prognosis but not for general screening purposes.

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D - Desmin

Explanation Why

Desmin is a muscle-specific, immunohistochemical tumor marker that can be used to screen for skeletal muscle tumors (e.g., rhabdomyosarcoma). However, malignant tumors of the skeletal muscle are very rare and most commonly affect children.

E - S-100 protein

Explanation Why

S-100 protein is an immunohistochemical tumor marker associated with tumors that are derived from neural crest cells (e.g., melanoma). S-100 protein can be used to help in the diagnosis of melanoma, assess disease progression, and tumor recurrence after surgical resection. This patient is not at increased risk for neural crest cell tumors.

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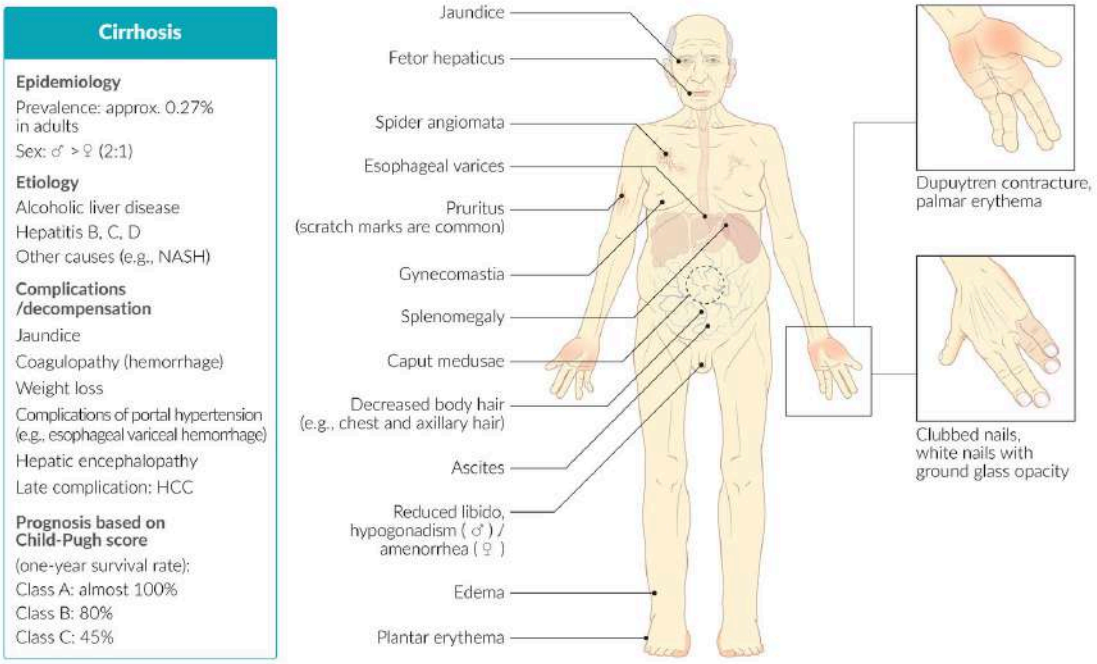
F - Alpha-fetoprotein

Image



Explanation Why

Periodic monitoring of alpha-fetoprotein along with abdominal ultrasound is the most appropriate surveillance method for hepatocellular carcinoma; approximately 80% of cases of HCC occur in patients with liver cirrhosis. The combined use of AFP and abdominal ultrasound increases detection rates of HCC compared to the use of ultrasound alone. AFP can also be used as a marker for yolk sac tumors (endodermal sinus tumors), mixed germ cell tumors, and ataxia telangiectasia.

G - Cancer antigen 125

Explanation Why

Cancer antigen 125 is a serum tumor marker associated with ovarian cancer. Cancer antigen 125 can be used to help in the diagnosis of ovarian cancer, assess treatment efficacy, and tumor recurrence

after surgical resection.

H - Cancer antigen 15-3

Explanation Why

Cancer antigen 15-3 (along with cancer antigen 27-29) is a serum tumor marker associated with breast cancer, which only rarely occurs in men. Cancer antigen 15-3 can be used to assess treatment efficacy and tumor recurrence after surgical resection but not for general screening purposes.

I - Carcinoembryonic antigen

Explanation Why

Carcinoembryonic antigen is a non-specific serum tumor marker associated with colorectal cancer and pancreatic cancer. This patient with a history of alcohol use disorder is at increased risk to develop pancreatic cancer. However, CEA is usually used to monitor the progression of colorectal and pancreatic cancer and to evaluate treatment efficacy, not for general screening purposes.

J - Cancer antigen 19-9

Explanation Why

Cancer antigen 19-9 is a serum tumor marker associated with pancreatic cancer and gastric cancer. This patient with a history of alcohol use disorder is at increased risk to develop pancreatic cancer. However, CA 19-9 is usually used to monitor the progression of pancreatic and gastric cancer and to evaluate treatment efficacy, not for general screening purposes.

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K - Beta-human chorionic gonadotropin

Explanation Why

Beta-human chorionic gonadotropin (ß hCG) is a tumor marker associated with choriocarcinomas and germ cell tumors. ß hCG is used to evaluate tumor stage, treatment efficacy, and prognosis but not for general screening purposes.

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Question # 38

A 48-year-old woman comes to the physician because of recurrent right upper abdominal pain for 3 weeks. The pain usually occurs after meals and tends to radiate to the right shoulder. She reports that she otherwise feels well. She has more energy since she started an intermittent fasting diet and has rapidly lost 9.0 kg (20 lbs). She is 160 cm (5 ft 3 in) tall and weighs 100 kg (220 lb); BMI is 39.1 kg/m^2. Physical examination shows a nontender abdomen. Abdominal ultrasonography shows several small stones in the gallbladder without calcification. When discussing treatment options, she states that she does not wish to undergo surgery and asks about other possibilities. Which of the following is the most appropriate pharmacotherapy to address the underlying cause of this patient's condition?

	Answer	Image
A	Gemfibrozil	
B	Ursodeoxycholic acid	
C	Ezetimibe	
D	Dicyclomine	
E	Colestipol	
F	Hydromorphone	

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Hint

This patient with biliary colic (postprandial right upper quadrant pain that radiates to the right shoulder) and radiologic evidence of gallstones has symptomatic cholelithiasis.

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Correct Answer

A - Gemfibrozil

Explanation Why

Gemfibrozil is a lipid-lowering agent that primarily decreases serum triglyceride concentrations. Gemfibrozil therapy is associated with an increased risk of developing gallstones and thus would be an inappropriate therapy for this patient.

B - Ursodeoxycholic acid

Explanation But

The success rate of ursodeoxycholic acid therapy for cholelithiasis is only ~ 50%.

Explanation Why

Bile cholesterol oversaturation, bile stasis, and impaired bile acid circulation promote the formation of cholesterol gallstones. Female sex, age > 40 years, obesity, and rapid weight loss, as seen in this patient, are also risk factors for gallstone formation. Cholecystectomy is the first-line therapy for symptomatic cholelithiasis. However, for patients who are unable or unwilling to receive cholecystectomy, ursodeoxycholic acid is the first-line nonsurgical treatment. It dissolves gallstones by solubilizing cholesterol and thus is appropriate for the management of small stones (i.e., < 10 mm) that have minimal calcification. Ursodeoxycholic acid also decreases hepatic secretion of cholesterol, decreases intestinal absorption of cholesterol, and promotes gallbladder emptying.

C - Ezetimibe

Explanation Why

Ezetimibe inhibits the absorption of cholesterol in the intestine and decreases biliary cholesterol secretion. Ezetimibe therapy leads to a marked reduction in LDL cholesterol. However, it is unclear

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whether it is effective for the prevention or treatment of cholelithiasis. Thus, this drug is not the most appropriate pharmacotherapy for this patient.

D - Dicyclomine

Explanation Why

Dicyclomine is an anticholinergic medication that decreases muscle spasms. Though it can be used to relieve pain associated with biliary colic, it does not address the underlying cause of this patient's symptoms and thus is not the most appropriate pharmacotherapy.

E - Colestipol

Explanation Why

Colestipol is a bile acid sequestrant that can be used to treat hyperlipidemia by binding to bile acids in the intestine and decreasing their absorption. Fecal loss of bile salts can increase the risk of developing gallstones and thus would be an inappropriate therapy for this patient.

F - Hydromorphone

Explanation Why

Hydromorphone is a potent opioid that can be used as analgesia for patients with severe pain. However, NSAIDs are typically sufficient to control pain caused by biliary colic. Moreover, analgesia does not address the underlying cause of this patient's symptoms and thus is not the most appropriate pharmacotherapy.

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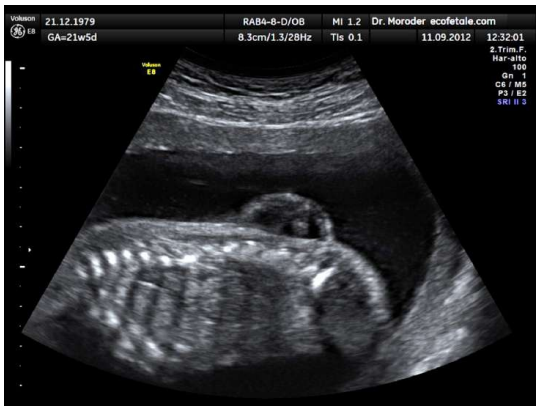
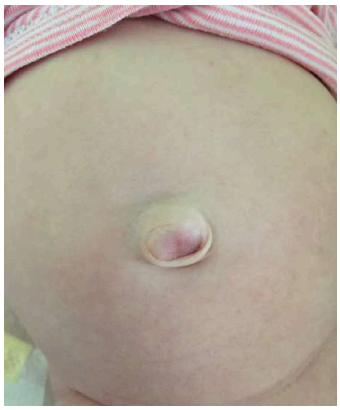
Question # 39

A 19-year-old woman, gravida 1, para 0, at 21 weeks' gestation comes to the physician for a follow-up prenatal visit. At her previous appointment, her serum α-fetoprotein concentration was elevated. She had smoked 1 pack of cigarettes daily for 3 years but quit at 6 weeks' gestation. Examination shows a uterus consistent in size with a 21-week gestation. Ultrasonography shows fetal viscera suspended freely into the amniotic cavity. Which of the following is the most likely diagnosis?

	Answer	Image
A	Vitelline fistula	
B	Diaphragmatic hernia	
C	Myelomeningocele	
D	Umbilical hernia	

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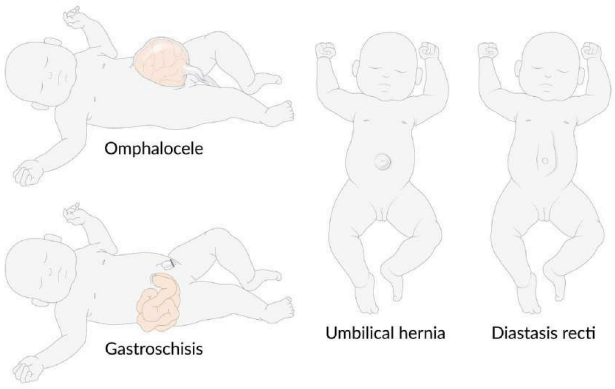
	Answer	Image
E	Vesicourachal diverticulum	
F	Gastroschisis	
G	Omphalocele	

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USMLE World Step 3 Qbank: https://t.me/USMLEWorldStep3

USMLE Anki: https://t.me/USMLEAnki

KissPrep: https://t.me/USMLEKissPrep

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Hint

Failure of lateral fold closure leads to a full-thickness abdominal wall defect that allows the growing bowel to herniate through at the weakest point.

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Correct Answer

A - Vitelline fistula

Explanation Why

Vitelline fistula (also known as patent omphalomesenteric duct) occurs when the vitelline duct fails to close during the 7th week of development, leading to a patent connection between the abdominal wall and ileum. It is diagnosed clinically after birth when meconium discharge through the umbilicus is observed. Elevated α-fetoprotein and fetal ultrasound findings of abdominal viscera in the amniotic fluid are not consistent with a vitelline fistula.

B - Diaphragmatic hernia

Explanation Why

Diaphragmatic hernias occur when the abdominal contents protrude into the thoracic cavity due to a defect in the diaphragm. Although congenital diaphragmatic hernias can be diagnosed on fetal ultrasound, imaging would show abdominal viscera within the thorax versus the free-floating contents in the amniotic fluid seen in this patient. In addition, elevated α-fetoprotein is not consistent with this condition.

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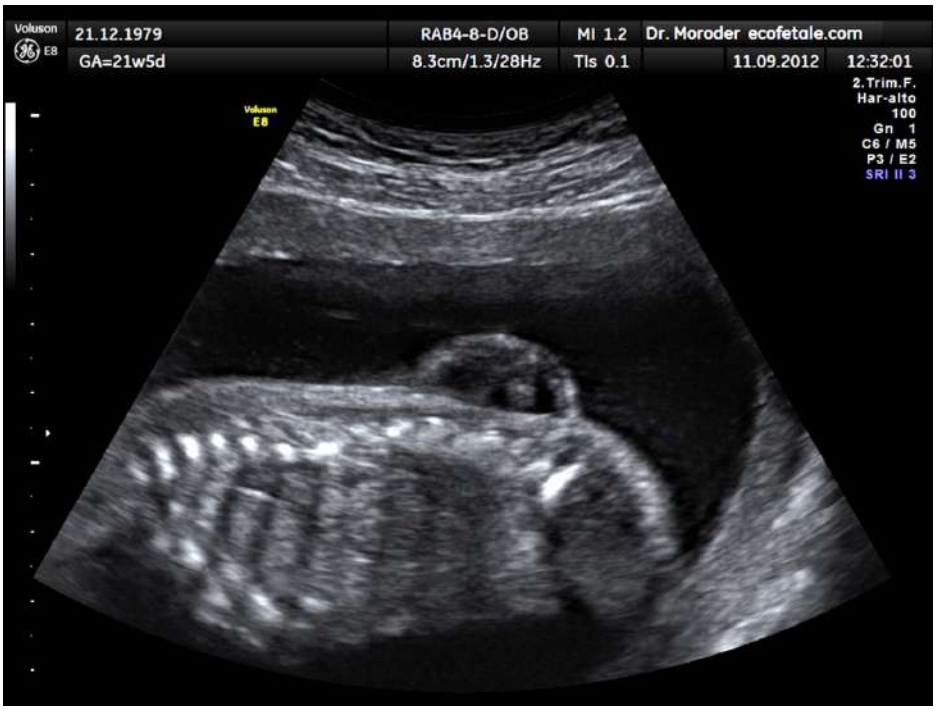
C - Myelomeningocele

Image



Explanation Why

Myelomeningocele is a neural tube defect that most commonly develops between the 3rd and 4th weeks of pregnancy from the incomplete closure of the spinal neural tube. It ultimately leads to the protrusion of the meninges and spinal cord within a membranous sac through a vertebral defect. Although elevated α-fetoprotein is associated with this condition, ultrasound findings of fetal viscera suspended freely in the amniotic cavity are inconsistent with myelomeningocele.

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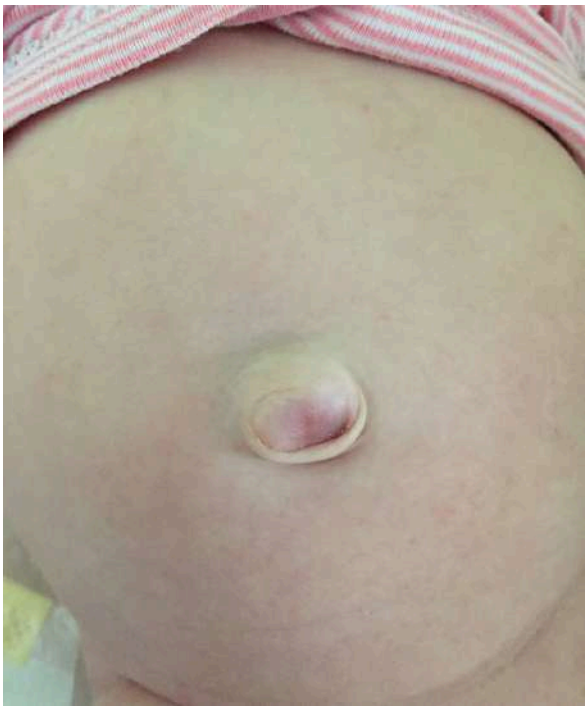
D - Umbilical hernia

Image



Explanation Why

Congenital umbilical hernias are abdominal wall defects that may occur when the umbilical ring fails to close during fetal development. The midgut initially develops outside of the abdominal cavity, until the second trimester, when it physiologically herniates back into the abdomen. Failure to close the umbilical ring or presence of underdeveloped fascia leads to abdominal weakness and may result in bulging of abdominal content through the umbilicus. It is diagnosed clinically after birth and is not associated with elevated α-fetoprotein levels or free-floating viscera on fetal ultrasound during the second trimester.

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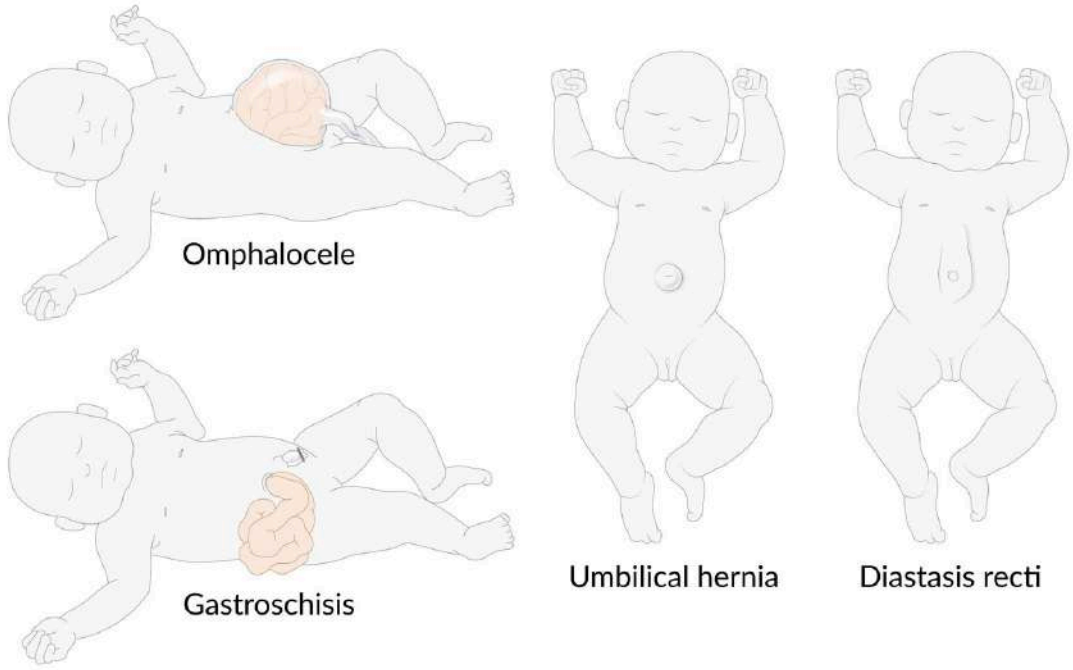
E - Vesicourachal diverticulum

Explanation Why

A vesicourachal diverticulum occurs when the connection between the urachus and bladder partially fails to obliterate during fetal development, leading to an outpouching of the bladder. Although typically asymptomatic and discovered incidentally, a vesicourachal diverticulum may manifest initially with infection, perforation, abscess formation, or neoplasm in early childhood. This anomaly can also be diagnosed on fetal ultrasound. However, the imaging findings (i.e., extruded abdominal contents) and elevated α-fetoprotein observed here are inconsistent with a vesicourachal diverticulum.

F - Gastroschisis

Image



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Explanation Why

Gastroschisis is a congenital ventral wall defect that leads to intestinal herniation through the involuted right umbilical vein, the weakest part of the fetal abdominal wall. As gastroschisis is an uncovered abdominal wall defect, α-fetoprotein (AFP) can diffuse freely into the amniotic fluid and maternal circulation, leading to elevated maternal serum AFP, which can be used as a screening test. As a confirmatory test, fetal ultrasound will show free-floating bowel without a membranous sac. Risk factors include young maternal age (i.e., under 20 years of age), and tobacco and alcohol use during pregnancy. Initial treatment of a newborn with gastroschisis includes placing the extruded abdominal contents in a protective silo, nasogastric decompression, and immediate surgical correction.

G - Omphalocele

Explanation Why

Omphalocele is a congenital ventral wall defect in which protrusion of the abdominal contents covered with peritoneum occurs at the site of umbilical cord insertion. Although maternal serum α-fetoprotein (AFP) is also elevated in this condition (due to leakage of AFP into the amniotic fluid and maternal circulation), fetal ultrasound shows midline herniation of abdominal contents within a hernia sac in contrast to the free-floating viscera seen on this patient's prenatal ultrasound. In addition, omphalocele is commonly associated with other congenital diseases, including trisomy 13, trisomy 18, and Beckwith-Wiedemann, evidence of which is not described in the fetus.

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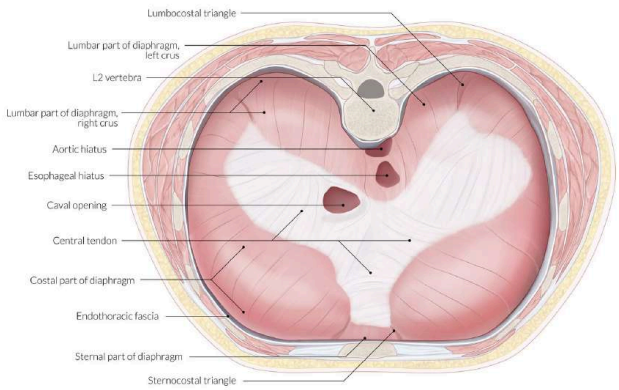
Question # 40

A 68-year-old man comes to the physician because of a 4-month history of difficulty swallowing. During this time, he has also had a 7-kg (15-lb) weight loss. Esophagogastroduodenoscopy shows an exophytic mass in the distal third of the esophagus. Histological examination of a biopsy specimen shows a well-differentiated adenocarcinoma. The patient is scheduled for surgical resection of the tumor. During the procedure, the surgeon damages a structure that passes through the diaphragm along with the esophagus at the level of the tenth thoracic vertebra (T10). Which of the following structures was most likely damaged?

	Answer	Image
A	Vagus nerve	
B	Inferior vena cava	
C	Thoracic duct	
D	Aorta	
E	Right phrenic nerve	
F	Azygos vein	

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Hint

Damage to this structure may cause gastroparesis.

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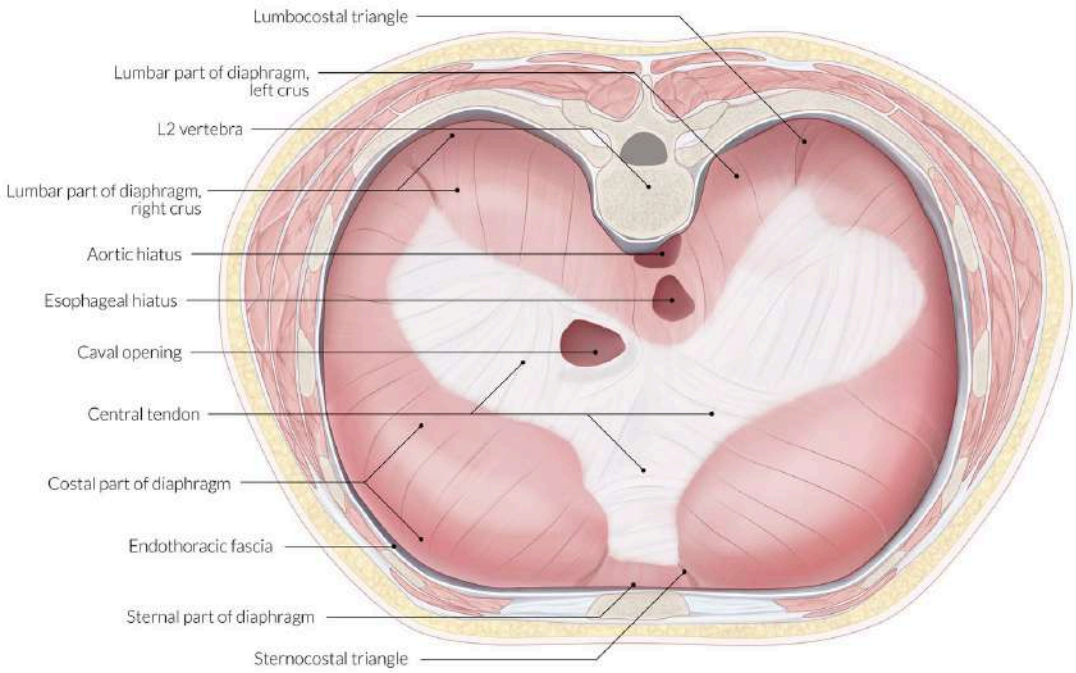
Correct Answer

A - Vagus nerve

Image



Explanation But

Further causes of vagus nerve injury include diabetic neuropathy, trauma, and inflammation.

Explanation Why

The vagus nerve (cranial nerve X) exits the thoracic cavity together with the esophagus through the esophageal hiatus, a diaphragmatic aperture at the level of T10, and innervates the smooth muscle cells of the digestive tract. Periesophageal vagus nerve injury, which may occur during thoracic or gastric surgery, typically manifests with delayed gastric emptying. Other symptoms of vagus nerve injury depend on the level at which the lesion is located and include loss of the gag reflex, vocal cord paralysis (manifesting as hoarseness), and autonomic dysfunction (e.g., impaired heart rate variability).

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B - Inferior vena cava

Explanation Why

Although the inferior vena cava can be damaged during thoracic surgery, it enters the thoracic cavity through the caval hiatus, a diaphragmatic aperture at the level of the eighth thoracic vertebra (T8).

C - Thoracic duct

Explanation Why

Although the thoracic duct can be damaged during thoracic surgery, it enters the thoracic cavity through the aortic hiatus, a diaphragmatic aperture at the level of the 12^{th} thoracic vertebra (T12).

D - Aorta

Explanation Why

Although the aorta can be damaged during thoracic surgery, it exits the thoracic cavity through the aortic hiatus, a diaphragmatic aperture at the level of the 12^{th} thoracic vertebra (T12).

E - Right phrenic nerve

Explanation Why

Although the right phrenic nerve can be damaged during thoracic surgery, it exits the thoracic cavity through the caval hiatus, a diaphragmatic aperture at the level of the eighth thoracic vertebra (T8).

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F - Azygos vein

Explanation Why

Although the azygos vein can be damaged during thoracic surgery, it enters the thoracic cavity through the aortic hiatus, a diaphragmatic aperture at the level of the 12^{th} thoracic vertebra (T12).

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Question # 1

A 46-year-old man with HIV infection comes to the physician because of a 1-week history of severe retrosternal pain while swallowing. He has not been adherent to his antiretroviral drug regimen. His CD4+ T-lymphocyte count is 98/mm^3. Endoscopy shows white plaques in the esophagus. The most appropriate immediate treatment is a drug that inhibits which of the following enzymes?

	Answer	Image
A	DNA polymerase	
B	Hydrogen-potassium ATPase	
C	Phospholipase A2	
D	Cytochrome p450 enzymes	
E	Squalene epoxidase	

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Hint

HIV infection with acute odynophagia, white plaques on upper GI endoscopy, and a low CD4+ T-cell count (especially < 100/mm^3) are consistent with esophageal candidiasis.

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Correct Answer

A - DNA polymerase

Explanation Why

Inhibition of DNA polymerase is the mechanism of action of certain antiviral medications (e.g., ganciclovir and acyclovir) and antifungal medications (e.g., flucytosine). Ganciclovir and acyclovir are used to treat infections caused by herpes simplex virus (HSV) and cytomegalovirus (CMV). Although immunocompromised patients with decreased CD4+ counts are at increased risk of viral infection, viral esophagitis caused by CMV manifests with linear ulcers and esophagitis caused by HSV with circumscribed ulcers in the distal esophagus, in contrast to this patient's white plaques. Flucytosine can be used to treat systemic fungal infections (e.g., disseminated candidiasis) when combined with amphotericin B and is particularly useful for the treatment of cryptococcal meningitis. It would not effectively treat esophageal candidiasis.

B - Hydrogen-potassium ATPase

Explanation Why

Inhibition of H^+/K^+ ATPase, which decreases gastric acid production, is the mechanism of action of PPIs. PPIs are the first-line treatment for gastroesophageal reflux disease (GERD), which manifests with retrosternal pain, odynophagia, and dysphagia, which are seen in this patient. However, GERD would not explain his white plaques, and PPIs play no role in the treatment of esophageal candidiasis.

C - Phospholipase A2

Explanation Why

Inhibition of phospholipase A2, an enzyme in the arachidonic acid synthesis pathway that leads to the formation of eicosanoids, is the mechanism of action of glucocorticoids. Glucocorticoids are prescribed for a variety of conditions, including hypersensitivity reactions, autoimmune conditions,

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and adrenal insufficiency. Because of their immunosuppressive effects, glucocorticoids are contraindicated in this patient; they would exacerbate his esophageal candidiasis and predispose him to further infections.

D - Cytochrome p450 enzymes

Explanation Why

Fluconazole is one of the first-line treatments for candida esophagitis. Fluconazole inhibits the yeast cytochrome p450 enzyme 14α-demethylase, which prevents ergosterol synthesis and therefore decreases cell membrane integrity, leading to cell destruction. It is also indicated for the treatment of systemic candidiasis, cryptococcal meningitis, and antifungal prophylaxis.

E - Squalene epoxidase

Explanation Why

Inhibition of squalene epoxidase, an enzyme that synthesizes squalene epoxide from squalene, is the mechanism of action of the antifungal terbinafine. Squalene epoxide is necessary for the synthesis of lanosterol, which, in turn, is required to synthesize ergosterol, an important element of the fungal cell membrane. Terbinafine therefore causes fungal cell death by ultimately disrupting cell membrane integrity. However, terbinafine is indicated for superficial dermatophyte infections (e.g., onychomycosis, tinea), not candida esophagitis.

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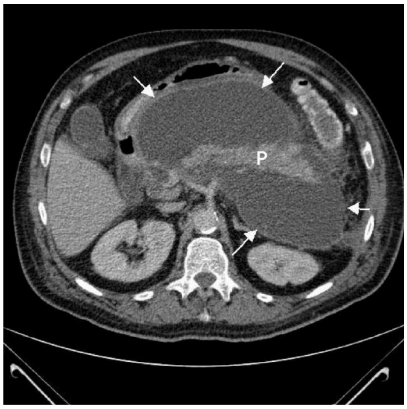
Question # 2

A 58-year-old man comes to the physician because of a 4-day history of abdominal pain and vomiting. Initially, the vomitus was food that he had recently eaten, but it is now bilious. He has had similar complaints several times in the past 6 years. He has smoked 1 pack of cigarettes daily for the past 25 years and drinks 18 oz of whiskey daily. He is 160 cm (5 ft 3 in) tall and weighs 48 kg (105 lb); BMI is 19 kg/m^2. His vital signs are within normal limits. Physical examination shows an epigastric mass. The remainder of the examination shows no abnormalities. Which of the following is the most likely diagnosis?

	Answer	Image
A	Chronic cholecystitis	
B	Retroperitoneal fibrosis	
C	Hypertrophic pyloric stenosis	
D	Pancreatic pseudocyst	
E	Gastric adenocarcinoma	

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Hint

This patient presents with recurrent abdominal pain, vomiting, and a palpable epigastric mass, while his vital signs and physical examination are otherwise unremarkable. His history of alcohol use suggests an underlying condition that is often caused by chronic alcohol use.

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Correct Answer

A - Chronic cholecystitis

Explanation Why

Chronic cholecystitis is the consequence of recurrent acute cholecystitis. Recurrent episodes of acute cholecystitis, which manifests with upper abdominal pain and bilious or non-bilious vomiting, could explain this patient's medical history. However, in chronic cholecystitis, the gallbladder is fibrosed and shrunken and would not explain this patient's abdominal mass.

B - Retroperitoneal fibrosis

Explanation Why

Retroperitoneal fibrosis is a rare condition that can manifest with recurrent abdominal pain (due to hydronephrosis or mesenteric ischemia) and vomiting (due to hydronephrosis and uremia). However, an abdominal mass in retroperitoneal fibrosis is typically due to hydronephrosis and so would be palpable in the flanks, not in the epigastrium. In addition, other typical manifestations of retroperitoneal fibrosis, such as lower limb edema, varicocele, and claudication are absent in this patient.

C - Hypertrophic pyloric stenosis

Explanation Why

Hypertrophic pyloric stenosis is a cause of gastric outlet obstruction (GOO) and manifests with vomiting and a palpable epigastric mass. However, it is a condition of infancy and does not manifest for the first time in adulthood. Moreover, vomitus is characteristically non-bilious, because the level of GOO by the pyloric hypertrophy is above the second part of the duodenum, into which the biliary duct drains.

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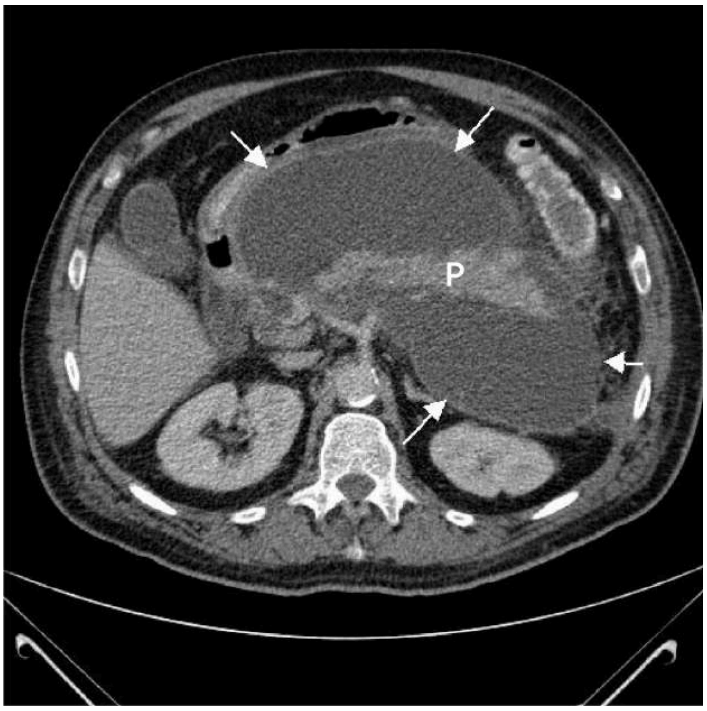
D - Pancreatic pseudocyst

Image



Explanation Why

A pancreatic pseudocyst, which is a complication of acute or chronic pancreatitis, is caused by leakage of pancreatic exocrine secretions from damaged ducts. This patient's history of recurrent epigastric pain, vomiting, and chronic alcohol consumption makes a diagnosis of pancreatitis highly likely. Patients with chronic pancreatitis and heavy alcohol use are often cachectic due to malnutrition. Pancreatic pseudocysts, when large enough, can manifest with a palpable epigastric mass and bilious vomiting (due to extrinsic compression of the distal duodenum) or non-bilious vomiting (due to gastric outlet obstruction). The diagnosis can be confirmed by imaging; a well-defined fluid collection would be seen in the vicinity of the pancreas.

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E - Gastric adenocarcinoma

Explanation Why

A gastric adenocarcinoma is a likely differential diagnosis in an individual who presents with abdominal pain, vomiting, an epigastric mass, cachexia, and certain risk factors (e.g., smoking, alcohol use). A history of similar symptoms in the past could have indicated a peptic ulcer that subsequently underwent malignant transformation. However, vomiting in gastric adenocarcinoma is a late manifestation and it is typically non-bilious because it is caused by gastric outlet obstruction.

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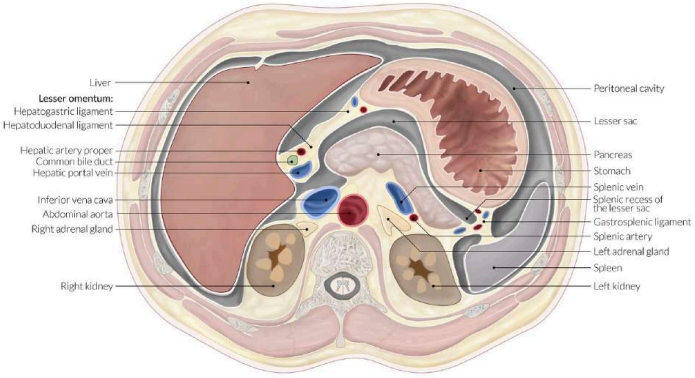
Question # 3

A 62-year-old woman with a pancreatic insulinoma is being prepared for a laparoscopic enucleation of the tumor. After induction of general anesthesia, preparation of a sterile surgical field, and port placement, the surgeon needs to enter the space posterior to the stomach to access the pancreatic tumor. Which of the following ligaments must be cut in order to access this space?

	Answer	Image
A	Phrenoesophageal ligament	
B	Hepatogastric ligament	
C	Phrenicocolic ligament	
D	Ligamentum venosum	
E	Falciform ligament	

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Hint

The space described is the lesser sac. The ligament that must be cut is a part of the lesser omentum.

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Correct Answer

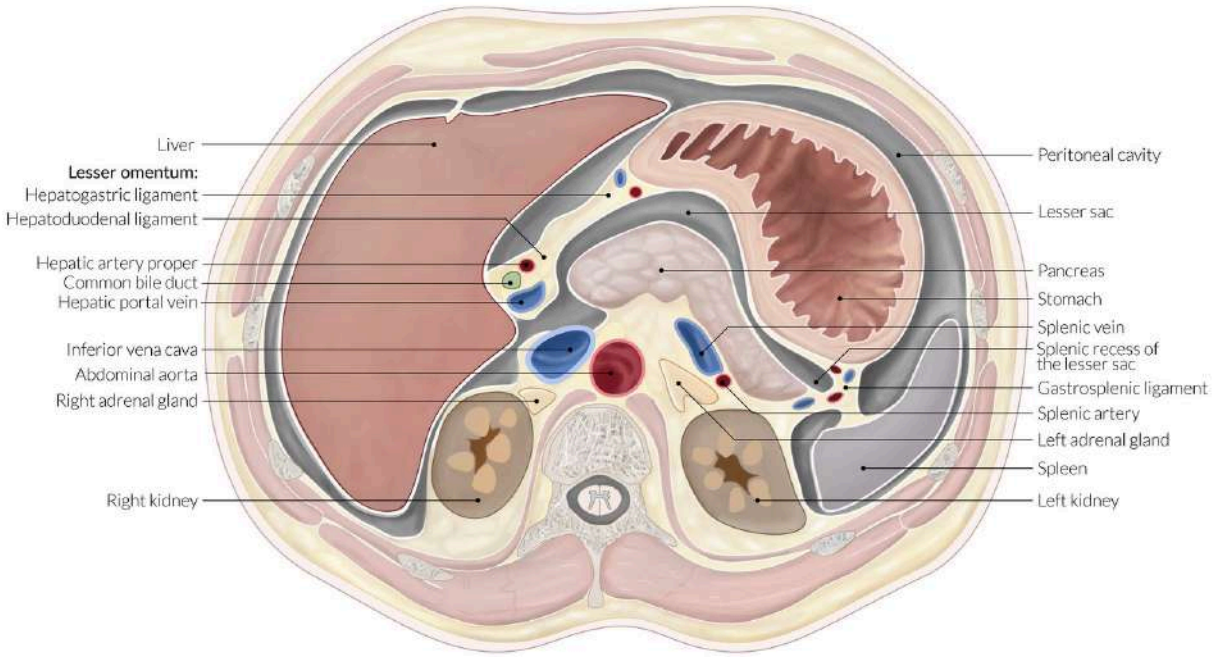
A - Phrenoesophageal ligament

Explanation Why

The phrenoesophageal ligament is a peritoneal fold that encircles the distal portion of the esophagus and gastroesophageal junction and connects them to the peritoneal surface of the diaphragm. It is typically cut in procedures that require mobilization of the distal esophagus or the fundus of the stomach (e.g., esophagectomy, fundoplication). However, it is not a boundary of the lesser sac and thus does not need to be cut to gain access to it.

B - Hepatogastric ligament

Image



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Explanation Why

The gastrohepatic ligament connects the lesser curvature of the stomach with the liver. Together with the hepatoduodenal ligament, it forms the lesser omentum, which separates the anterior greater sac from the posterior lesser sac. Access to the lesser sac, as during pancreatic surgery, can be achieved by cutting the gastrohepatic ligament. The lesser sac can also be accessed through the gastrocolic ligament (part of the greater omentum), gastrosplenic ligament, splenorenal ligament, and through the transverse mesocolon.

C - Phrenicocolic ligament

Explanation Why

The phrenicocolic ligament is a peritoneal fold that extends from the splenic flexure of the colon to the peritoneal surface of the diaphragm. It can be cut to gain access to the spleen and the structures posterior to it (e.g., the left kidney and adrenal gland). However, it is not a boundary of the lesser sac and thus does not need to be cut to gain access to it.

D - Ligamentum venosum

Explanation Why

The ligamentum venosum is a remnant of the fetal ductus venosus that lies between the caudate lobe and left lobe of the liver (dorsal aspect). It does not form a boundary of the lesser sac and thus does not need to be cut to gain access to it.

E - Falciform ligament

Explanation Why

The falciform ligament is a derivative of ventral mesentery that attaches the liver to the anterior abdominal wall. It contains the ligamentum teres hepatis and paraumbilical veins and is typically cut during surgical procedures on the liver (e.g., hepatectomy). However, it is not a boundary of the

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lesser sac and thus does not need to be cut to gain access to it.

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Question # 4

A 66-year-old woman with hypertension comes to the physician because of crampy, dull abdominal pain and weight loss for 1 month. The pain is located in the epigastric region and typically occurs within the first hour after eating. She has had a 7-kg (15.4-lb) weight loss in the past month. She has smoked 1 pack of cigarettes daily for 20 years. Physical examination shows a scaphoid abdomen and diffuse tenderness to palpation. Laboratory studies including carbohydrate antigen 19-9 (CA 19-9), carcinoembryonic antigen (CEA), and lipase concentrations are within the reference range. Which of the following is the most likely cause of this patient's symptoms?

	Answer	Image
A	Narrowing of the celiac artery	
B	Malignant mass at the head of the pancreas	
C	Narrowing of the gastric pylorus	
D	Embolus in the superior mesenteric artery	
E	Focal wall thickening in the colon	
F	Decreased motility of gastric smooth muscle	

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Hint

An elderly woman with multiple atherosclerotic risk factors (hypertension, smoking) who presents with chronic postprandial pain, food avoidance, and unintentional weight loss, is concerning for chronic mesenteric ischemia.

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Correct Answer

A - Narrowing of the celiac artery

Explanation Why

Slow progressive narrowing of the celiac artery secondary to atherosclerosis can lead to chronic mesenteric ischemia, which presents with the signs and symptoms seen in this patient. She likely also has atherosclerotic narrowing of the SMA or IMA. If only one main artery is affected, collateral connections will typically compensate for the reduced flow and the patient will often be asymptomatic.

B - Malignant mass at the head of the pancreas

Explanation Why

Pancreatic cancer causes abdominal pain and weight loss, as in this patient, and smoking is also a known risk factor. However, this patient lacks other common signs of pancreatic cancer, including nausea and vomiting. Pancreatic cancer involving the head typically also causes obstructive jaundice, which is not present. Lastly, laboratory values typically elevated in patients with pancreatic cancer, including CA 19-9, CEA, and lipase, are all normal. This combination of findings makes pancreatic cancer an unlikely cause of this patient's symptoms.

C - Narrowing of the gastric pylorus

Explanation Why

Gastric outlet obstruction results from narrowing of the gastric pylorus and presents with postprandial pain and weight loss, as seen in this patient. However, she lacks the vomiting that is seen in nearly all patients with gastric outlet obstruction, making this diagnosis unlikely.

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D - Embolus in the superior mesenteric artery

Explanation Why

Arterial thromboembolism to the superior mesenteric artery causes acute mesenteric ischemia. This presents with sudden, severe, periumbilical pain, often accompanied by nausea and vomiting. The pain is classically disproportionate to abdominal examination findings. Instead, this patient presents with chronic mesenteric ischemia and has a gradual onset of symptoms associated with post-prandial pain and weight loss.

E - Focal wall thickening in the colon

Explanation Why

Focal wall thickening in the colon can represent a colonic mass or infectious colitis. Although both could potentially cause weight loss, these diagnoses do not explain the postprandial pain seen in this patient. Furthermore, she lacks other typical symptoms for colonic mass or infectious colitis, such as hematochezia.

F - Decreased motility of gastric smooth muscle

Explanation Why

Decreased motility of gastric smooth muscle causes gastroparesis, a condition that presents with postprandial pain and in severe cases, weight loss. However, this patient lacks other typical symptoms of gastroparesis, including nausea and vomiting. She also lacks risk factors such as diabetes or a history of upper GI surgery, making this diagnosis unlikely.

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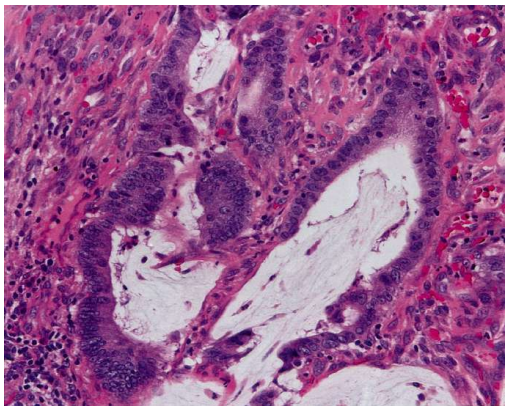
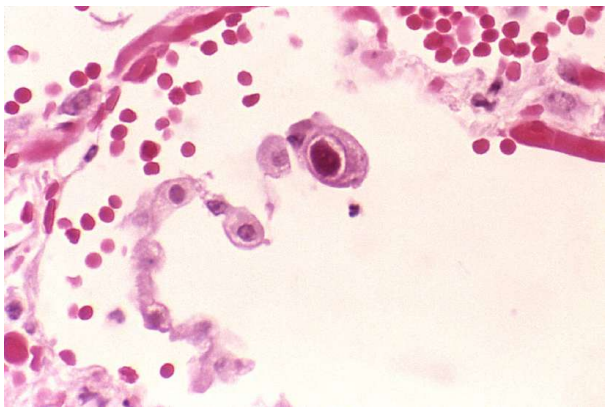
Question # 5

A 49-year-old man with HIV comes to the physician because of a 1-month history of intermittent diarrhea and abdominal pain. Abdominal examination shows mild, diffuse tenderness throughout the lower quadrants. His CD4+ T-lymphocyte count is 180/mm^3. Colonoscopy shows multiple hemorrhagic nodules in the rectum and descending colon. Polymerase chain reaction of the lesions is positive for HHV-8. Histologic examination of the lesions is most likely to show which of the following findings?

	Answer	Image
A	Cords of atypical cells with extracellular mucin	
B	Enlarged cells with ground-glass nuclei and central clearing	
C	Enlarged cells with intranuclear inclusion bodies	
D	Polygonal cells with racket-shaped organelles	

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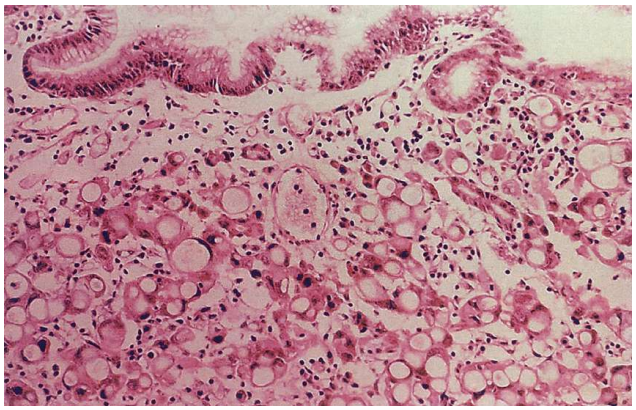
	Answer	Image
E	Spindle-shaped cells with lymphocytic infiltration	
F	Mucin-filled cell with peripheral nucleus	

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Hint

This HIV-positive patient with a very low CD4+ T-lymphocyte count (< 200/mm^3) presents with HHV-8-positive lesions, making Kaposi sarcoma the most likely diagnosis.

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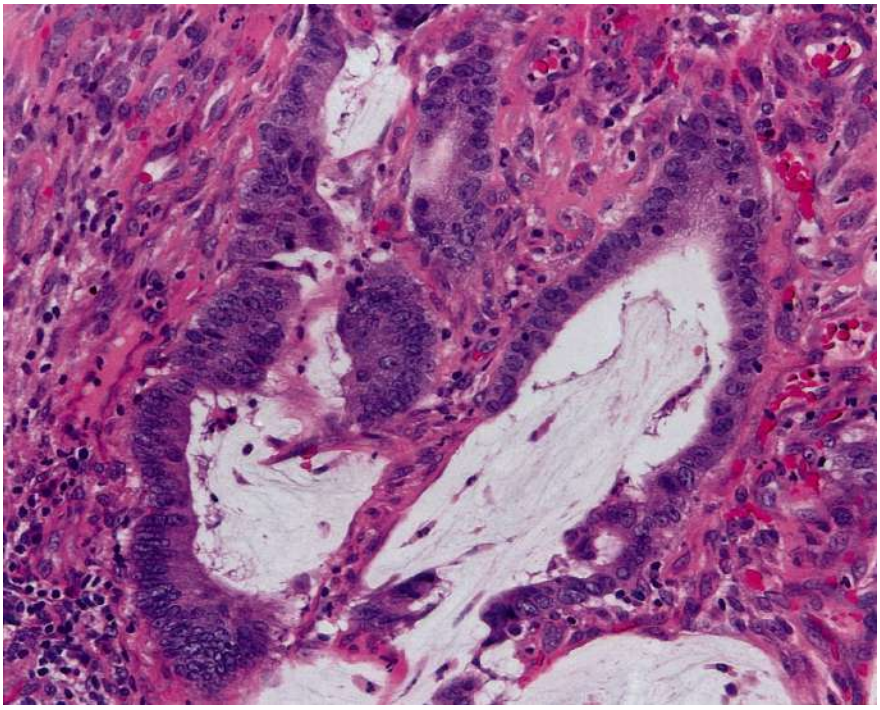
Correct Answer

A - Cords of atypical cells with extracellular mucin

Image



Explanation Why

A biopsy of colonic lesions showing cords of atypical cells with extracellular mucin is concerning for colorectal mucinous adenocarcinoma, which could explain this patient's diarrhea and abdominal pain. Colon cancers may also cause GI bleeding, but it would usually occur at a rate too slow to support a colonoscopy finding of occult hemorrhage. In addition, mucinous adenocarcinoma is not associated with HHV-8 infection.

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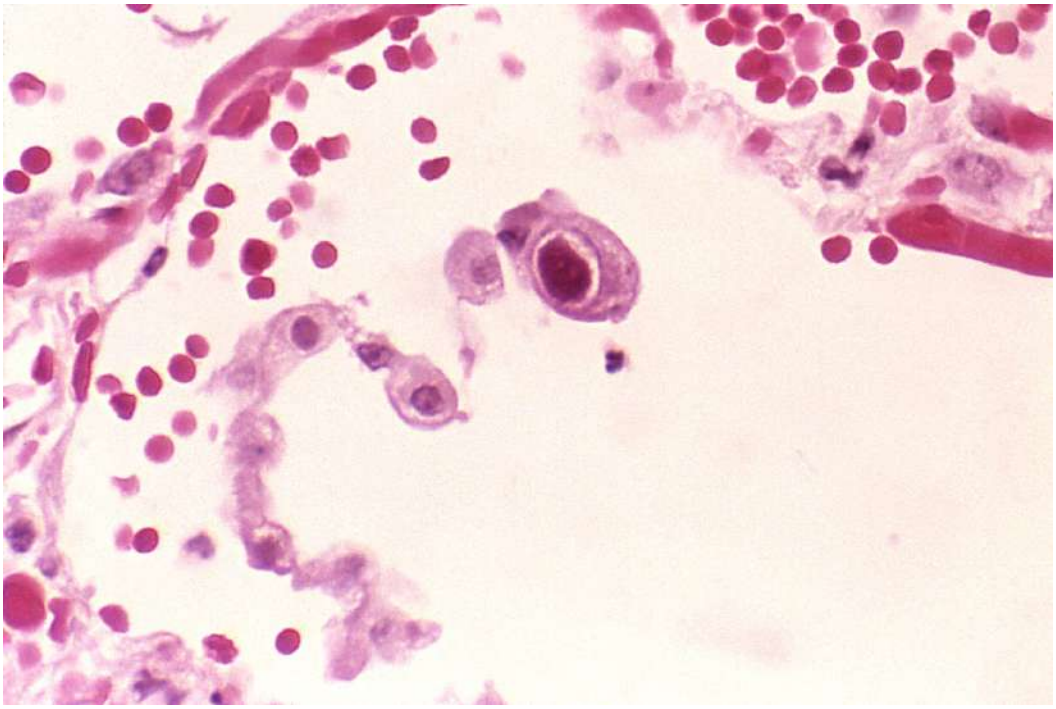
B - Enlarged cells with ground-glass nuclei and central clearing

Explanation Why

Enlarged cells with ground-glass nuclei and central clearing describe "Orphan Annie eye" nuclear inclusions, which are characteristic of papillary thyroid carcinoma and autoimmune thyroiditis (i.e., Hashimoto disease). Neither of these conditions is associated with HHV-8 infection or colonic lesions. In addition, the patient has neither a neck mass to suggest thyroid cancer nor metabolic symptoms (e.g., weight changes, temperature intolerance) to suggest thyroiditis.

C - Enlarged cells with intranuclear inclusion bodies

Image



Explanation Why

A finding of enlarged cells with intranuclear inclusion bodies in an immunocompromised patient with gastrointestinal symptoms is concerning for CMV colitis. Patients with CMV colitis can present

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with abdominal pain and bloody diarrhea. However, endoscopy of CMV colitis usually shows linear ulcers rather than the hemorrhagic nodules seen in this patient. Furthermore, CMV infections (e.g., colitis, retinitis, esophagitis) in patients with HIV typically present when the CD4+ count is < 50 cells/mm^3 and would be unlikely in this patient with a CD4+ count of 180/mm^3.

D - Polygonal cells with racket-shaped organelles

Explanation Why

Polygonal cells with tennis racket-shaped organelles describe Birbeck granules, which are seen in Langerhans cell histiocytosis. Unlike this patient's condition, Langerhans cell histiocytosis rarely involves the gastrointestinal tract. It also would not lead to a low CD4 count and has no known association with HHV-8 infection.

E - Spindle-shaped cells with lymphocytic infiltration

Explanation But

Kaposi sarcoma of the skin appears similar to bacillary angiomatosis, which can also occur in HIV patients. However, bacillary angiomatosis is caused by *Bartonella* species, not HHV-8, and a skin biopsy of bacillary angiomatosis shows a neutrophilic rather than a lymphocytic infiltrate.

Explanation Why

Vascular lesions showing spindle-shaped cells with lymphocytic infiltration are consistent with Kaposi sarcoma, an AIDS-defining condition that is caused by HHV-8 infection. Kaposi sarcomas originate from endothelial cells and usually manifest with asymptomatic vascular tumors of the skin. These tumors can also involve the lymph nodes and gastrointestinal tract, potentially causing diarrhea and abdominal pain. Additional histologic features of Kaposi sarcoma include slit-like vascular spaces and extravasated erythrocytes.

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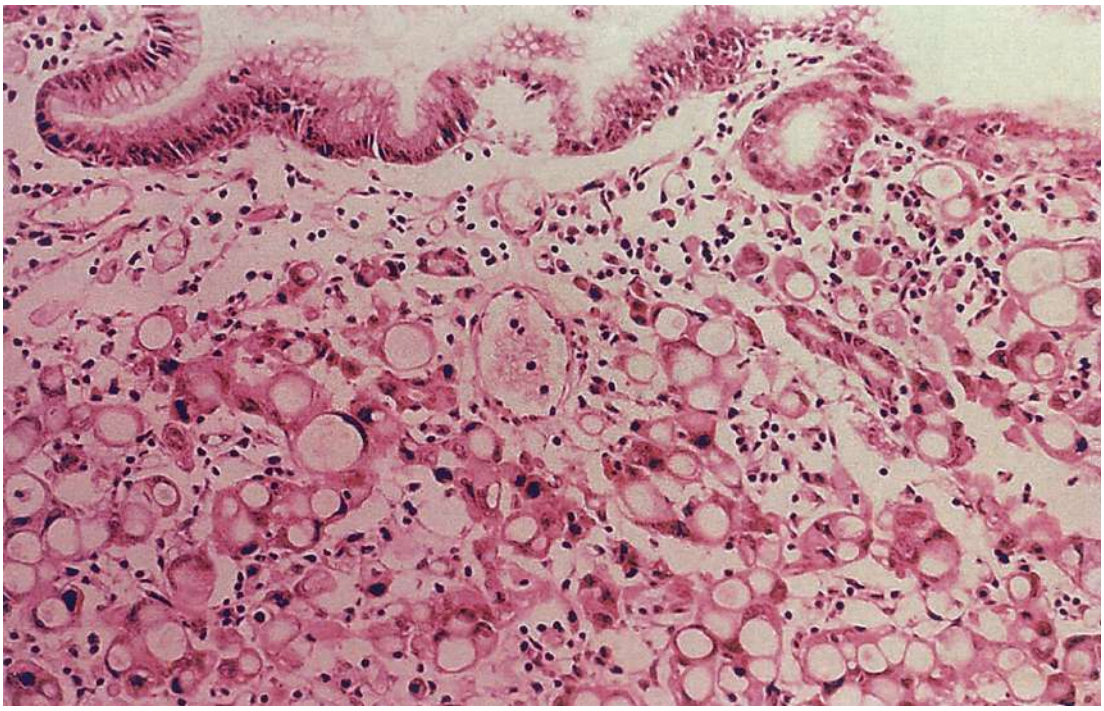
F - Mucin-filled cell with peripheral nucleus

Image



Explanation Why

Cells with large mucin-filled vacuoles that displace the nucleus to the periphery are called Signet ring cells. Signet ring cell carcinoma is a type of adenocarcinoma and usually arises from the stomach. While this form of cancer can cause gastrointestinal upset such as diarrhea and abdominal pain, these lesions are not associated with HHV-8 infection.

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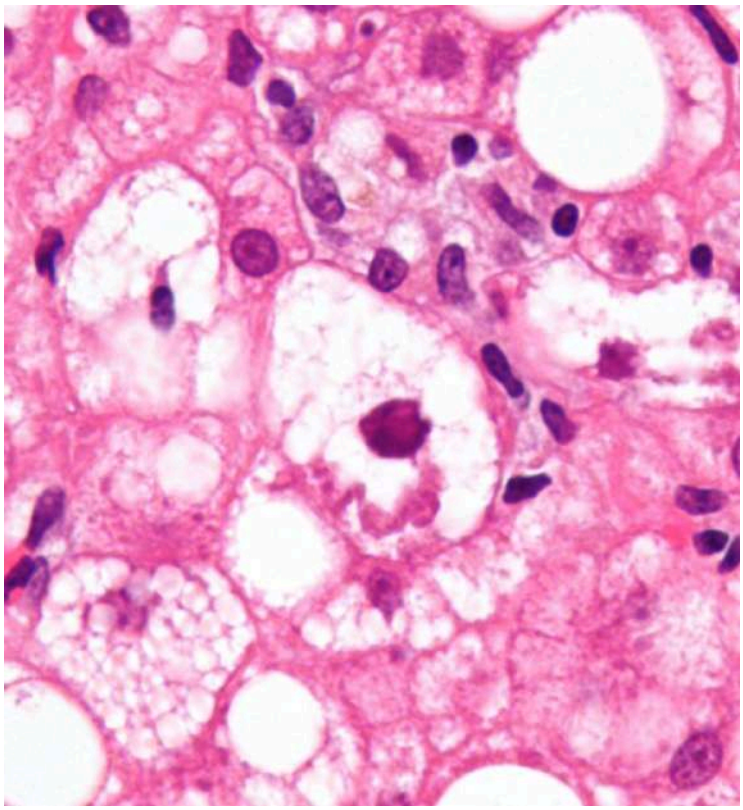
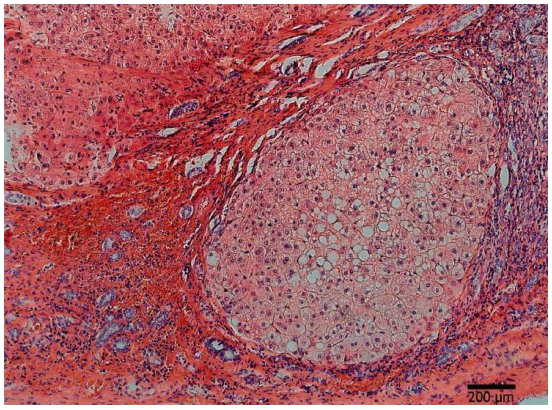
Question # 6

A 43-year-old woman comes to the physician because of a 2-week history of malaise, nausea, and a 3-kg (6.6-lb) weight loss. She has been drinking 8–9 alcoholic beverages daily for the past 20 years. Her temperature is 37.8°C (100°F) and pulse is 105/min. Examination shows jaundice and hepatosplenomegaly. A photomicrograph of a section of a biopsy specimen of the liver is shown. Which of the following mechanisms best explains the findings shown?



	Answer	Image
A	Excessive interstitial TGF-β activity	

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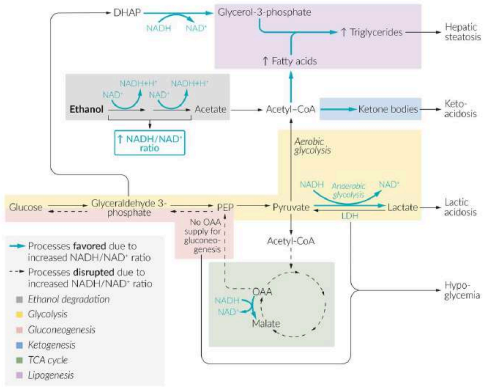
	Answer	Image
B	Decreased clearance of N-acetyl-p-benzoquinone imine	
C	Intracellular accumulation of lactate	
D	Increased glycerol 3-phosphate formation	
E	Estrogen-mediated glandular hyperplasia	

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Hint

This patient has a history of chronic alcoholism and presents with signs and symptoms of hepatic injury. The central hepatocyte in the photomicrograph shows ballooning degeneration, as well as a twisted rope-like cytoplasmic inclusion, called a Mallory body; these are both findings that are strongly associated with steatohepatitis.

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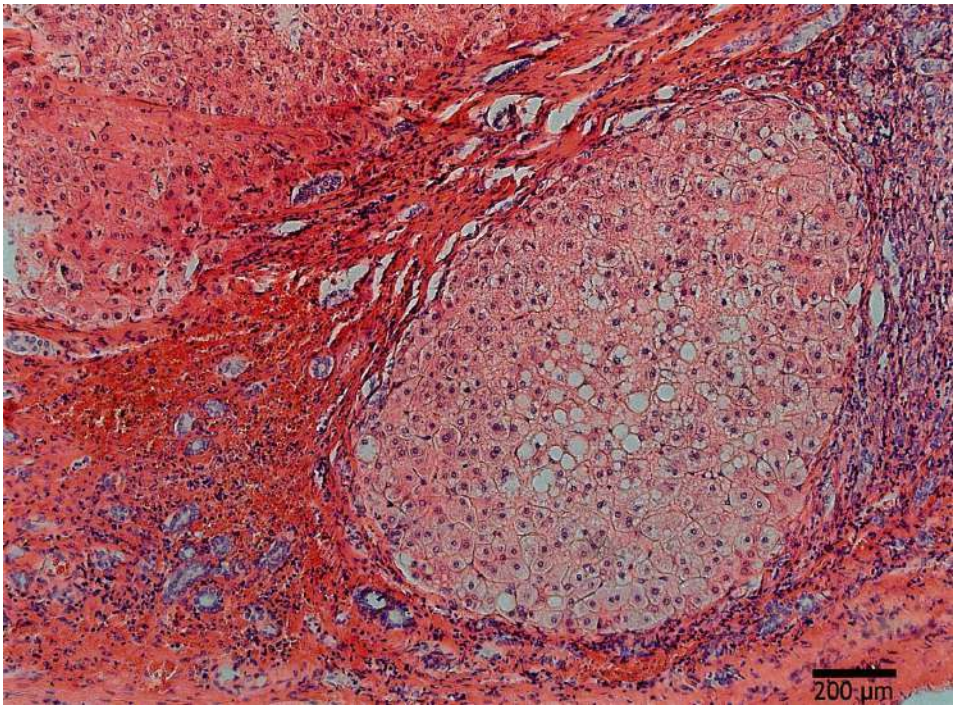
Correct Answer

A - Excessive interstitial TGF-β activity

Image



Explanation Why

Excessive interstitial TGF-β activity is associated with hepatocyte necrosis and would not be expected at this patient's stage of disease. TGF-β is involved in the development of liver cirrhosis, the final, irreversible form of alcoholic liver disease, which is usually preceded by steatohepatitis.

B - Decreased clearance of N-acetyl-p-benzoquinone imine

Explanation Why

Decreased clearance of N-acetyl-p-benzoquinone imine (NAPQI) is the pathomechanism of acetaminophen-induced hepatotoxicity. Increased NAPQI concentrations due to overdose cause acute

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liver failure, not the steatohepatitis seen in this patient.

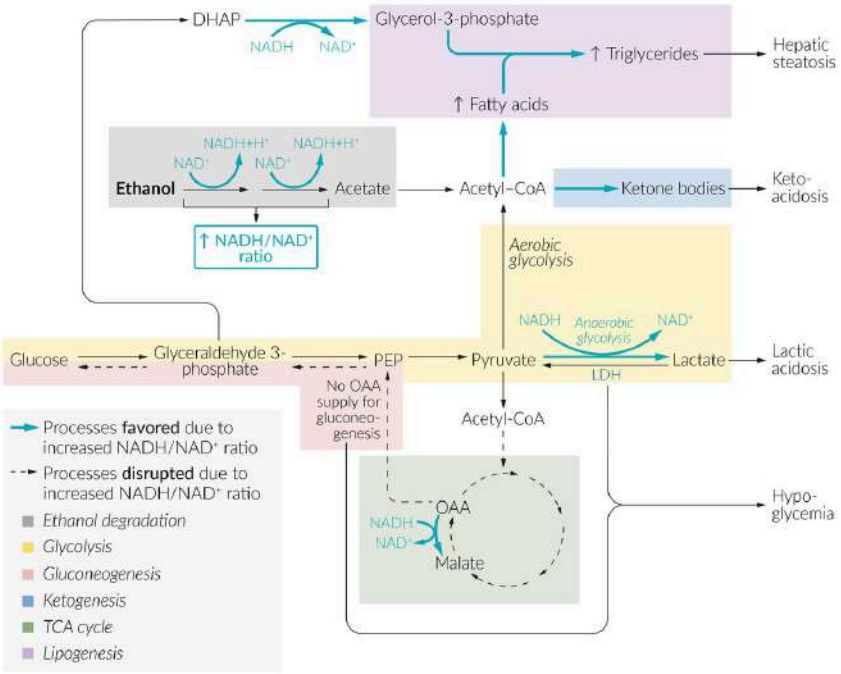
C - Intracellular accumulation of lactate

Explanation Why

Intracellular accumulation of lactate and lactate acidosis can occur with increased activity of alcohol dehydrogenase, which breaks down ethanol by reducing NAD^+ to NADH. An increased concentration of NADH within cells favors the conversion of pyruvate to lactate in an attempt to recycle NAD^+. Increased NADH concentrations play an important role in the pathogenesis of alcohol-induced steatohepatitis. However, intracellular accumulation of lactate is not the mechanism underlying steatohepatitis, which is seen here.

D - Increased glycerol 3-phosphate formation

Image



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Explanation Why

Increased glycerol 3-phosphate formation from dihydroxyacetone phosphate (DHAP) tends to occur when there is a high concentration of reduced nicotinamide adenine dinucleotide (NADH), which is present in individuals who engage in heavy drinking. In this case, massive hepatic degradation of ethanol to acetyl-CoA causes NADH excess. An increase in both glycerol 3-phosphate concentration and availability of fatty acids causes increased triglyceride synthesis, leading to the development of steatohepatitis.

E - Estrogen-mediated glandular hyperplasia

Explanation Why

Estrogen-mediated glandular hyperplasia is typically seen in patients with hepatocellular adenoma. Accordingly, it is strongly associated with the use of oral contraceptives. Even though plasma estrogen levels are elevated in women with chronic, heaving drinking, like this patient, steatohepatitis is caused by a different mechanism.

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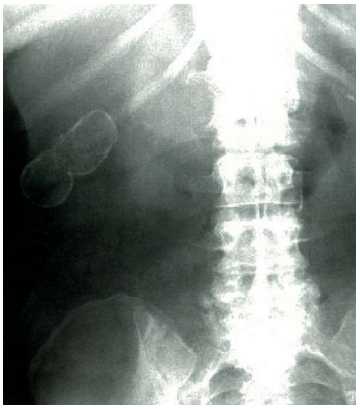
Question # 7

An otherwise healthy 56-year-old woman comes to the physician because of a 3-year history of intermittent upper abdominal pain. She has had no nausea, vomiting, or change in weight. Physical examination shows no abnormalities. Laboratory studies are within normal limits. Abdominal ultrasonography shows a hyperechogenic rim-like calcification of the gallbladder wall. The finding in this patient's ultrasonography increases the risk of which of the following conditions?

	Answer	Image
A	Hepatocellular carcinoma	
B	Pancreatic adenocarcinoma	
C	Gallbladder empyema	
D	Pyogenic liver abscess	
E	Emphysematous cholecystitis	
F	Gallbladder carcinoma	

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	Answer	Image
G	Gallstone ileus	
H	Acute pancreatitis	

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Hint

The imaging findings in this patient are pathognomonic for porcelain gallbladder.

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Correct Answer

A - Hepatocellular carcinoma

Explanation Why

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer. Risk factors for HCC include pre-existing cirrhosis, alcohol use, aflatoxin, or hemochromatosis. However, there are no signs in the patient's history suggesting these underlying conditions. Porcelain gallbladder, which this patient has, is not a known risk factor for hepatocellular carcinoma.

B - Pancreatic adenocarcinoma

Explanation Why

Pancreatic adenocarcinomas are highly aggressive cancers that arise from pancreatic ductal epithelium. Risk factors include tobacco use, chronic pancreatitis, diabetes, age > 50 years, Ashkenazi Jewish descent, African Americans ethnicity. However, porcelain gallbladder, which this patient has, is not associated with an increased risk for pancreatic adenocarcinoma.

C - Gallbladder empyema

Explanation Why

Gallbladder empyema refers to a collection of pus in the gallbladder. Both porcelain gallbladder, which this patient has, and gallbladder empyema are complications of cholelithiasis and cholecystitis. However, porcelain gallbladder itself is not known to cause empyema of the gallbladder.

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D - Pyogenic liver abscess

Explanation Why

Pyogenic liver abscess refers to the formation of a bacterial abscess within the liver. Although pyogenic liver abscesses usually present with upper abdominal pain and often develop from biliary obstruction as a result of chronic cholelithiasis, the condition typically also causes fever, which is absent in this patient. Regardless, porcelain gallbladder is not a known risk factor for pyogenic liver abscess.

E - Emphysematous cholecystitis

Explanation Why

Emphysematous cholecystitis is a rare complication of cholecystitis in which air accumulates in the walls of the gallbladder. It is caused by ischemia of the gallbladder wall due to constriction of blood vessels and subsequent infection with gas-forming bacteria. The inflammatory background of porcelain gallbladder, which this patient has, is not a known risk factor for such a disease.

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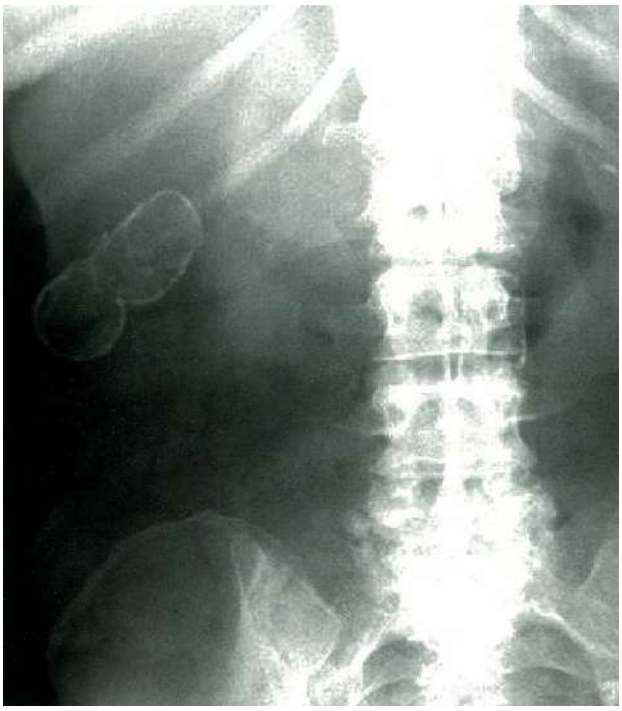
F - Gallbladder carcinoma

Image



Explanation Why

Porcelain gallbladder is a calcification of the gallbladder caused by chronic inflammation as a result of cholecystitis. It is often identified incidentally during abdominal imaging, although it may present with right upper quadrant pain, as in this patient. Porcelain gallbladder causes a significant risk of developing gallbladder adenocarcinoma. Therefore, the recommended treatment is cholecystectomy.

G - Gallstone ileus

Explanation Why

Gallstone ileus occurs when a gallstone finds passage into the small intestines, usually through a biliary-enteric fistula, and gets impacted. Gallstone ileus is frequently preceded by episodes of acute cholecystitis and cholelithiasis, which are both risk factors of porcelain gallbladder, which this

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patient has. However, porcelain gallbladder itself is not a known risk factor for gallstone ileus.

H - Acute pancreatitis

Explanation Why

Acute pancreatitis is the sudden and painful onset of pancreatic inflammation. The most common risk factors for acute pancreatitis are excessive alcohol consumption and cholelithiasis. Although this patient likely has cholelithiasis, porcelain gallbladder itself is not a known risk factor for acute pancreatitis.

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Question # 8

A 48-year old man comes to the physician for the evaluation of an 8-month history of fatigue and profuse, watery, odorless diarrhea. He reports that he has had a 10.5-kg (23-lb) weight loss during this time. Physical examination shows conjunctival pallor and poor skin turgor. Laboratory studies show:

Hemoglobin	9.8 g/dl
Serum	
Glucose (fasting)	130 mg/dl
K^+	2.5 mEq/L
Ca^{2+}	12 mg/dl

A CT scan of the abdomen with contrast shows a 3.0 × 3.2 × 4.4 cm, well-defined, enhancing lesion in the pancreatic tail. Further evaluation of this patient is most likely to show which of the following findings?

	Answer	Image
A	Achlorhydria	
B	Cholelithiasis	
C	Hyperinsulinemia	
D	Peptic ulcers	

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	Answer	Image
E	Tricuspid insufficiency	
F	Deep vein thrombosis	
G	Episodic hypertension	

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Hint

Watery diarrhea, hypokalemia, and a pancreatic mass are pathognomonic of a rare type of pancreatic neuroendocrine tumor. The hypercalcemia in this patient is most likely due to coexistent hyperparathyroidism of multiple endocrine neoplasia 1 syndrome (MEN1).

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Correct Answer

A - Achlorhydria

Explanation Why

Achlorhydria would most likely be seen on further evaluation of this patient with a VIPoma. VIPomas are usually solitary and occur in the pancreatic tail. VIPoma can occur sporadically (> 95% of cases) or as part of the MEN1. VIPoma syndrome is caused by the excessive secretion of vasoactive intestinal peptide (VIP) by the tumor. This results in excess fluid and electrolyte secretion into the lumen, leading to secretory diarrhea and hypokalemia. VIP also inhibits gastric acid secretion, leading to achlorhydria. Reduced gastric acid can lead to iron and vitamin B_{12} malabsorption, which can result in anemia, as seen in this patient. The hyperglycemia often noted in patients with WDHA syndrome is secondary to enhanced glycogenolysis caused by the effect of high portal vein VIP signaling on the liver.

B - Cholelithiasis

Explanation Why

Cholelithiasis is a finding associated with somatostatinomas, which would arise in the pancreas and can present with weight loss, diarrhea, and glucose intolerance. However, diarrhea in a patient with a somatostatinoma is typically caused by fat malabsorption. Therefore, stools would be foul-smelling (steatorrhea), unlike the odorless watery diarrhea in this patient. Moreover, somatostatinomas are among the least common pancreatic neuroendocrine tumors in patients with MEN1 syndrome. They are more commonly associated with neurofibromatosis type I (von Recklinghausen disease).

C - Hyperinsulinemia

Explanation Why

Hyperinsulinemia can be seen in the case of insulinomas, which would arise in the pancreas and can occur as a part of MEN1 syndrome. However, insulinomas would cause recurrent hypoglycemia and patients present with Whipple's triad. Diarrhea and anemia would not be expected with an

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insulinoma.

D - Peptic ulcers

Explanation Why

Peptic ulcers are seen in patients with a gastrinoma (Zollinger-Ellison syndrome) due to high levels of gastrin causing increased gastric acid secretion. Gastrinomas often arise in the pancreas, can cause diarrhea as well as anemia (due to chronic GI bleeding from peptic ulcers), and can occur a part of MEN1 syndrome. However, gastrinomas have no effect on blood glucose levels.

E - Tricuspid insufficiency

Explanation Why

Tricuspid insufficiency can be seen in carcinoid syndrome, which is caused by carcinoid tumors. This patient's profuse watery diarrhea is consistent with carcinoid syndrome. However, carcinoid tumors are most commonly found in the appendix, terminal ileum, or bronchi, unlike the pancreatic mass in this patient, and other features characteristic of carcinoid syndrome (e.g., flushing, wheezing) are not present in this case.

F - Deep vein thrombosis

Explanation Why

Deep vein thrombosis can be associated with a glucagonoma, which most commonly occurs as part of MEN1 syndrome. Although patients may also present with diarrhea, weight loss, and hyperglycemia, glucagonomas are typically associated with necrolytic migratory erythema (seen in 70% of patients). Neuropsychiatric symptoms may also occur. Other symptoms include abdominal pain and angular cheilitis.

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G - Episodic hypertension

Explanation Why

Episodic hypertension is associated with pheochromocytomas. Pheochromocytoma can occur in conjunction with hypercalcemia in patients with MEN2A. Hyperglycemia and hypokalemia can also occur in patients with pheochromocytoma due to the effects of catecholamines. However, a pheochromocytoma arises in the adrenal medulla, not the pancreas. Moreover, patients with a pheochromocytoma typically have symptoms such as episodic headaches, diaphoresis, and palpitations. Diarrhea is not a clinical feature of pheochromocytoma.

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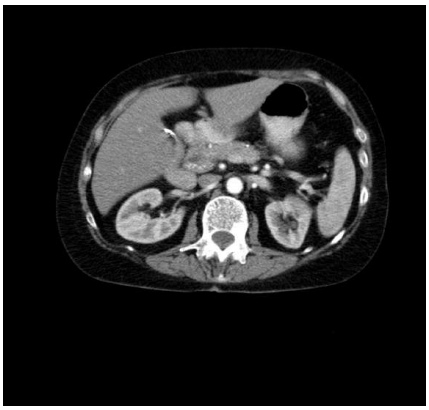
Question # 9

A 47-year-old woman with chronic epigastric pain comes to the physician because of a 1-month history of intermittent, loose, foul-smelling stools. She has also had a 6-kg (13-lb) weight loss. She has consumed 9–10 alcoholic beverages daily for the past 25 years. Seven years ago, she traveled to Mexico on vacation; she has not been outside the large metropolitan area in which she resides since then. She appears malnourished. The stool is pale and loose; fecal fat content is elevated. An immunoglobulin A serum anti-tissue transglutaminase antibody assay is negative. Further evaluation is most likely to show which of the following?

	Answer	Image
A	Inflammation of subcutaneous fat	
B	Trophozoites on stool microscopy	
C	Pancreatic calcifications	
D	Villous atrophy of duodenal mucosa	
E	Positive lactulose breath test	

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Hint

The patient's chronic and heavy alcohol consumption is the key driver of a process that leads to fat malabsorption, which manifests as steatorrhea (bulky, greasy, foul-smelling stool due to increased fat content).

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Correct Answer

A - Inflammation of subcutaneous fat

Explanation Why

Erythema nodosum (inflammation of subcutaneous fat) is associated with ulcerative colitis (UC), which can also present with diarrhea, abdominal pain, and weight loss. However, it is typically associated with bloody diarrhea rather than steatorrhea.

B - Trophozoites on stool microscopy

Explanation Why

Trophozoites on stool microscopy are consistent with giardiasis, which can manifest with steatorrhea and weight loss, and occurs in individuals who travel to resource-limited areas with poor sanitation and limited water treatment facilities. Although this patient has a history of travel, giardiasis is unlikely given that she has not left her metropolitan residential area in the US in the past 7 years.

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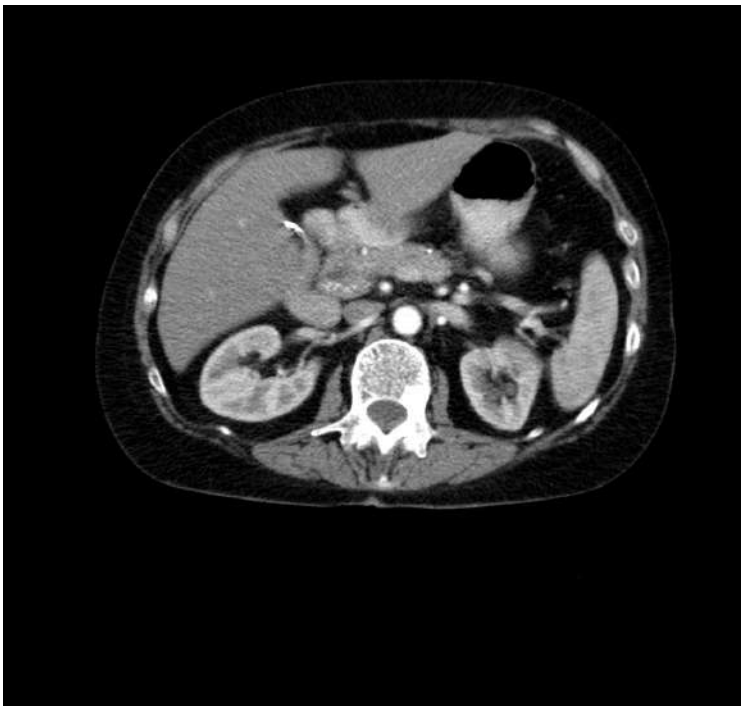
C - Pancreatic calcifications

Image



Explanation Why

Chronic pancreatitis is the most likely diagnosis in a patient with a history of chronic epigastric pain and features of pancreatic insufficiency (e.g., steatorrhea, weight loss). Alcohol use disorder is the most common etiology of chronic pancreatitis, accounting for 60–70% of cases. Diagnosis is confirmed on abdominal CT imaging, which can show pancreatic calcifications, ductal strictures, and ductal dilatation. A “chain of lakes” appearance can sometimes be seen, which is caused by the alternating dilation and stricture of the main pancreatic duct. Pancreatic function tests (e.g., fecal elastase-1 measurement, 72-hour quantitative fecal fat test) can be used to assess the degree of pancreatic exocrine and enzyme deficiency.

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D - Villous atrophy of duodenal mucosa

Explanation Why

Atrophy of the duodenal villi is associated with celiac disease, which can present with abdominal pain, steatorrhea, malnourishment, and weight loss. However, this patient tested negative for anti-tissue transglutaminase antibodies (anti-tTG), which are present in over 90% of patients with celiac disease, making celiac disease an unlikely diagnosis here.

E - Positive lactulose breath test

Explanation Why

The lactulose breath testing is used to diagnose small intestinal bacterial overgrowth (SIBO), which can manifest with chronic abdominal pain, steatorrhea, and weight loss. However, epigastric pain would not be expected with SIBO. Moreover, SIBO is caused by anatomical abnormalities (adhesions or strictures, small intestinal diverticulosis) or motility disorders (e.g., irritable bowel syndrome, radiation enteritis or scleroderma). There is no history of suggestive of any of these conditions in this patient.

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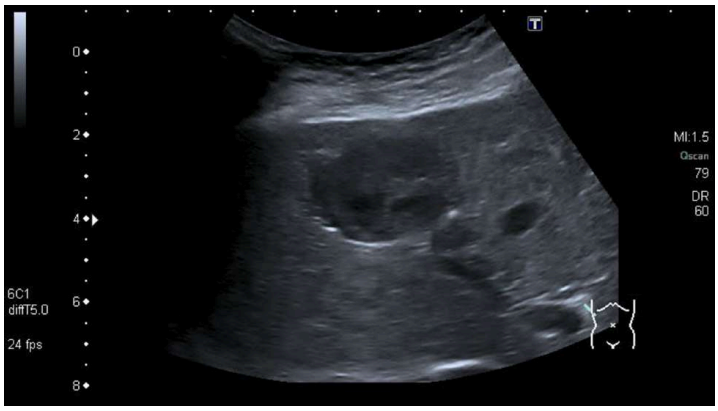
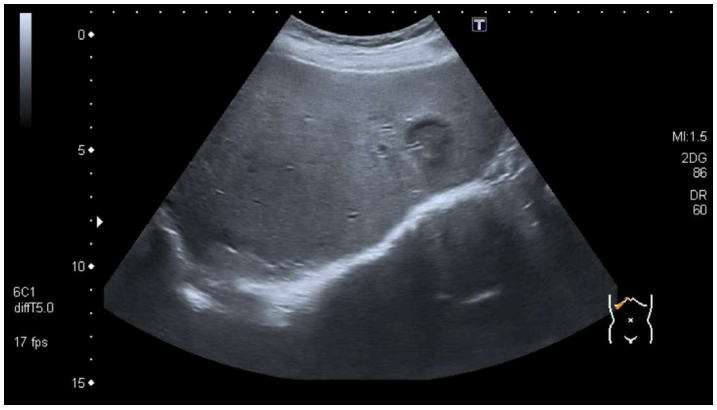
Question # 10

A 71-year-old woman comes to the physician with a 2-month history of fatigue, anorexia, abdominal swelling, shortness of breath, and a 5-kg (11-lb) weight loss. She appears chronically ill. Examination shows jaundice, bilateral temporalis muscle wasting, hepatosplenomegaly, and tense ascites. Ultrasonography of the abdomen shows multiple hepatic masses and enlargement of the portal vein. Which of the following is the most likely cause of these masses?

	Answer	Image
A	Metastatic spread of malignant cells from the colon	
B	Malignant transformation of hepatocytes	

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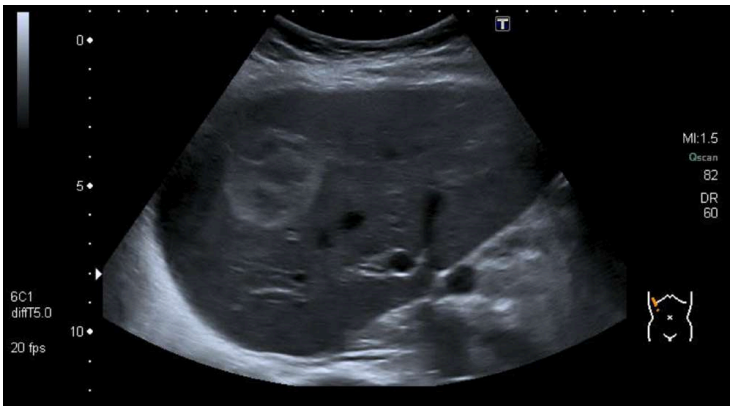
	Answer	Image
C	Proliferation of hepatic capillaries	
D	Hyperplasia of atypical bile duct tissue	
E	Lymphoproliferative disorder of hepatic sinusoids	

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Hint

Processed meats are a risk factor for the causative condition.

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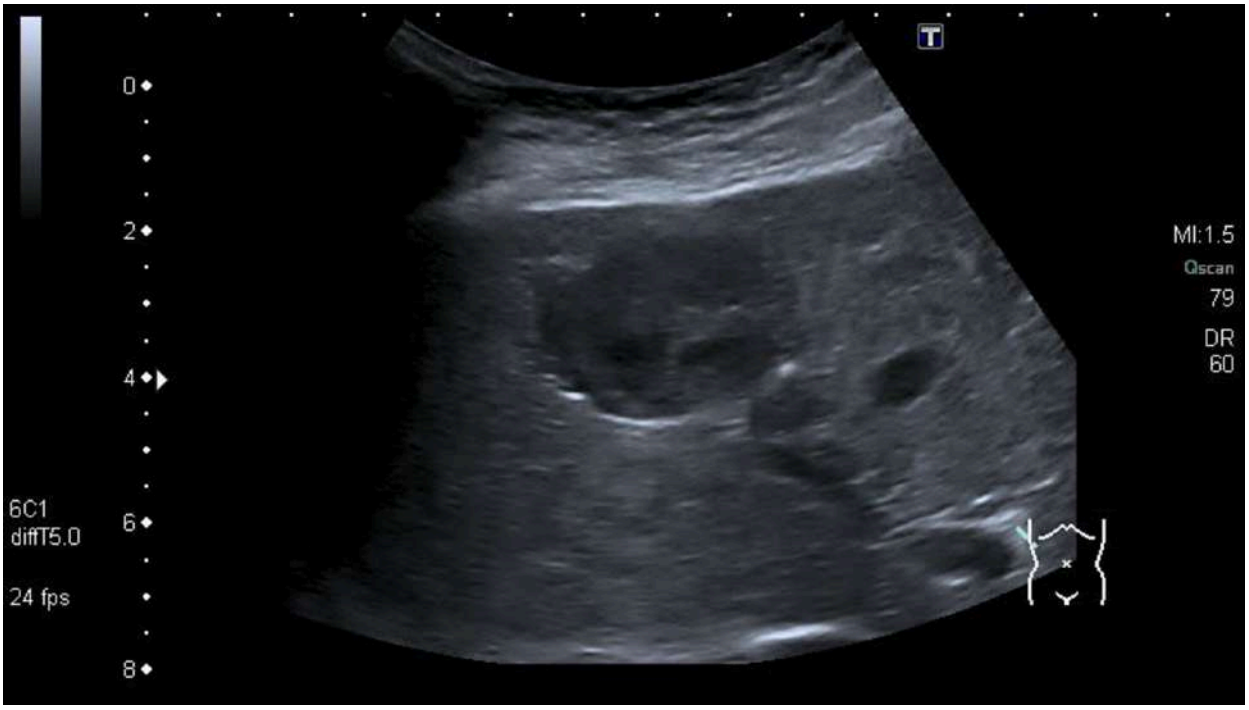
Correct Answer

A - Metastatic spread of malignant cells from the colon

Image



Explanation Why

The most common malignant lesion of the liver is metastatic liver disease, which can manifest with muscle wasting (due to cancer cachexia), hepatosplenomegaly, and features of portal hypertension (e.g., enlarged portal vein, ascites). A liver ultrasound typically shows multiple lesions, as seen in this patient. The most common primary tumor in the case of liver metastases is a colorectal carcinoma, which can be caused by a diet rich in processed meats and low in fiber. Other primary tumor sites for hepatic metastases include the lungs and breasts.

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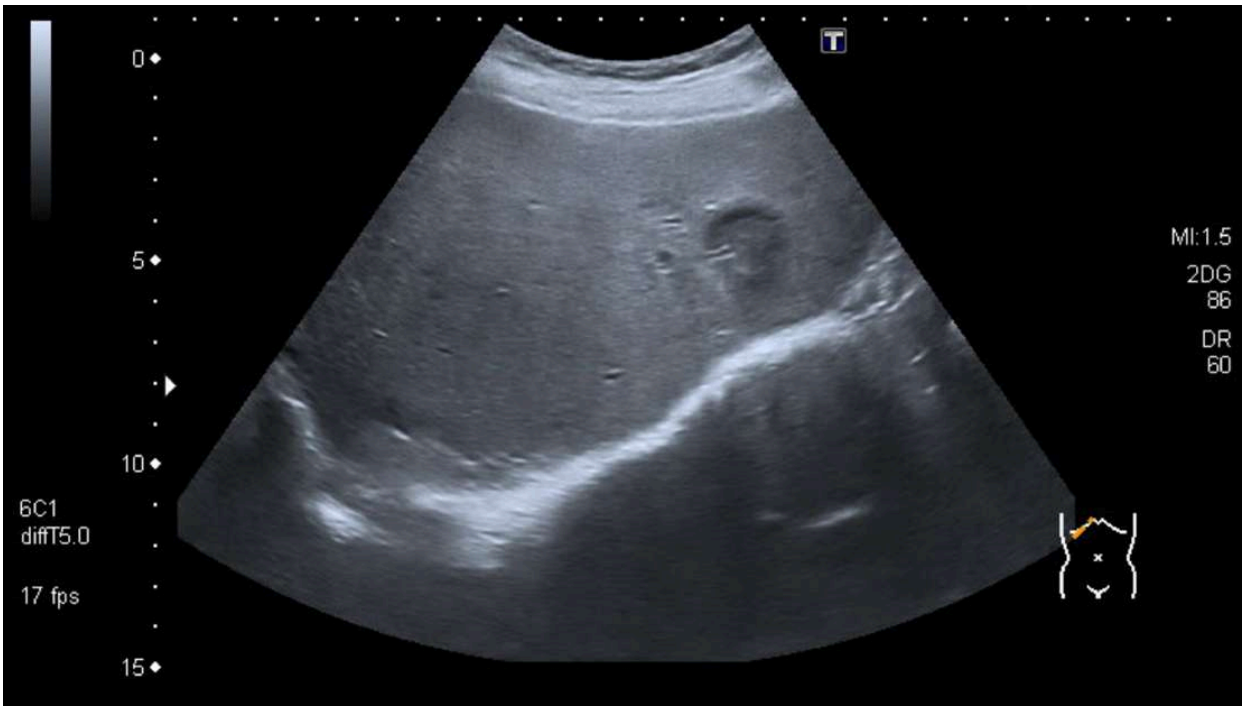
B - Malignant transformation of hepatocytes

Image



Explanation Why

Malignant transformation of hepatocytes leads to hepatocellular carcinoma (HCC). Although HCC can manifest with ascites, jaundice, and hepatomegaly, ultrasound would be more likely to show a single mass with irregular borders than multiple masses, which are more consistent with a secondary liver tumor.

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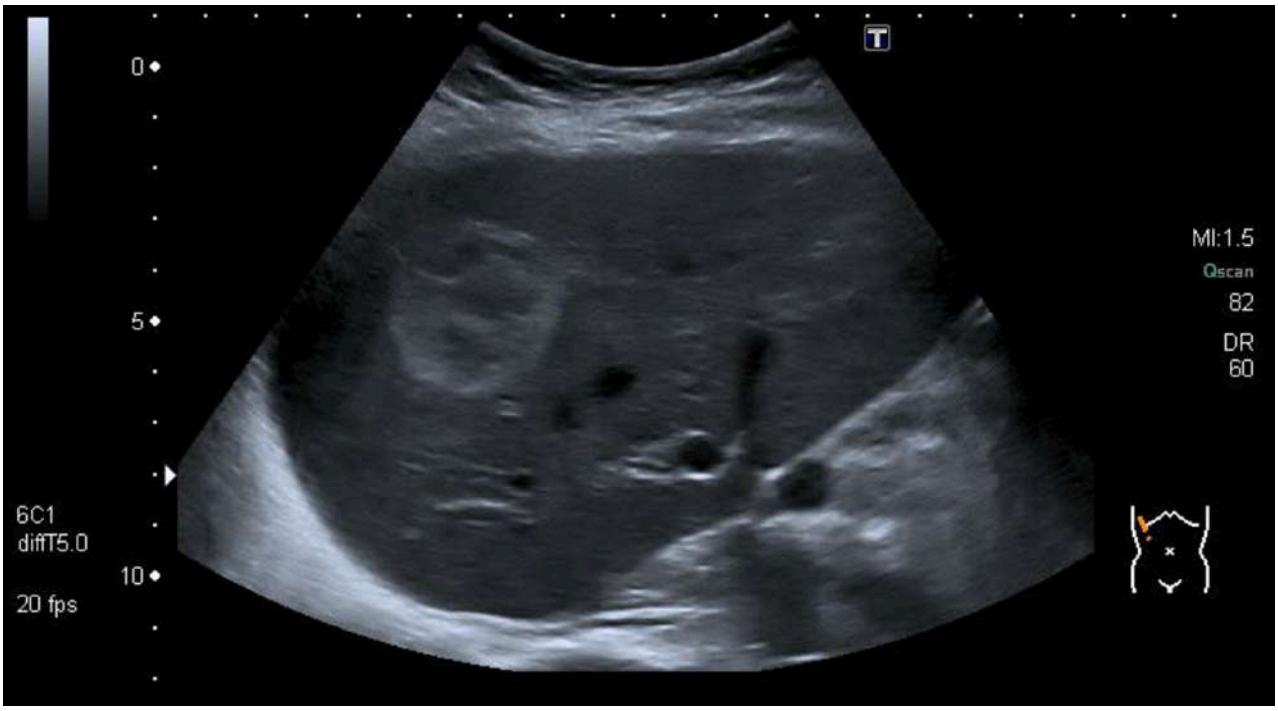
C - Proliferation of hepatic capillaries

Image



Explanation Why

The proliferation of hepatic capillaries leads to a hepatic hemangioma. Large hemangiomas can rarely cause hepatomegaly and abdominal pain, but symptoms such as jaundice, ascites, and muscle wasting are not typical. Also, liver ultrasound would most likely show a single, sharply demarcated, hyperechoic lesion, not multiple masses.

D - Hyperplasia of atypical bile duct tissue

Explanation Why

Hyperplasia of atypical bile duct tissue is seen in cholangiocarcinoma, which can manifest with jaundice (due to cholestasis) and abdominal discomfort. However, ultrasound typically shows a poorly defined mass involving the biliary tree rather than multiple hepatic masses. Moreover, the

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main risk factors for cholangiocarcinoma are primary sclerosing cholangitis and choledochal cysts, of which this patient has no history.

E - Lymphoproliferative disorder of hepatic sinusoids

Explanation Why

Lymphoproliferative disorder of hepatic sinusoids is seen in hepatosplenic T-cell lymphoma (HSTL). Although HSTL can manifest with hepatosplenomegaly, it does not typically cause jaundice, ascites, or multiple masses on ultrasound. Furthermore, lymphoma typically also causes B symptoms, which are not seen in this patient.

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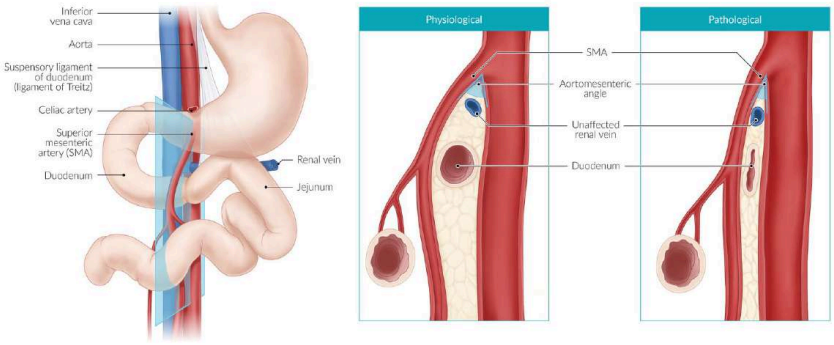
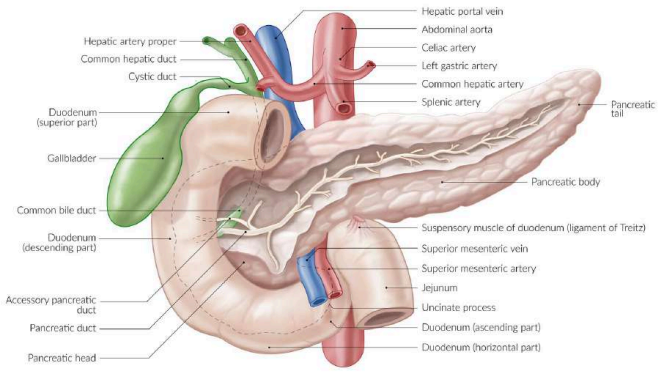
Question # 11

Two days after undergoing abdominal surgery for lysis of adhesions, a 52-year-old man has nausea and one episode of bilious vomiting. The patient's nausea is somewhat alleviated in the prone position. The patient has had a 70-kg (154-lb) weight loss since undergoing bariatric surgery 1 year ago. Physical examination shows abdominal distention. Sudden movement of the patient elicits a sloshing sound on auscultation of the abdomen. An upper gastrointestinal series of the abdomen with oral contrast shows no passage of contrast past the third segment of the duodenum. The obstruction in this patient is most likely caused by which of the following structures?

	Answer	Image
A	Superior mesenteric artery	
B	Body of pancreas	

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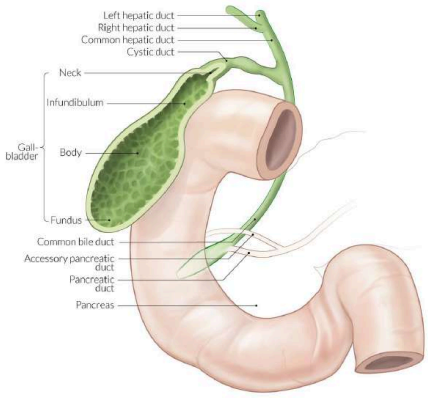
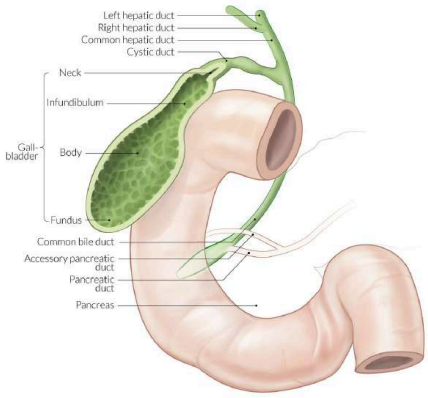
	Answer	Image
C	Gallbladder	
D	Common bile duct	
E	Portal vein	
F	Inferior vena cava	

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Hint

The structure in question can compress the part of the duodenum lying between it and the aorta, leading to features of small bowel obstruction such as nausea, bilious vomiting, abdominal distention, and succussion splash (a sloshing sound heard on abdominal auscultation after moving the patient suddenly).

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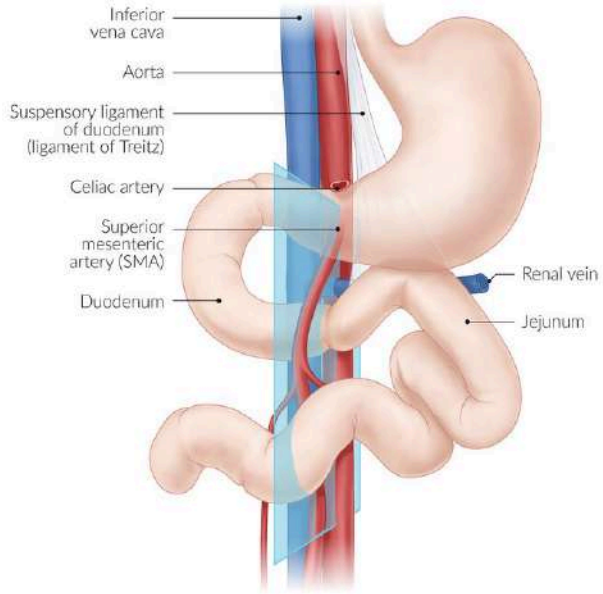
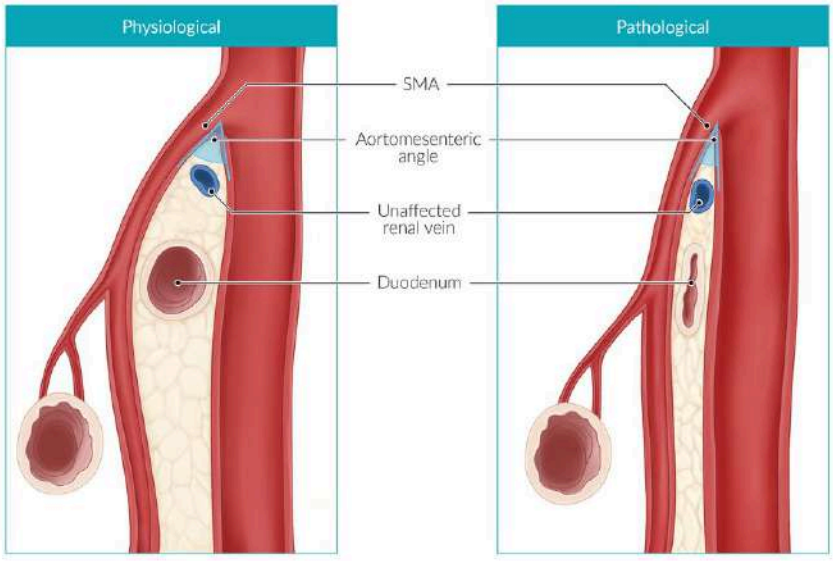
Correct Answer

A - Superior mesenteric artery

Image





Explanation But

Rapid weight loss causes shrinkage of the fat pad between the superior mesenteric artery and the duodenum, leading to compression of the intestinal lumen. Pediatric patients with congenitally abnormal arterial anatomy or those undergoing corrective surgery for scoliosis are also at risk.

Explanation Why

The superior mesenteric artery passes anterior to the third segment of the duodenum (transverse duodenum), and the aorta is located directly posterior to this part of the intestine. Compression of the duodenum by this artery is called superior mesenteric artery syndrome. The classic presentation includes postprandial pain and bilious emesis following extreme weight loss.

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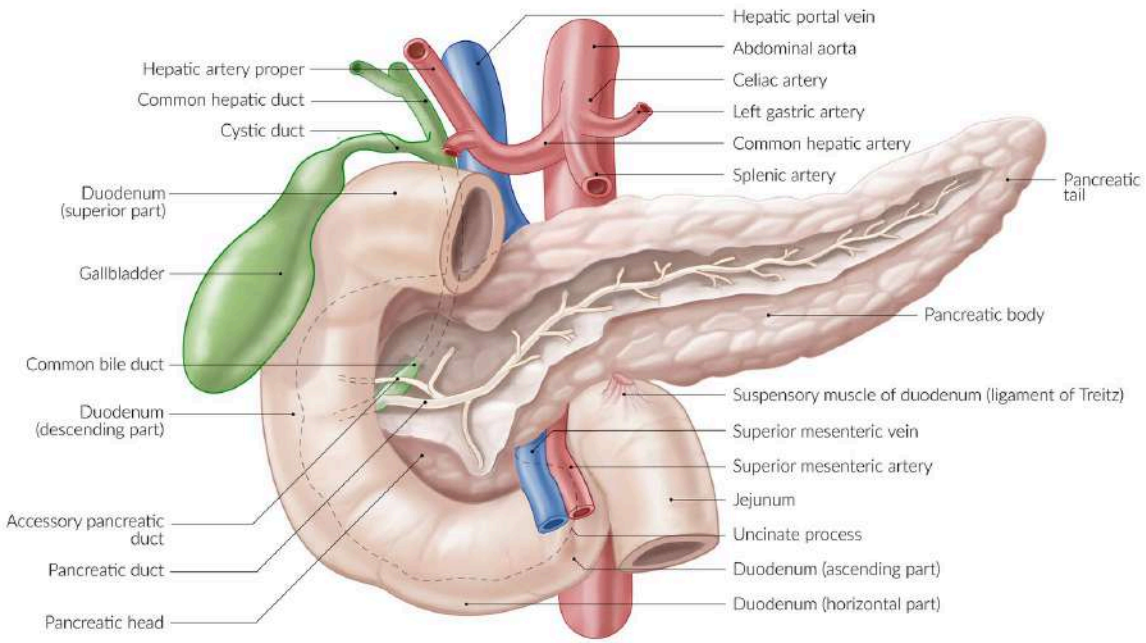
B - Body of pancreas

Image



Explanation Why

The distal second and proximal third segments of duodenum curve around the pancreas. Inflammation of the pancreas, e.g., in severe pancreatitis, or pancreatic mass effect, e.g., from a tumor, could lead to duodenal obstruction. However, this would be expected from a process involving the head of the pancreas. Because the body of the pancreas is not in close contact with the duodenum, a pathology in this area would be very unlikely to account for an obstruction of the intestinal lumen.

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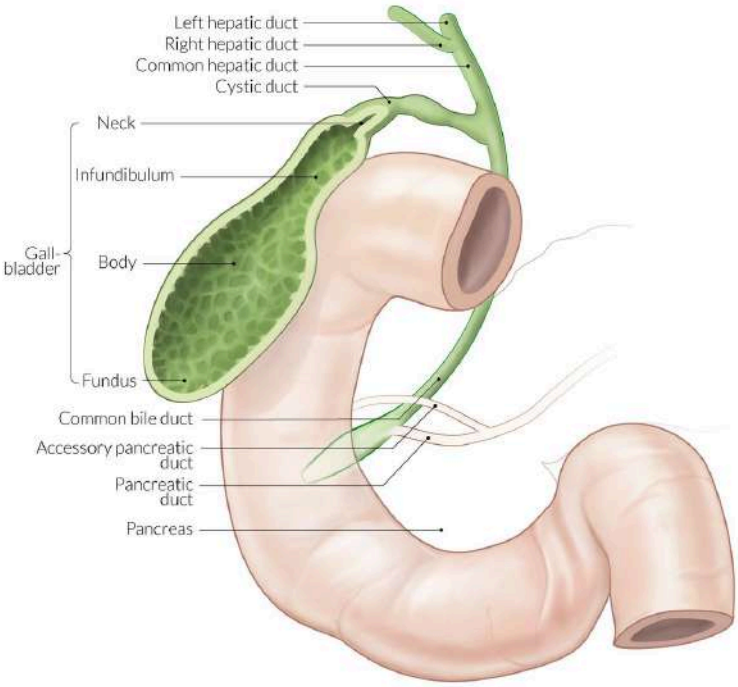
C - Gallbladder

Image



Explanation Why

The gallbladder empties into the second segment of the duodenum. Direct obstruction of the duodenum by an enlarged gallbladder is very unlikely and would not cause third segment obstruction. In the very rare event of a fistula between the gallbladder and the duodenum, a gallstone can enter the intestinal lumen and cause an obstruction, which is known as gallstone ileus. However, gallstone ileus most often manifests with obstruction at the ileocecal valve.

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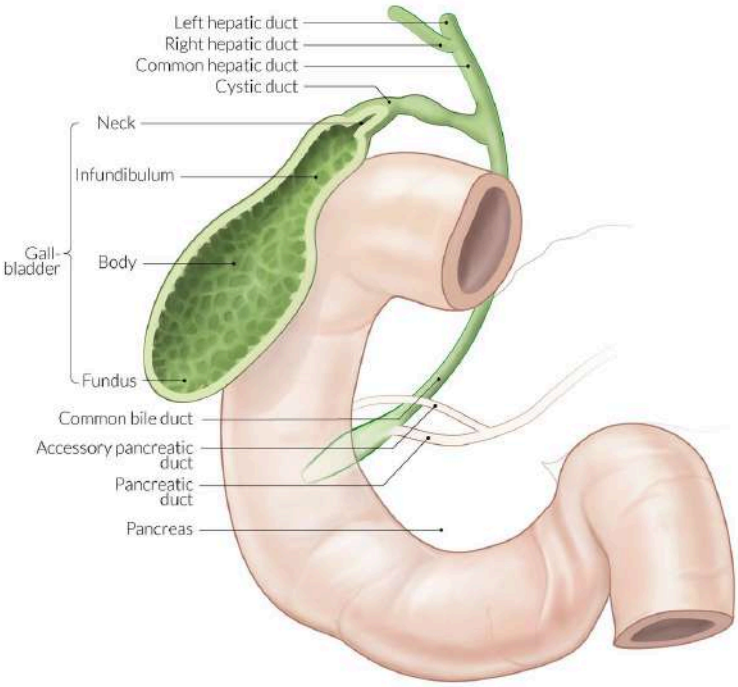
D - Common bile duct

Image



Explanation Why

The common bile duct enters the second segment of the duodenum. Cholangiocarcinoma of the bile duct at its junction with the duodenum can cause obstruction of the duodenum. However, this would result in second segment obstruction, not the third segment obstruction seen in this patient. Additionally, bilious emesis would not be expected, as bile flow through the common bile duct would be severely reduced or blocked entirely.

E - Portal vein

Explanation Why

The portal vein arises from the confluence of the superior mesenteric and splenic vein posterior to the pancreas. It then travels superolaterally to the liver. It does not have contact with the duodenum

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and is not known to cause duodenal obstruction.

F - Inferior vena cava

Explanation Why

The inferior vena cava is located in the retroperitoneum where it passes posterior to the second and third segments of the duodenum and the pancreas. The inferior vena cava can easily be compressed due to its low intravascular pressure but is unlikely to cause obstruction of adjacent structures such as the duodenum.

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Question # 12

Eight weeks after starting a new weight-loss medication, a 43-year-old woman with obesity comes to the physician because of greasy diarrhea, excessive belching, and flatulence. She also complains of progressively worsening night-time vision. She has had no fever, chills, or vomiting. Physical examination shows dry, scaly skin on her extremities and face. Which of the following is the most likely mechanism of action of the drug she is taking?

	Answer	Image
A	Stimulation of monoamine neurotransmitter release	
B	Inhibition of serotonin reuptake	
C	Stimulation of norepinephrine release	
D	Inhibition of lipase	
E	Secretion of glucose-dependent insulin	

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Hint

This patient's greasy diarrhea and symptoms of vitamin A deficiency (poor night vision, xeroderma) are characteristic adverse effects related to orlistat, a commonly used weight-loss medication.

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Correct Answer

A - Stimulation of monoamine neurotransmitter release

Explanation Why

Amphetamines stimulate the release of monoamine neurotransmitters and can be used to induce weight loss. The most common adverse effects of amphetamines include tachycardia, hypertension, and appetite suppression. Steatorrhea and symptoms of fat-soluble vitamin malabsorption are not consistent with amphetamine use.

B - Inhibition of serotonin reuptake

Explanation Why

SSRIs can be prescribed to reduce weight in patients with binge eating disorder, especially in those with concomitant depression. Although adverse effects of SSRIs include diarrhea, steatorrhea and other symptoms of fat malabsorption are not common. More typical side effects of SSRIs such as somnolence/insomnia, dizziness, headaches, and nausea would be expected instead. This patient has no history of binge eating disorder or depression, which makes this medication unlikely.

C - Stimulation of norepinephrine release

Explanation Why

Phentermine, which stimulates norepinephrine release, can be used as a weight-loss agent. However, the most common adverse effects include cardiovascular symptoms (e.g., tachycardia, hypertension, and palpitations) and constipation, rather than diarrhea and symptoms associated with fat malabsorption, which is seen here.

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D - Inhibition of lipase

Explanation Why

Lipase inhibitors such as orlistat inactivate gastric and pancreatic lipase enzymes within the intestine, preventing the complete hydrolyzation of dietary fats into monoglycerides and fatty acids. This decreases the amount of fat absorbed in the gastrointestinal tract and increases fecal fat excretion. Adverse effects of orlistat, therefore, include symptoms of fat malabsorption, such as steatorrhea, abdominal cramps, and bloating. It may also cause fat-soluble vitamin deficiencies (in this case, vitamin A deficiency).

E - Secretion of glucose-dependent insulin

Explanation Why

GLP1 agonists facilitate insulin secretion in response to food. They can be used to achieve weight loss, especially in patients with pre-existing T2DM and cardiovascular disease, which this patient does not have. Although common adverse effects of this class of medications include GI disturbances, steatorrhea and other symptoms of fat malabsorption would not be expected.

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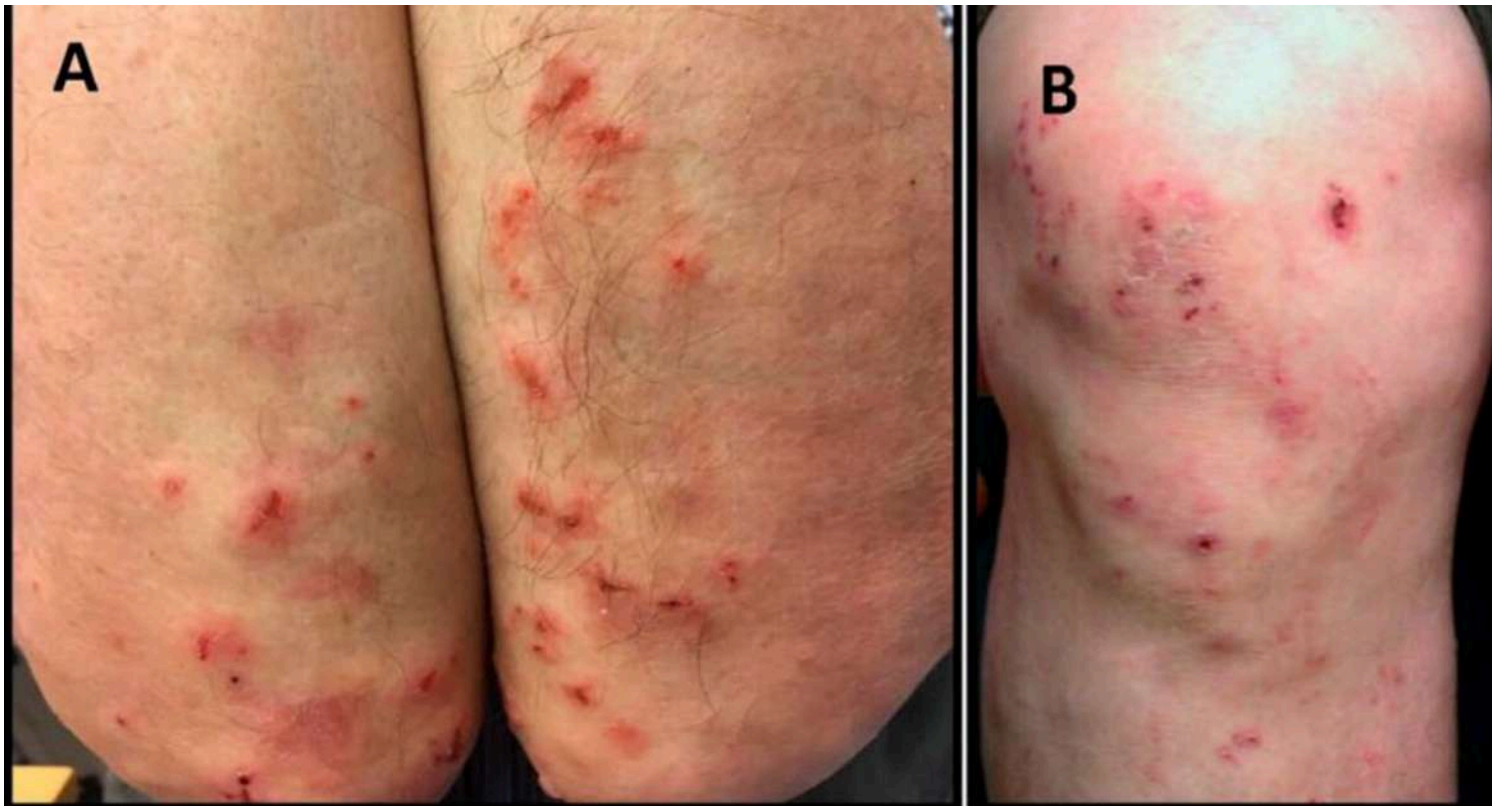
Question # 13

A 23-year-old woman comes to the physician because of a 2-month history of diarrhea, flatulence, and fatigue. She reports having 3–5 episodes of loose stools daily that have an oily appearance. The symptoms are worse after eating. She also complains of an itchy rash on her elbows and knees. A photograph of the rash is shown. Further evaluation of this patient is most likely to show which of the following findings?



	Answer	Image
A	Macrocytic, hypochromic red blood cells	
B	Low fecal elastase levels	
C	PAS-positive intestinal macrophages	

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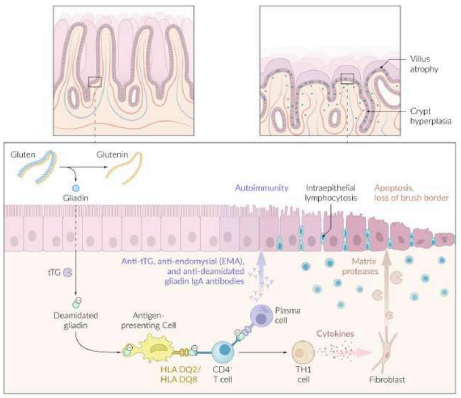
	Answer	Image
D	HLA-DQ2 serotype	
E	Elevated exhaled hydrogen concentration	
F	Elevated urine tryptophan levels	

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Hint

This woman's rash is consistent with dermatitis herpetiformis and her symptoms of malabsorption (e.g., fatty diarrhea, flatulence, fatigue) are suggestive of celiac disease.

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Correct Answer

A - Macrocytic, hypochromic red blood cells

Explanation Why

Malabsorptive conditions that cause macrocytic, hypochromic anemia due to vitamin B_{12} and/or folate deficiency include tropical sprue, atrophic gastritis, and chronic pancreatitis. Celiac disease causes malabsorption of iron in the duodenum and may result in a microcytic, hypochromic anemia.

B - Low fecal elastase levels

Explanation Why

Decreased fecal elastase levels are seen in patients with exocrine pancreatic insufficiency (e.g., from chronic pancreatitis). Although this condition can manifest with diarrhea and flatulence, it is not associated with dermatitis herpetiformis. In addition, patients with chronic pancreatitis typically have epigastric abdominal pain that radiates to the back and improves upon leaning forward (though in the later stages of chronic pancreatitis, patients may not have any pain).

C - PAS-positive intestinal macrophages

Explanation Why

Biopsy results that show PAS-positive intestinal macrophages confirm a diagnosis of Whipple disease. Although this condition can manifest with diarrhea and flatulence, it is not associated with dermatitis herpetiformis. In addition, this patient lacks other characteristic findings of Whipple disease, such as sacroiliitis, polyserositis, and/or lymphadenopathy.

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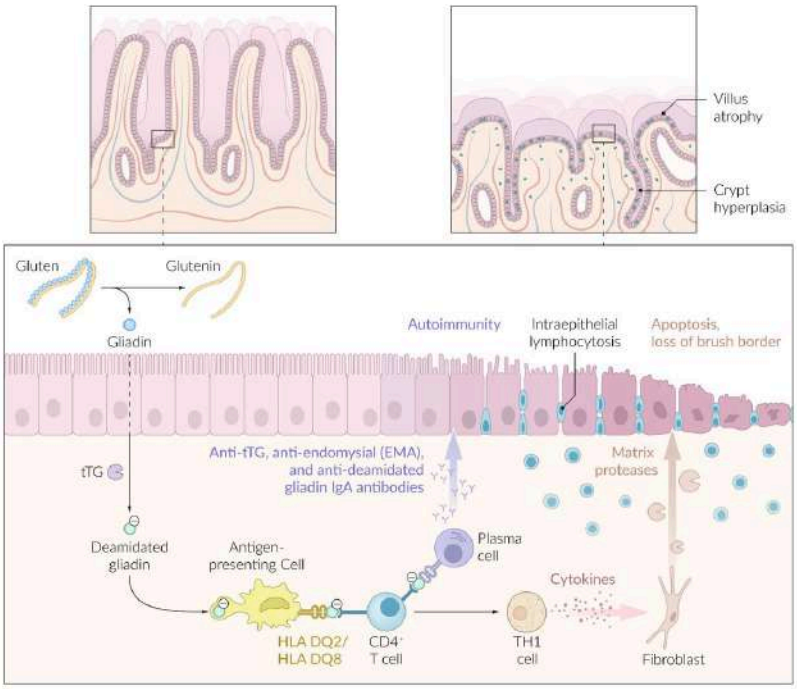
D - HLA-DQ2 serotype

Image



Explanation Why

HLA-DQ2 is a cell surface receptor of antigen-presenting cells associated with 90–95% of cases of celiac disease. Expression of HLA-DQ2 is thought to predispose patients to celiac disease due to increased binding of gluten peptides to this HLA subtype, triggering a T-cell mediated autoimmune reaction and inflammation of the intestinal epithelium. Dermatitis herpetiformis is associated with celiac disease and is caused by deposition of IgA and complement C3 in dermal papillae of the dermis.

E - Elevated exhaled hydrogen concentration

Explanation Why

Elevation in exhaled hydrogen concentration when performing a lactose or hydrogen breath test is

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seen in patients with lactose intolerance or small intestinal bacterial overgrowth (SIBO). Although both of these conditions can manifest with diarrhea and flatulence, neither is associated with dermatitis herpetiformis.

F - Elevated urine tryptophan levels

Explanation Why

Elevation in urine tryptophan levels is seen in patients with Hartnup disease. This condition can cause diarrhea and a skin rash (due to niacin deficiency); however, the typical rash involves the neck (Casal necklace) and manifests with hyperpigmentation of sun-exposed areas. In addition, patients with Hartnup disease often develop features of dementia and glossitis, which this patient does not have.

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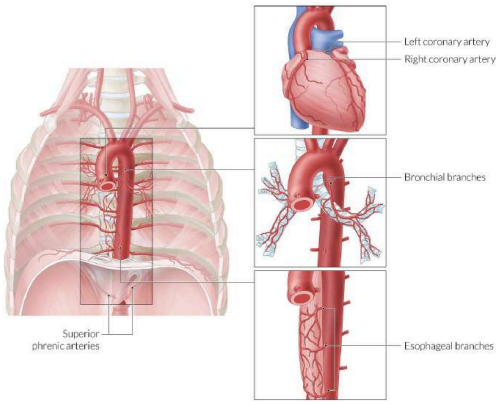
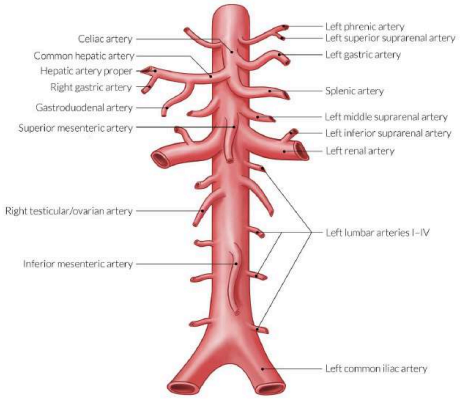
Question # 14

A 63-year-old man comes to the physician because of a 1-month history of difficulty swallowing, low-grade fever, and weight loss. He has smoked one pack of cigarettes daily for 30 years. An esophagogastroduodenoscopy shows an esophageal mass just distal to the upper esophageal sphincter. Histological examination confirms the diagnosis of locally invasive squamous cell carcinoma. A surgical resection is planned. Which of the following structures is at greatest risk for injury during this procedure?

	Answer	Image
A	Esophageal branch of thoracic aorta	
B	Left inferior phrenic artery	

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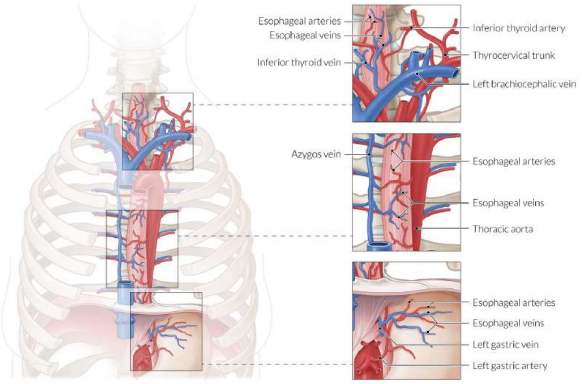
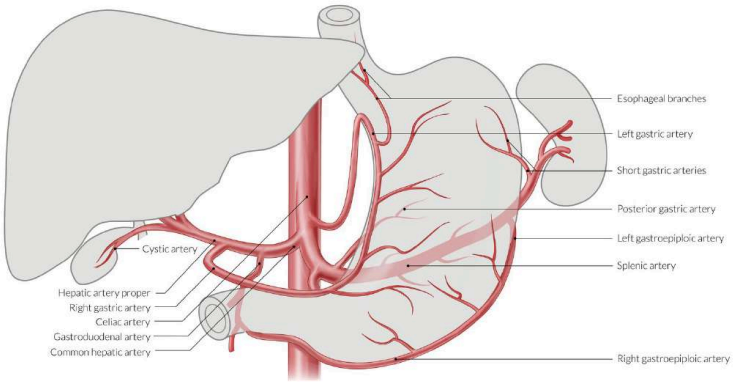
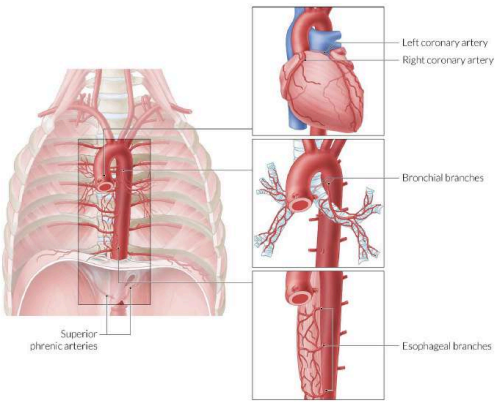
	Answer	Image
C	Inferior thyroid artery	
D	Left gastric artery	
E	Bronchial branch of thoracic aorta	

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Hint

This patient presents with squamous cell carcinoma in the cervical portion of the esophagus.

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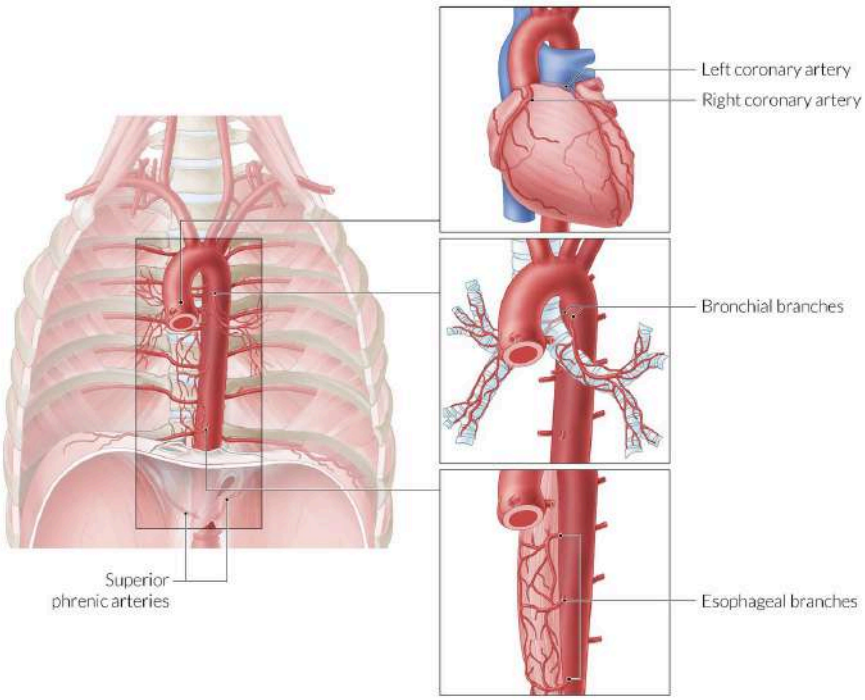
Correct Answer

A - Esophageal branch of thoracic aorta

Image



Explanation Why

The esophageal branch of thoracic aorta supplies the thoracic portion of the esophagus, which extends between the thoracic inlet and the gastroesophageal junction. A different structure is at higher risk of injury given the location of the mass.

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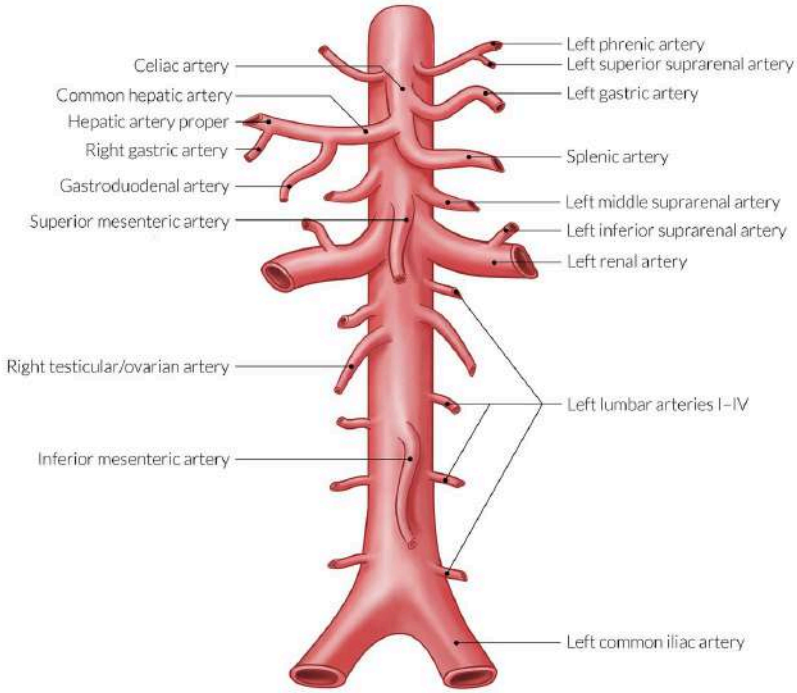
B - Left inferior phrenic artery

Image



Explanation Why

The left inferior phrenic artery originates from the aorta and supplies the abdominal portion of the esophagus, which is located below the esophageal hiatus of the diaphragm. A different structure is at higher risk of injury given the location of the mass.

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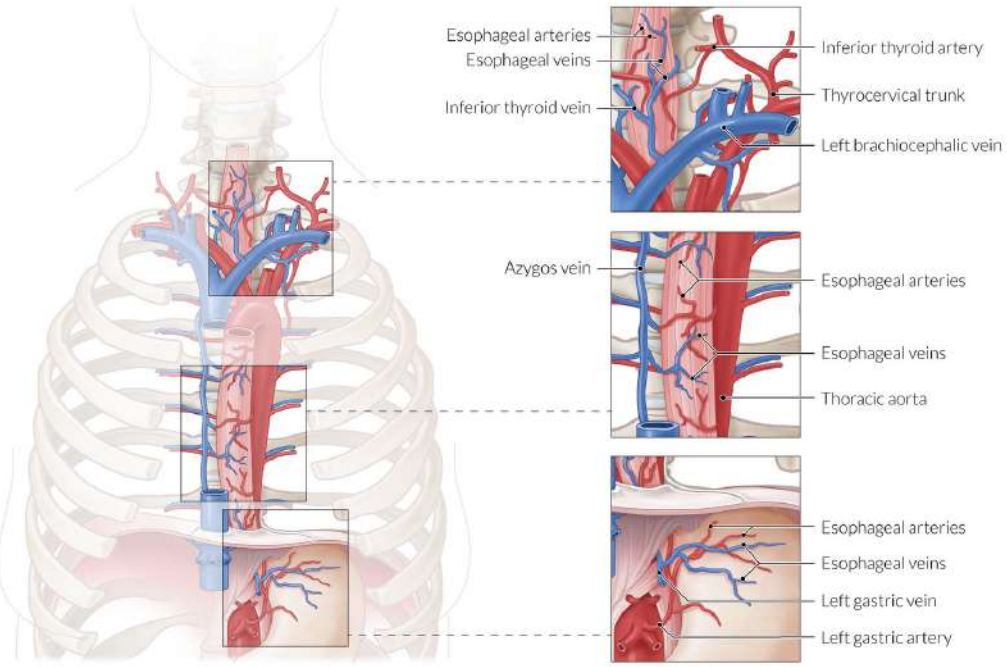
C - Inferior thyroid artery

Image



Explanation Why

The inferior thyroid artery originates from the thyrocervical trunk, a branch of the subclavian artery. It supplies the cervical portion of the esophagus, which is 6–8 cm long and extends between the hypopharynx (lower border of the cricoid cartilage) and the thoracic inlet (suprasternal notch). Since this tumor is located in the cervical portion of the esophagus, care should be taken to avoid injuring this artery during the surgery.

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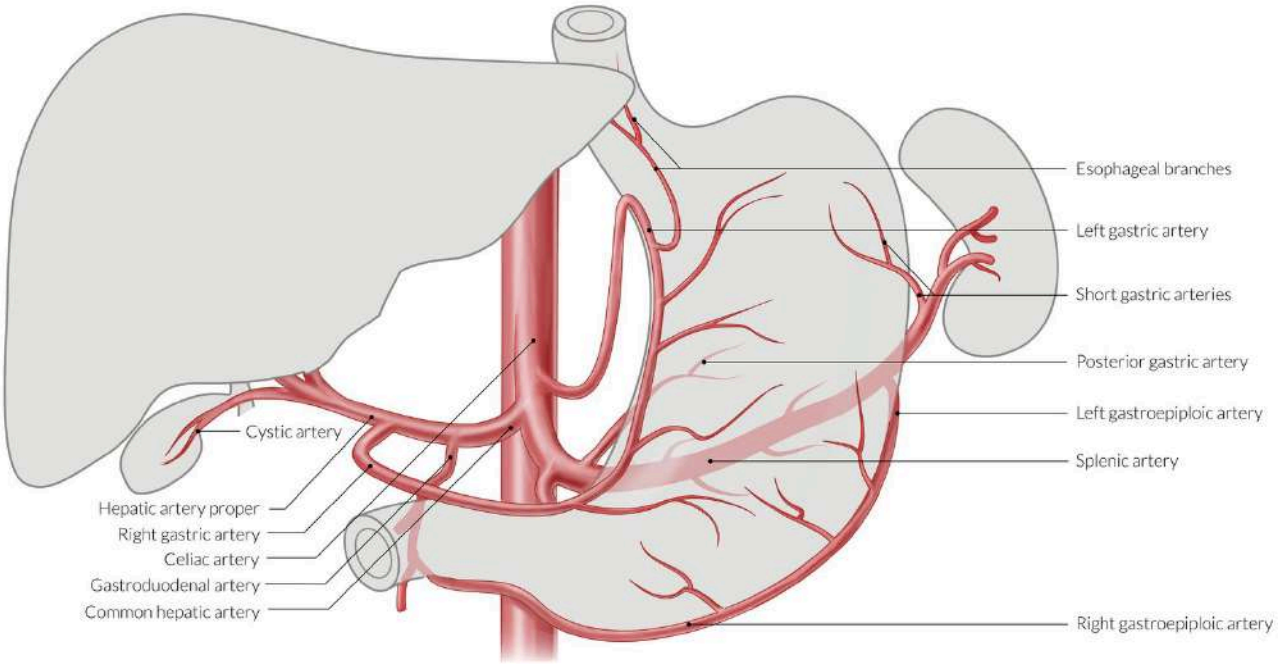
D - Left gastric artery

Image



Explanation Why

The left gastric artery originates from the celiac trunk and supplies the abdominal portion of the esophagus, which is located below the esophageal hiatus of the diaphragm.

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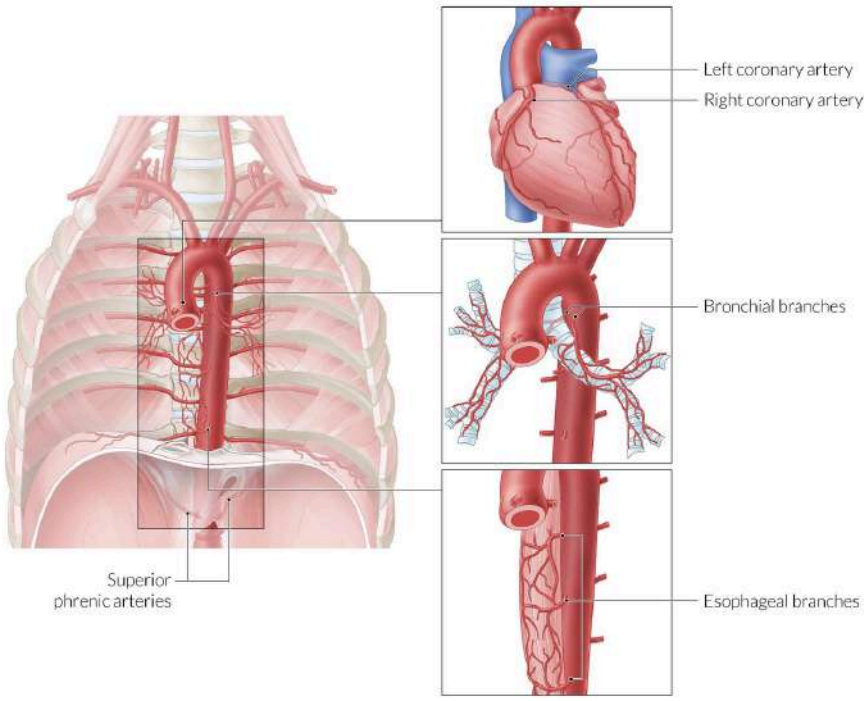
E - Bronchial branch of thoracic aorta

Image



Explanation Why

The bronchial branch of the thoracic aorta supplies parts of the trachea, bronchi, and thoracic portion of the esophagus, which extends between the thoracic inlet and the gastroesophageal junction. A different structure is at higher risk of injury given the location of the mass.

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Question # 15

A 21-year-old woman comes to the physician because of a 4-day history of abdominal cramps and bloody diarrhea 5 times per day. Her symptoms began after she ate an egg sandwich from a restaurant. Her vital signs are within normal limits. Physical examination shows diffuse abdominal tenderness. Stool culture shows gram-negative rods that produce hydrogen sulfide and do not ferment lactose. Which of the following effects is most likely to occur if she receives antibiotic therapy?

	Answer	Image
A	Self-limiting systemic inflammatory response	
B	Pruritic maculopapular rash on the extensor surface	
C	Thrombocytopenia and hemolytic anemia	
D	Orange discoloration of bodily fluids	
E	Prolonged fecal excretion of the pathogen	

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Hint

Salmonella are gram-negative rods that produce hydrogen sulfide and do not ferment lactose. Nontyphoidal species of salmonella (e.g., *Salmonella enterica*) can cause dysentery. Uncooked poultry products are a common source of salmonella infections.

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Correct Answer

A - Self-limiting systemic inflammatory response

Explanation Why

A self-limiting systemic inflammatory response describes the Jarisch-Herxheimer reaction, which is a reaction to bacterial endotoxins that are released after antibiotic therapy initiation. This reaction is commonly seen following the treatment of spirochete infections, such as syphilis or Lyme disease. However, this patient does not show signs of syphilis (primary skin lesions and regional nontender lymphadenopathy) or Lyme disease (e.g., erythema chronicum migrans, migratory arthritis, cranial nerve palsy, polyneuropathy, carditis). In addition, the patient's stool culture shows rods, not spirochetes, and uncooked poultry products are not a common source of spirochete infections.

B - Pruritic maculopapular rash on the extensor surface

Explanation Why

A pruritic maculopapular rash that is more prominent on the extensor surfaces describes a side effect that patients with infectious mononucleosis can develop when they are incorrectly prescribed ampicillin. However, this patient has no signs of infectious mononucleosis (e.g., splenomegaly, pharyngitis, bilateral cervical lymphadenopathy) and therefore would not develop this reaction. Furthermore, pathogen detection shows rods, not a double-stranded, enveloped DNA virus, and uncooked poultry products are not a source of EBV infections.

C - Thrombocytopenia and hemolytic anemia

Explanation Why

Thrombocytopenia with hemolytic anemia describes hemolytic uremic syndrome, a complication sometimes seen when antibiotics are initiated in *Shigella* or EHEC infection. *E. coli* and *Shigella* are gram-negative rods, which can be transmitted by uncooked poultry products. However, in contrast to salmonella, *E. coli* ferments lactose and *Shigella* does not produce hydrogen sulfide. In addition, salmonellosis can be treated with ceftriaxone, which can induce hemolytic anemia; however, this

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treatment would not cause thrombocytopenia.

D - Orange discoloration of bodily fluids

Explanation Why

Orange discoloration of bodily secretions such as urine, sweat, and saliva is a common side-effect of rifampin treatment. Rifampin is used for the treatment of tuberculosis or as a prophylaxis when in contact with patients infected with *N. meningitidis*. However, this patient does not show signs of tuberculosis (e.g., dyspnea, productive cough, weight loss, night sweats, lymphadenopathy) and has not been in contact with patients infected with *N. meningitidis*. Pathogen detection also shows rods, not gram-positive, acid-fast bacilli, and uncooked poultry products are not a common source of *M. tuberculosis* infections.

E - Prolonged fecal excretion of the pathogen

Explanation Why

Salmonella gastroenteritis may be treated with antibiotics, such as fluoroquinolones (e.g., ciprofloxacin). However, a potential side effect of this treatment is the prolonged fecal excretion of salmonella. The mechanism behind this is not known. Because of this side effect, antibiotics should only be used if clinically indicated and for an adequate duration. Antibiotics are only indicated for severe cases of salmonella gastroenteritis, which include diarrhea that occurs more than 9 times per day or the presence of systemic symptoms (e.g., fever, tachycardia, hypotonia). This patient only has local symptoms with normal vital signs, hence she would not qualify for antibiotics.

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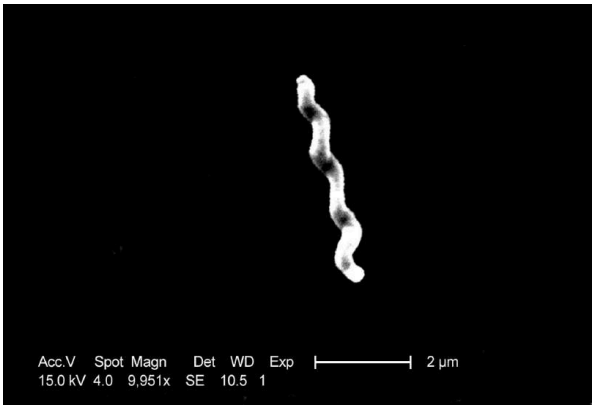
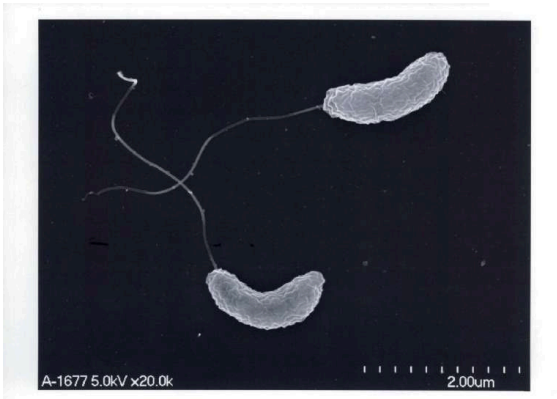
Question # 16

A 59-year-old woman comes to the emergency department because of abdominal pain and bloody diarrhea that began 12 hours ago. Three days ago, she ate undercooked chicken at a local restaurant. Blood cultures grow spiral and comma-shaped, oxidase-positive organisms at 42°C. This patient is at greatest risk for which of the following complications?

	Answer	Image
A	Segmental myelin degeneration	
B	Seizures	
C	Toxic megacolon	
D	Erythema nodosum	

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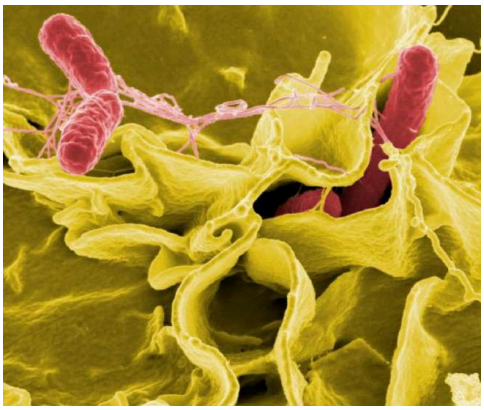
	Answer	Image
E	Peyer patch necrosis	

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Hint

Campylobacter jejuni is a spiral and comma-shaped, oxidase-positive organism that grows at 42°C and is a common cause of gastroenteritis with bloody diarrhea. It is associated with consumption of undercooked meat, especially poultry.

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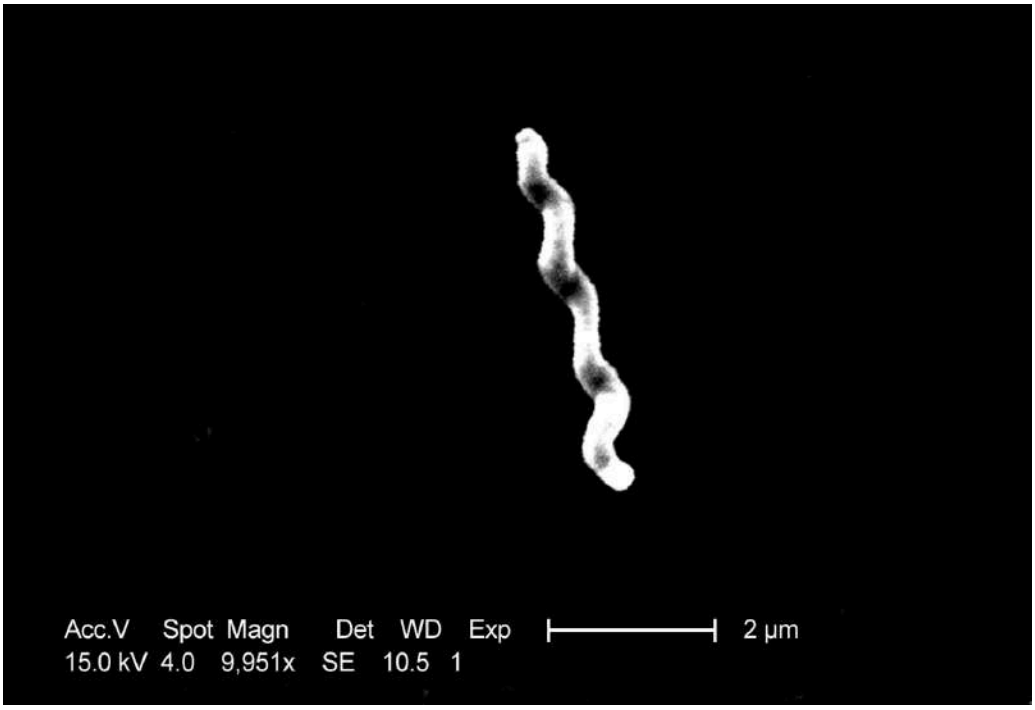
Correct Answer

A - Segmental myelin degeneration

Image



Explanation Why

Segmental myelin degeneration is the hallmark of Guillain-Barre syndrome (GBS). It is hypothesized that the inciting infection prompts the development of antibodies with cross-reactivity to antigens on Schwann cells. This molecular mimicry results in damage to the myelin sheaths of peripheral nerves. *Campylobacter jejuni* enteritis is classically associated with GBS.

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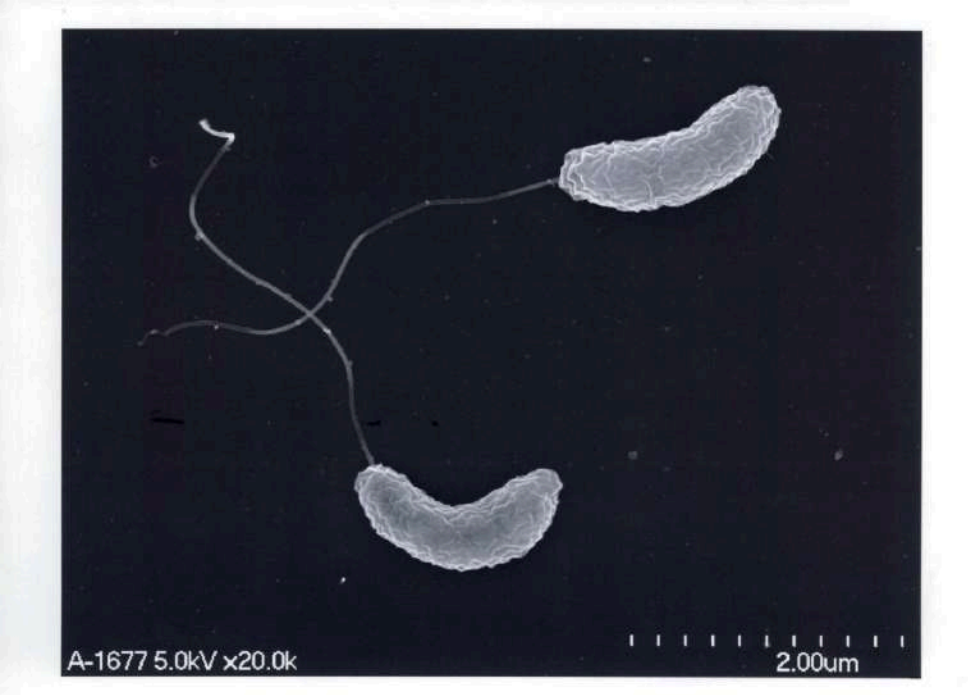
B - Seizures

Image



Explanation Why

Seizures can occur as a result of electrolyte imbalances in cases of profuse diarrhea (e.g., due to *Vibrio cholerae* infection). *Vibrio cholerae* is also oxidase-positive and comma-shaped but infection is typically contracted after eating undercooked seafood, and classically presents with copious watery diarrhea ("rice water diarrhea"), not bloody diarrhea.

C - Toxic megacolon

Explanation Why

Toxic megacolon is a serious complication of *Clostridioides difficile* colitis and also presents with abdominal pain and diarrhea. However, the vast majority of patients with toxic megacolon caused by *C. difficile* have a history of recent antibiotic exposure. Moreover, *C. difficile* is a gram-positive,

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oxidase-negative, and obligate anaerobe bacillus that forms spores, unlike the spiral and comma-shaped, oxidase-positive organism found in this patient.

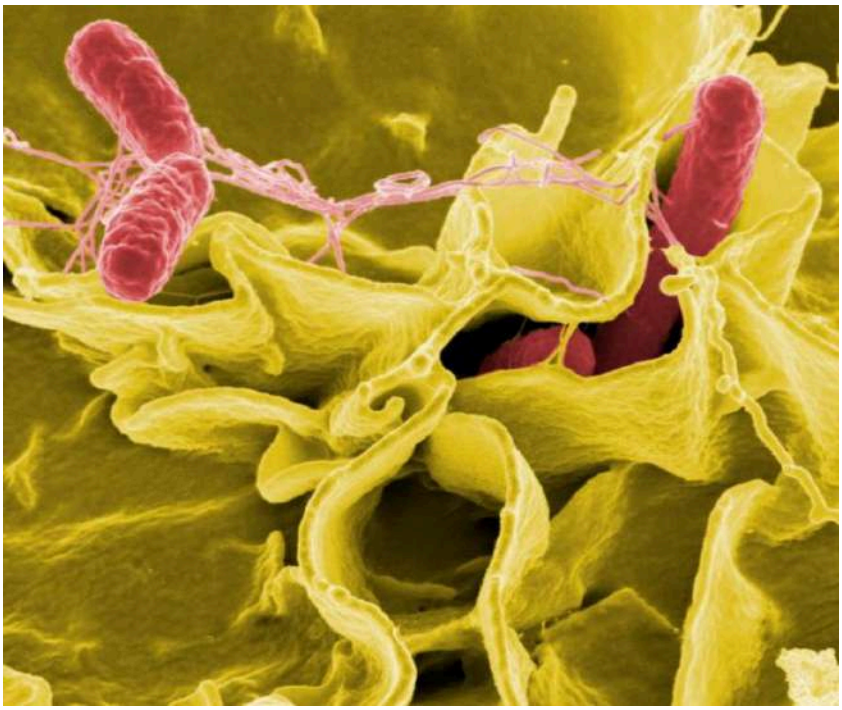
D - Erythema nodosum

Explanation Why

Erythema nodosum can be a complication of *Yersinia enterocolitica* gastroenteritis, which can also present with abdominal pain and bloody or watery diarrhea after consumption of undercooked meat. However, *Y. enterocolitica* is an oxidase-negative pathogen that can grow at refrigeration temperatures (3–5 °C), unlike the pathogen seen here.

E - Peyer patch necrosis

Image



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Explanation Why

Peyer patch necrosis can occur as a complication of typhoid fever and lead to profuse rectal bleeding. Infection with *Salmonella typhi* is via the fecal-oral route and would not be due to consumption of undercooked poultry. This infection develops over a period of weeks and is initially characterized by a fluctuating temperature with malaise, followed by profound fatigue and high fevers. Diarrhea is a relatively late finding. Moreover, *Salmonella typhi* is an oxidase-negative pathogen, unlike the oxidase-positive organism found in this patient.

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Question # 17

A 66-year-old man comes to the physician because of a 3-month history of constipation and streaks of blood in his stool. He has had a 10-kg (22-lb) weight loss during this period. Colonoscopy shows an exophytic tumor in the sigmoid colon. A CT scan of the abdomen shows liver metastases and enlarged mesenteric and para-aortic lymph nodes. A diagnosis of stage IV colorectal cancer is made, and palliative chemotherapy is initiated. The chemotherapy regimen includes a monoclonal antibody that inhibits tumor growth by preventing ligand binding to a protein directly responsible for epithelial cell proliferation and organogenesis. Which of the following proteins is most likely inhibited by this drug?

	Answer	Image
A	ALK	
B	EGFR	
C	TNF-α	
D	VEGF	
E	CD52	

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Hint

The absence of this protein or complete inhibition of its receptor results in lack of epithelial development in multiple organ systems.

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Correct Answer

A - ALK

Explanation Why

Anaplastic lymphoma kinase (ALK) is a transmembrane receptor with intrinsic tyrosine kinase activity that is important for the development of the brain and nervous system. Mutation of ALK is implicated in multiple cancers such as large cell lymphoma, adenocarcinoma of the lung, familial cases of neuroblastoma, and colorectal carcinoma. However, ALK inhibitors (e.g., crizotinib) are not typically used to treat colorectal carcinoma. Moreover, ALK is not directly responsible for epithelial cell proliferation and organogenesis.

B - EGFR

Explanation Why

Epidermal growth factor receptor (EGFR) is a ubiquitous tyrosine kinase receptor found in almost all adult human tissues. Ligand binding to its extracellular domain triggers a signaling cascade that ultimately promotes cellular proliferation and survival. EGFR is pathologically overexpressed by colorectal carcinoma and facilitates angiogenesis, invasiveness, and metastatic ability. Cetuximab is a monoclonal antibody EGFR inhibitor used to treat metastatic stage IV colorectal cancer and squamous cell carcinoma of the head and neck. This drug binds to the extracellular domain of EGFR to prevent signal transduction and thus impairs malignant cell proliferation and growth.

C - TNF-α

Explanation Why

Tumor necrosis factor alpha (TNF-α) is a signal protein involved in systemic inflammation, the immune response, and apoptosis. Antibodies against TNF-α (e.g., adalimumab, certolizumab, golimumab, and infliximab) are used to treat chronic inflammatory disorders (e.g, rheumatoid arthritis, inflammatory bowel disease); they are not used to treat colorectal cancer. Moreover, TNF-α is not directly responsible for epithelial cell proliferation and organogenesis.

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D - VEGF

Explanation Why

Vascular endothelial growth factor (VEGF) is a signal protein that stimulates vasculogenesis and angiogenesis, which is essential for tumor growth and metastasis. Antibodies against VEGF (e.g., bevacizumab) can be used to treat colorectal carcinoma. However, VEGF is not directly responsible for epithelial cell proliferation and organogenesis.

E - CD52

Explanation Why

CD52 is a surface glycoprotein found on almost all mature lymphocytes and immune cells. CD52 inhibition is the mechanism of action of alemtuzumab, a monoclonal antibody used to treat chronic lymphocytic leukemia and multiple sclerosis. This agent is not used to treat colorectal cancer. Moreover, CD52 is not directly responsible for epithelial cell proliferation and organogenesis

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Question # 18

A 17-year-old girl comes to the physician because of a 12-hour history of profuse watery diarrhea with flecks of mucus that started shortly after she returned from a trip to South America. She has not had any fever or nausea. Pulse is 104/min and blood pressure is 110/65 mm Hg. Physical examination shows dry mucous membranes and decreased skin turgor. Stool culture shows gram-negative, comma-shaped, flagellated bacilli. Therapy with oral rehydration solution is initiated. Which of the following is the most likely mechanism of this patient's diarrhea?

	Answer	Image
A	Reduced ability of water absorption in the colon due to rapid intestinal transit	
B	Fluid and electrolyte loss due to inflammation of luminal surface epithelium	
C	Luminal chloride hypersecretion due to overactivation of adenylate cyclase	
D	Impaired intestinal motility due to degeneration of autonomic nerves	
E	Excessive water excretion due to osmotically active solutes in the lumen	

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Hint

Vibrio cholera is a gram-negative flagellated bacterium that is transmitted via the fecal-oral route in endemic areas such as South America. This patient's travel history, acute onset of 'rice water' stool, signs of dehydration (dry mucous membranes, decreased skin turgor, tachycardia, and arterial hypotension), and stool studies are consistent with *Vibrio cholera* infection.

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Correct Answer

A -

Reduced ability of water absorption in the colon due to rapid intestinal transit

Explanation Why

Increased gut motility, as the result of hyperthyroidism or a carcinoid tumor, leads to diarrhea secondary to inadequate colonic water reabsorption. They present as postprandial, large-volume, watery stools with negative cultures. The patient's travel history, positive stool culture, and acute presentation of profuse non-bloody 'rice water' stools and resulting dehydration are not suggestive of diarrhea secondary to rapid intestinal transit.

B -

Fluid and electrolyte loss due to inflammation of luminal surface epithelium

Explanation Why

Inflammation of the luminal epithelium is seen in exudative-inflammatory diarrhea caused by IBD or bacterial infections with *Salmonella, Campylobacter*, and *E.coli*. Blood, pus, and leukocytes in stool, as well as systemic illness such as fever, are common in exudative-inflammatory diarrhea. This patient's travel history, afebrile presentation of profuse non-bloody 'rice water' stools, and stool culture negative for leukocytes make inflammatory-mediated diarrhea unlikely.

C - Luminal chloride hypersecretion due to overactivation of adenylate cyclase

Explanation But

Enterotoxic *E.coli* (ETEC), the most common cause of traveler's diarrhea, is also a gram-negative bacteria transmitted via the fecal-oral route in endemic areas. Similar to cholera, it produces enterotoxins that increase intestinal cellular adenylate cyclase, leading to secretory diarrhea via luminal water and electrolyte hypersecretion. ETEC infection would typically manifest with nausea, and possibly vomiting, and fever that last 24–72 hours. Treatment is supportive and includes oral

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rehydration therapy.

Explanation Why

Cholera toxin activates the G_s α subunit, thereby stimulating adenylate cyclase activity to increase cAMP within the intestinal epithelial cells. Increased cAMP concentration overactivates cytosolic PKA, which phosphorylates CFTR chloride channel proteins, causing excess secretion of Cl^- (and subsequently water, Na^+, K^+, and HCO_3^-). This process leads to watery, greyish stools and severe dehydration, as seen in this patient. Oral rehydration therapy (ORT) is the mainstay of treatment to replenish intravascular volume because, in diarrheal disease, neutral NaCl absorption and electrogenic Na^+ absorption are disrupted, while coupled absorption of Na^+ and glucose via sodium/glucose cotransporter 1 (SGLT 1) is preserved. Glucose enhances absorption of electrolytes and water, which is what makes ORT so effective.

D - Impaired intestinal motility due to degeneration of autonomic nerves

Explanation Why

Visceral autonomic neuropathy, which may be caused by DM, can lead to dysfunctional intestinal motility resulting in chronic diarrhea. This condition presents as intermittent, painless diarrhea during both day and night that may result in fecal incontinence. The patient's travel history, positive stool culture, and acute presentation of profuse non-bloody 'rice water' stools and resulting dehydration are atypical for chronic diarrhea as the result of autonomic neuropathy.

E - Excessive water excretion due to osmotically active solutes in the lumen

Explanation Why

An increased luminal osmotic load and the resulting excessive water excretion (osmotic diarrhea) could be a consequence of laxative use, excess magnesium intake, or lactose intolerance. The patient's travel history, positive stool culture, and acute presentation of profuse non-bloody 'rice water' stools with severe dehydration are not typical of osmotic diarrhea, which would present with normal stool cultures and diarrhea only following ingestion of those substances.

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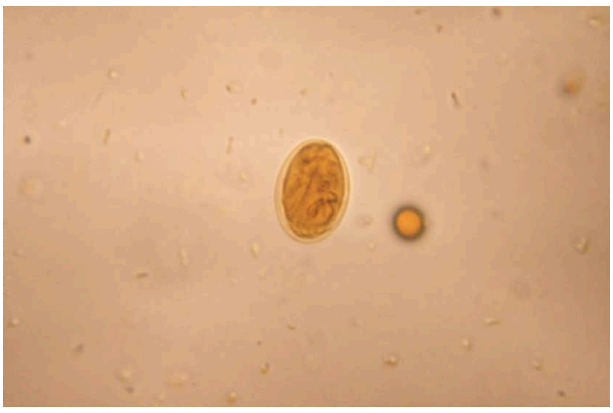
Question # 19

A 31-year-old man comes to the physician because of diarrhea, bloating, nausea, and vomiting for the past week. He describes his stool as greasy, frothy, and soft; it is not red or darkened. The patient went on a hiking trip in Brazil 3 weeks ago. He has no history of serious illness and takes no medications. The patient appears dehydrated. His vital signs are within normal limits. Examination shows dry mucous membranes and diffuse abdominal tenderness. Microscopy of the stool shows egg-shaped cysts with prominent two-layered cell wall and multiple nuclei. Which of the following is the most appropriate treatment?

	Answer	Image
A	Supportive treatment only	
B	Vancomycin therapy	
C	Trimethoprim-sulfamethoxazole therapy	
D	Ciprofloxacin therapy	
E	Metronidazole therapy	
F	Octreotide therapy	

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Hint

The patient's recent hiking trip and the detection of cysts in his stool make giardiasis the most likely diagnosis. The infection impairs absorption, which leads to greasy and frothy diarrhea.

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Correct Answer

A - Supportive treatment only

Explanation Why

Supportive treatment is important in the context of diarrhea to replace fluid and electrolyte losses. However, this patient's diarrhea is caused by a parasite and therefore also demands causative treatment.

B - Vancomycin therapy

Explanation Why

Oral vancomycin is the second-line therapy for *Clostridioides difficile* infection, which may present with watery, rather than frothy, and greasy diarrhea. Moreover, *C. difficile* mainly causes infections in elderly patients (> 65 years) who have received treatment with an antibiotic like clindamycin or cephalosporin. This patient has no history of prior antibiotic treatment and most likely has giardiasis, against which vancomycin is not effective.

C - Trimethoprim-sulfamethoxazole therapy

Explanation Why

TMP-SMX is used for maintenance therapy in Whipple's disease, which may also present with malabsorption and greasy stools. However, there are usually also extraintestinal symptoms such as migratory arthritis, lymphadenopathy, and/or neurologic deficits. Moreover, Whipple's disease would not present with cysts in a stool sample. TMP-SMX is not effective against giardiasis.

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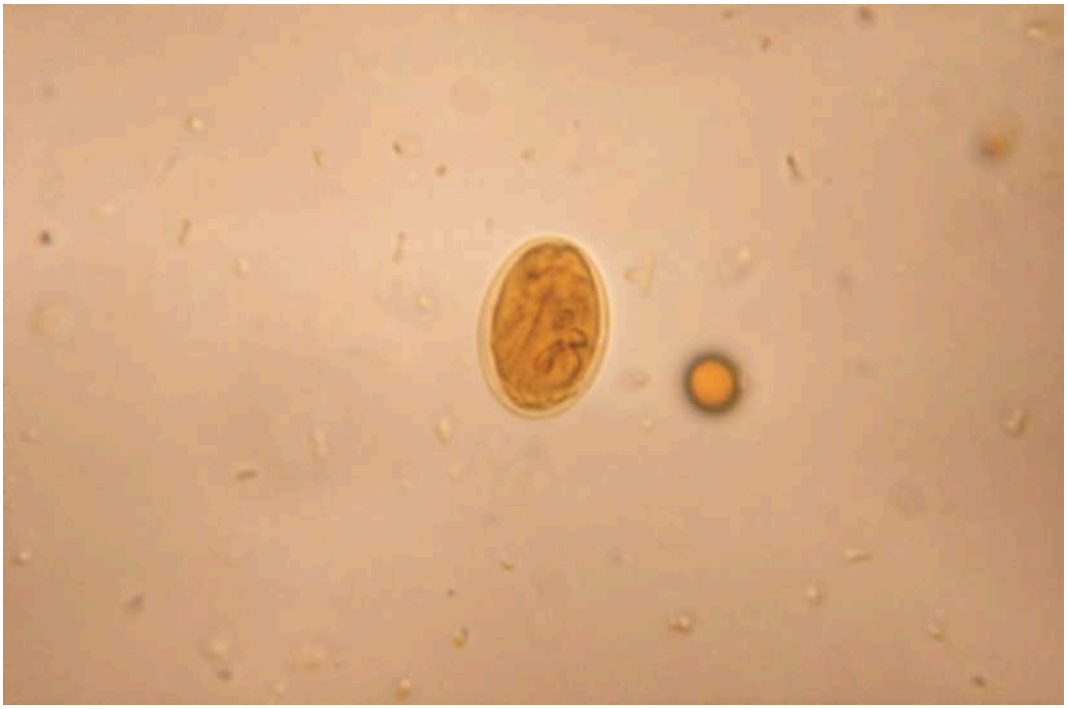
D - Ciprofloxacin therapy

Explanation Why

Ciprofloxacin can be used to treat traveler's diarrhea caused by enterotoxigenic Escherichia coli endemic in many tropical countries. This patient visited Brazil 3 weeks ago and might have contracted traveler's diarrhea (watery diarrhea) during that time, which resolved without further treatment. At this time, however, the patient most likely has giardiasis, against which ciprofloxacin is not effective.

E - Metronidazole therapy

Image



Explanation Why

Giardiasis is the most common parasitic cause of diarrhea in the US. It is caused by *Giardia lamblia*, which can be acquired from drinking untreated water (natural springs, streams). Metronidazole is an

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antibiotic that is effective against anaerobes and protozoa and is commonly used for giardiasis. Side effects include nausea and a metallic taste in the mouth. Patients should be advised not to consume alcohol while taking metronidazole because it can lead to a disulfiram-like reaction with nausea and vomiting.

F - Octreotide therapy

Explanation Why

Octreotide is used to relieve symptoms in patients with carcinoid tumors, which classically present with diarrhea, cutaneous flushing, and asthma-like attacks. This patient does not complain of any flushing or dyspnea.

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Question # 20

A 52-year-old man comes to the physician because of a 5-month history of progressive lethargy, shortness of breath, and difficulty concentrating. His friends have told him that he appears pale. He has smoked half a pack of cigarettes daily for the past 20 years. Neurological examination shows reduced sensation to light touch and pinprick in the toes bilaterally. Laboratory studies show:

Hemoglobin	8.2 g/dL
Mean corpuscular volume	108 μm^3
Serum	
Vitamin B_{12} (cyanocobalamin)	51 ng/L (N = 170–900)
Folic acid	13 ng/mL (N = 5.4–18)

An oral dose of radiolabeled vitamin B_{12} is administered, followed by an intramuscular injection of nonradioactive vitamin B_{12}. A 24-hour urine sample is collected and urine vitamin B_{12} levels are unchanged. The procedure is repeated with the addition of oral intrinsic factor, and 24-hour urine vitamin B_{12} levels increase. This patient's findings indicate an increased risk for which of the following conditions?

	Answer	Image
A	Colorectal carcinoma	
B	Pancreatic carcinoma	
C	Gastric carcinoma	
D	De Quervain thyroiditis	

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	Answer	Image
E	Type 2 diabetes mellitus	
F	Celiac disease	

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Hint

This patient has macrocytic anemia and peripheral neuropathy due to vitamin B_{12} deficiency. The results of the Schilling test are consistent with intrinsic factor deficiency, which suggests pernicious anemia.

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Correct Answer

A - Colorectal carcinoma

Explanation Why

A history of smoking is a risk factor for colorectal carcinoma, and patients with colorectal cancer may present with anemia (due to chronic GI hemorrhage). However, chronic GI hemorrhage typically results in iron-deficiency anemia (microcytic anemia) rather than pernicious anemia (macrocytic anemia). There is currently no clear evidence that patients with pernicious anemia are at an increased risk of colorectal carcinoma.

B - Pancreatic carcinoma

Explanation But

Chronic pancreatitis, which is a risk factor for pancreatic carcinoma, may also result in vitamin B_{12} deficiency. However, urinary excretion of radiolabeled B_{12} would not normalize after repeating the Schilling test with orally administered intrinsic factor because B_{12} malabsorption in chronic pancreatitis is caused by trypsin deficiency, which results in the impaired breakdown of salivary haptocorrin. Instead, urinary excretion of radiolabelled B_{12} would normalize only after the ingestion of pancreatic enzymes. Moreover, this patient does not have a history of alcohol use disorder or recurrent abdominal pain, which would suggest chronic pancreatitis.

Explanation Why

Although this patient's history of smoking is a risk factor for pancreatic carcinoma, the presence of pernicious anemia significantly increases his risk of another disease. Studies have shown that there is no statistically significant association between pernicious anemia and pancreatic carcinoma.

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C - Gastric carcinoma

Explanation But

Patients with newly diagnosed pernicious anemia should undergo an endoscopic examination and gastric biopsy within 6 months to confirm the presence of atrophic gastritis and rule out dysplastic changes. Patients should undergo a repeat endoscopy if they develop dyspeptic symptoms. Surveillance endoscopies may also be performed every 3 years in certain high-risk patients (e.g., those with severe columnar metaplasia at the initial biopsy).

Explanation Why

Patients with pernicious anemia are at increased risk of developing gastric adenocarcinoma. Approx. 90% of patients with pernicious anemia have chronic atrophic gastritis, which likely accounts for the increased incidence of gastric carcinoma. These patients are also at increased risk for gastric carcinoid tumor as a result of chronic hypergastrinemia, which induces gastric cell hyperplasia.

D - De Quervain thyroiditis

Explanation Why

There is no evidence to suggest that patients with pernicious anemia are at increased risk of developing de Quervain thyroiditis (subacute granulomatous thyroiditis), which usually occurs following a viral upper respiratory infection. Given the autoimmune etiology of their condition, patients with pernicious anemia are at increased risk of developing autoimmune thyroid diseases, including Hashimoto disease and Graves disease.

E - Type 2 diabetes mellitus

Explanation But

Atrophic gastritis, which causes pernicious anemia, and type 1 DM are both caused by autoimmune damage. Given this autoimmune association, the median probability that patients with pernicious

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anemia will have type 1 DM is about 15 times greater than in the general population. However, the onset of type 1 DM, which usually occurs before the age of 20, will typically precede the onset of clinical features of pernicious anemia, which usually appear during adulthood.

Explanation Why

Patients with type 2 DM are at increased risk of vitamin B_{12} deficiency for multiple reasons, the most significant being metformin use because metformin affects the calcium-dependent ileal absorption of the intrinsic factor-B_{12} complex. Increased gut transit time due to diabetic autonomic neuropathy may lead to bacterial overgrowth, which can also cause vitamin B_{12} deficiency. However, there is no data to suggest that patients with pernicious anemia are at an increased risk of developing type 2 DM.

F - Celiac disease

Explanation Why

Patients with celiac disease may also present with symptoms of B_{12} deficiency due to malabsorption. However, if the cause of vitamin B_{12} deficiency was malabsorption due to celiac disease, urinary excretion of radiolabeled B_{12} would not normalize after repeating the Schilling test with orally administered intrinsic factor (IF). This patient's increased absorption of B_{12} with oral IF on the Schilling test is diagnostic of pernicious anemia. Because pernicious anemia and celiac disease are both autoimmune diseases, there could theoretically be an association between the two. However, there is currently little evidence to suggest a clear association.

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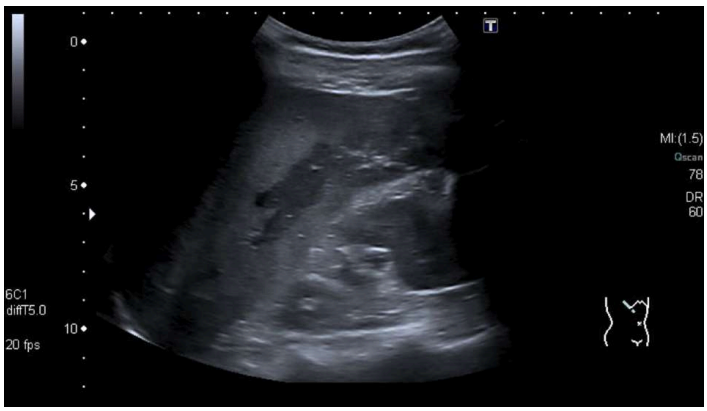
Question # 21

A 45-year-old man comes to the physician because of a 5-day history of fever, malaise, and right upper abdominal pain. Examination of the abdomen shows tenderness in the right upper quadrant. His leukocyte count is 18,000/mm^3 (90% neutrophils) and serum alkaline phosphatase is 130 U/L. Ultrasonography of the abdomen shows a 3-cm hypoechoic lesion in the right lobe of the liver with a hyperemic rim. Which of the following is the most likely underlying cause of this patient's condition?

	Answer	Image
A	Colorectal cancer	
B	Infectious endocarditis	
C	Echinococcosis	
D	Diverticulitis	
E	Cholangitis	
F	Perinephric infection	

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	Answer	Image
G	Candidiasis	

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Hint

A triad of fever, malaise, and right upper abdominal pain in a patient with neutrophilic leukocytosis and a hepatic lesion with a hyperemic rim (due to surrounding edema and inflammation) on ultrasonography is diagnostic of a liver abscess.

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Correct Answer

A - Colorectal cancer

Explanation Why

Colorectal cancer commonly metastasizes into the liver, leading to right upper quadrant pain with fever and malaise, as seen in this patient. However, liver metastases typically present as multiple lesions on ultrasound, and this patient has only a single lesion. Neutrophilic leukocytosis would not be expected. Secondary bacterial infection of a metastatic deposit, on the other hand, is a rare cause of hepatic abscess. Moreover, colorectal cancer is unlikely in this 45-year old patient without a known genetic mutation or symptoms such as changes in bowel habits, rectal bleeding, and weight loss.

B - Infectious endocarditis

Explanation Why

Bacteremia in conditions such as infectious endocarditis (IE) may cause a hepatic abscess due to dissemination via the hepatic artery (< 15% of hepatic abscesses). IE presents with fever and malaise, as in this patient; however, it is also associated with cardiac manifestations (e.g., new or changed heart murmur, heart failure signs), and signs such as Janeway lesions, Osler nodes, and Roth spots. Moreover, IE is unlikely in this patient without risk factors like a predamaged or prosthetic heart valve, IV drug abuse, or recent dental surgery.

C - Echinococcosis

Explanation Why

Echinococcosis is a helminthic infection resulting in the formation of a hepatic cyst, which can cause right upper quadrant pain and malaise, as seen in this patient. However, it is a rare infection in the US and risk factors for tapeworm exposure (e.g., contact with dogs or other potentially infected definitive hosts) would be expected. Moreover, this patient's laboratory and ultrasound findings are inconsistent with echinococcosis, which is associated with leukopenia and anechoic, well-defined

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cysts with eggshell calcifications on ultrasound.

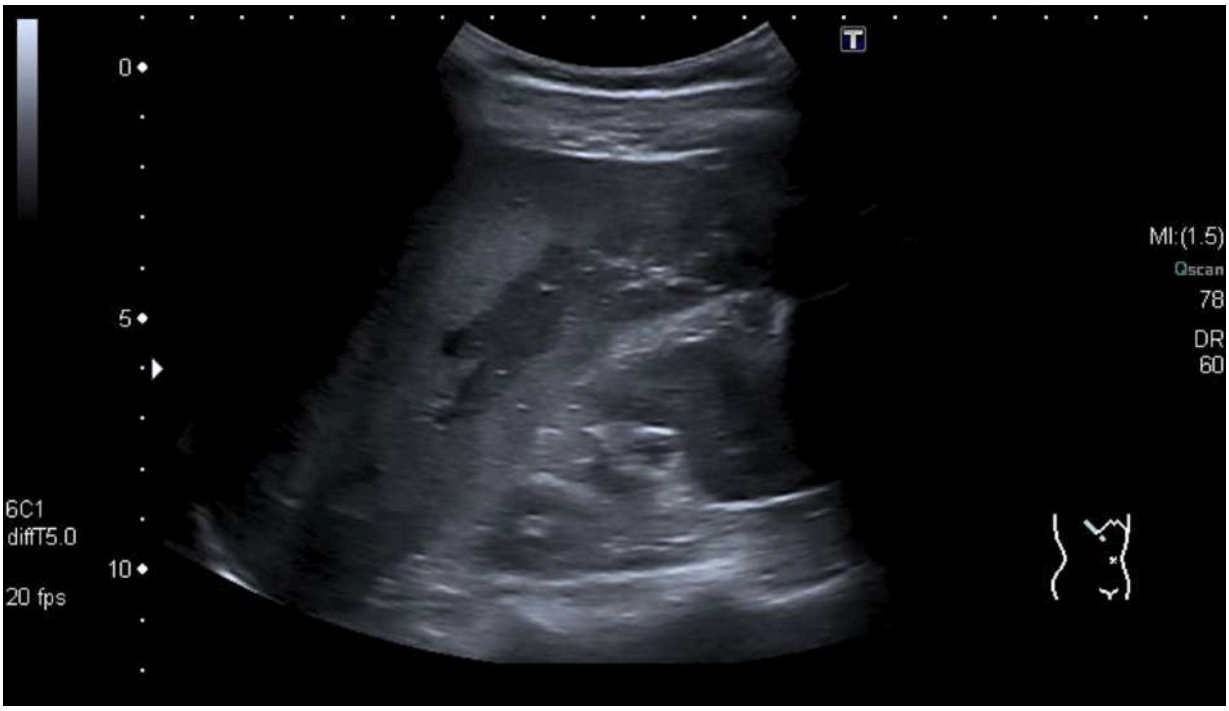
D - Diverticulitis

Explanation Why

Diverticulitis may cause a hepatic abscess due to bacterial infection spread via the portal vein; however, this is a rare complication and associated with high bacterial loads. Moreover, diverticulitis is less common in this patient's age group and is typically associated with symptoms such as left lower quadrant pain and a change in bowel habits.

E - Cholangitis

Image



Explanation Why

Ascending infection from a biliary tract pathology, such as cholangitis, is the most common cause of

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hepatic abscesses. The infection is typically caused by bacteria and mainly is polymicrobial, with *E. coli* being the most frequent causative pathogen. Hepatic abscesses may also result from intraabdominal infections (e.g., acute appendicitis, peritonitis), or hematogenous spread from systemic circulation (e.g., sepsis).

F - Perinephric infection

Explanation Why

Perinephric infection may rarely lead to a hepatic abscess via contiguous spread. Since such an infection typically occurs as a complication of pyelonephritis, accompanying symptoms such as dysuria, hematuria, and flank pain would be expected.

G - Candidiasis

Explanation Why

Candidiasis and other fungal infections account for < 10% of all hepatic abscesses. Fungal hepatic abscesses are seen especially in immunocompromised/neutropenic individuals (e.g., with diabetes, HIV), which is why this patient's neutrophilic leukocytosis is inconsistent with this diagnosis. Mortality rates in patients with fungal hepatic abscesses are high.

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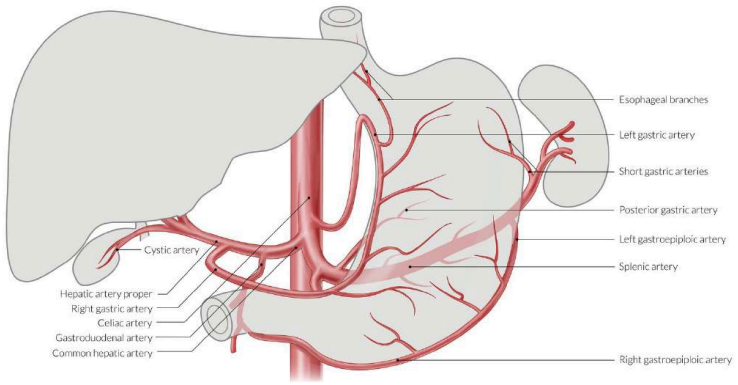
Question # 22

A 55-year-old man comes to the physician because of a 3-week history of intermittent burning epigastric pain. His pain improves with antacid use and eating but returns approximately 2 hours following meals. He has a history of chronic osteoarthritis and takes ibuprofen daily. Upper endoscopy shows a deep ulcer located on the posterior wall of the duodenal bulb. This ulcer is most likely to erode into which of the following structures?

	Answer	Image
A	Splenic vein	
B	Pancreatic duct	
C	Liver capsule	
D	Descending aorta	
E	Gastroduodenal artery	
F	Transverse colon	

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Hint

The structure most at risk of damage lies directly posterior to the first part of the duodenum (the duodenal bulb).

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Correct Answer

A - Splenic vein

Explanation Why

The splenic vein courses along the posterior gastric fundus and can be damaged by gastric ulcers in this location (although gastric ulcers more commonly develop along the lesser curvature of the stomach). Peptic ulcers located on the posterior wall of the duodenal bulb are not likely to injure the splenic vein.

B - Pancreatic duct

Explanation Why

Damage to the pancreatic duct is a rare complication of duodenal ulcers. The pancreatic duct is located posterior to the second part of the duodenum and is not likely to be damaged by a peptic ulcer located on the posterior wall of the duodenal bulb.

C - Liver capsule

Explanation Why

Damage to the liver capsule, which can cause a perihepatic abscess, is a rare complication of duodenal ulcers. The liver capsule is located superior to the proximal duodenum and is not likely to be damaged by a peptic ulcer located on the posterior wall of the duodenal bulb.

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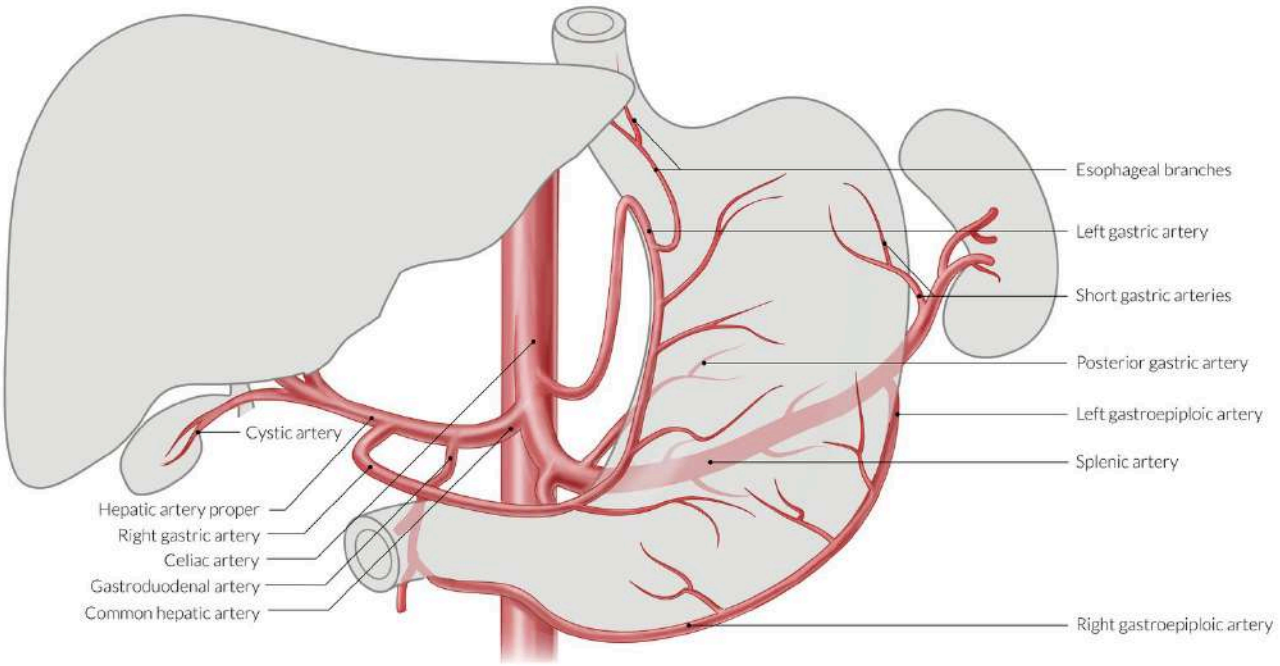
D - Descending aorta

Explanation Why

Damage to the descending aorta is a rare complication of gastric ulcers located along the posterior gastric antrum. This structure is not likely to be damaged by a peptic ulcer located on the posterior wall of the duodenal bulb.

E - Gastroduodenal artery

Image



Explanation But

Anterior duodenal ulcers can cause perforation that results in free air under the diaphragm.

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Explanation Why

The gastroduodenal artery runs directly posterior to the first part of the duodenum after originating from the common hepatic artery. It supplies the pylorus, proximal duodenum, and head of the pancreas. A peptic ulcer located on the posterior wall of the duodenal bulb can erode into the gastroduodenal artery and cause significant gastrointestinal bleeding. Bleeding is the most common complication of peptic ulcer disease.

F - Transverse colon

Explanation Why

Damage to the transverse colon is a rare complication of peptic ulcers (primarily gastric ulcers located along the greater curvature of the stomach and anterior duodenal ulcers). This structure is not likely to be damaged by a peptic ulcer located on the posterior wall of the duodenal bulb.

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Question # 23

A 57-year-old woman is brought to the emergency department because of crampy abdominal pain and foul-smelling, watery diarrhea. One week ago, she underwent treatment of cellulitis with clindamycin. Her temperature is 38.4°C (101.1°F). Abdominal examination shows mild tenderness in the left lower quadrant. Her leukocyte count is 12,800/mm^3. An enzyme immunoassay is positive for glutamate dehydrogenase antigen and toxins A and B. Treatment is begun with a drug that inhibits the sigma subunit of the RNA polymerase. The patient was most likely treated with which of the following drugs?

	Answer	Image
A	Vancomycin	
B	Clindamycin	
C	Moxifloxacin	
D	Metronidazole	
E	Fidaxomicin	

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Hint

Foul-smelling, watery diarrhea shortly after antibiotic use (especially clindamycin) should raise suspicion for *Clostridioides difficile* infection. The positive enzyme immunoassays for *C. difficile* glutamate dehydrogenase antigen and toxins A and B confirm this suspicion.

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Correct Answer

A - Vancomycin

Explanation Why

Vancomycin is a first-line treatment option for *C. difficile* infection. When given orally it is neither systemically absorbed nor metabolized, leading to high concentrations in the colon, which makes vancomycin an effective drug in the treatment of *C. difficile* colitis. However, vancomycin's mechanism of action is via inhibition of cell wall peptidoglycan formation rather than through inhibition of the sigma subunit of the RNA polymerase.

B - Clindamycin

Explanation Why

Clindamycin is an antibiotic that is most commonly used in the treatment of anaerobic, staphylococcal, and streptococcal infections. However, clindamycin has a propensity for causing *C. difficile* infections, as seen here, so its further use in this case should be avoided. Moreover, clindamycin's mechanism of action is via inhibition of protein synthesis at the 50S ribosomal subunit.

C - Moxifloxacin

Explanation Why

Moxifloxacin is a fluoroquinolone antibiotic with a broad clinical spectrum and a high oral bioavailability. However, fluoroquinolones have numerous drug-drug interactions and can cause many serious adverse effects, including predisposing patients to *C. difficile* infections, so their use use in this case should be avoided. Moreover, fluoroquinolones act via inhibition of bacterial topoisomerases II and IV.

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D - Metronidazole

Explanation Why

Metronidazole is an antibiotic effective against obligate anaerobic organisms and is considered a second-line therapy for *C. difficile* infections. However, metronidazole's mechanism of action occurs via the generation of toxic free radical metabolites. Therefore, another antibiotic was initiated for the treatment of this patient.

E - Fidaxomicin

Explanation But

In contrast to previous recommendations, metronidazole is now considered a second-line therapy.

Explanation Why

Fidaxomicin is a first-line treatment for nonsevere *C. difficile* infection (e.g., WBC count ≤ 15,000 cells/mL), as seen in this patient. Fidaxomicin is a bactericidal antibiotic that acts through inhibition of the RNA polymerase sigma subunit. Based upon recent revisions to guidelines, oral fidaxomicin is now considered a first-line treatment for nonsevere *C. difficile* infection. Fidaxomicin is administered less frequently than oral vancomycin, the other first-line treatment option for this condition, because it is significantly more expensive; however, fidaxomicin has been shown to lower recurrence rates.

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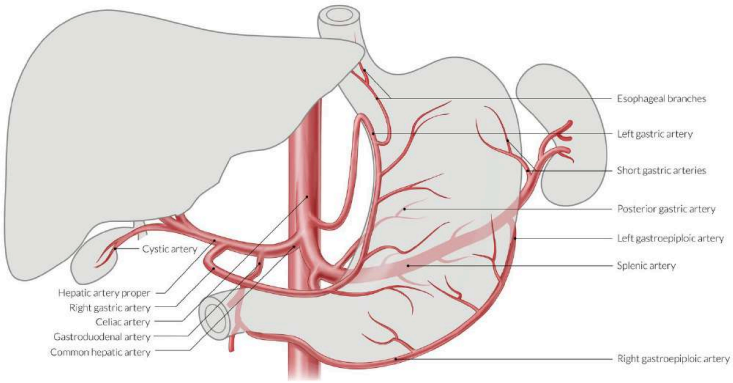
Question # 24

A 45-year-old man is brought to the emergency department because of severe abdominal pain for the past 2 hours. He has a 2-year history of burning epigastric pain that gets worse with meals. His pulse is 120/min, respirations are 22/min, and blood pressure is 60/40 mm Hg. Despite appropriate lifesaving measures, he dies. At autopsy, examination shows erosion of the right gastric artery. Perforation of an ulcer in which of the following locations most likely caused this patient's findings?

	Answer	Image
A	Anterior duodenum	
B	Posterior duodenum	
C	Fundus of the stomach	
D	Greater curvature of the stomach	
E	Lesser curvature of the stomach	

Hint

This patient has a history of epigastric pain, suggesting peptic ulcer disease. Pain that gets worse with meals and erosion of the right gastric artery suggest that the ulcer is located in the stomach.

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Correct Answer

A - Anterior duodenum

Explanation Why

The anterior duodenum is supplied by the superior pancreaticoduodenal artery via its anterior branches. An ulcer in the anterior duodenum could perforate this artery and extend into the anterior abdominal cavity. However, erosion of the right gastric artery, as found in this patient, would not be expected.

B - Posterior duodenum

Explanation Why

The posterior duodenum is supplied by the gastroduodenal artery, which originates from the common hepatic artery. An ulcer in the posterior duodenum could penetrate into the gastroduodenal artery and cause massive hemorrhage. However, erosion of the right gastric artery, as found in this patient, would not be expected.

C - Fundus of the stomach

Explanation Why

The gastric fundus is supplied by the short gastric arteries, which are branches of the splenic artery. An ulcer in the fundus could perforate into those arteries. However, erosion of the right gastric artery, as found in this patient, would not be expected.

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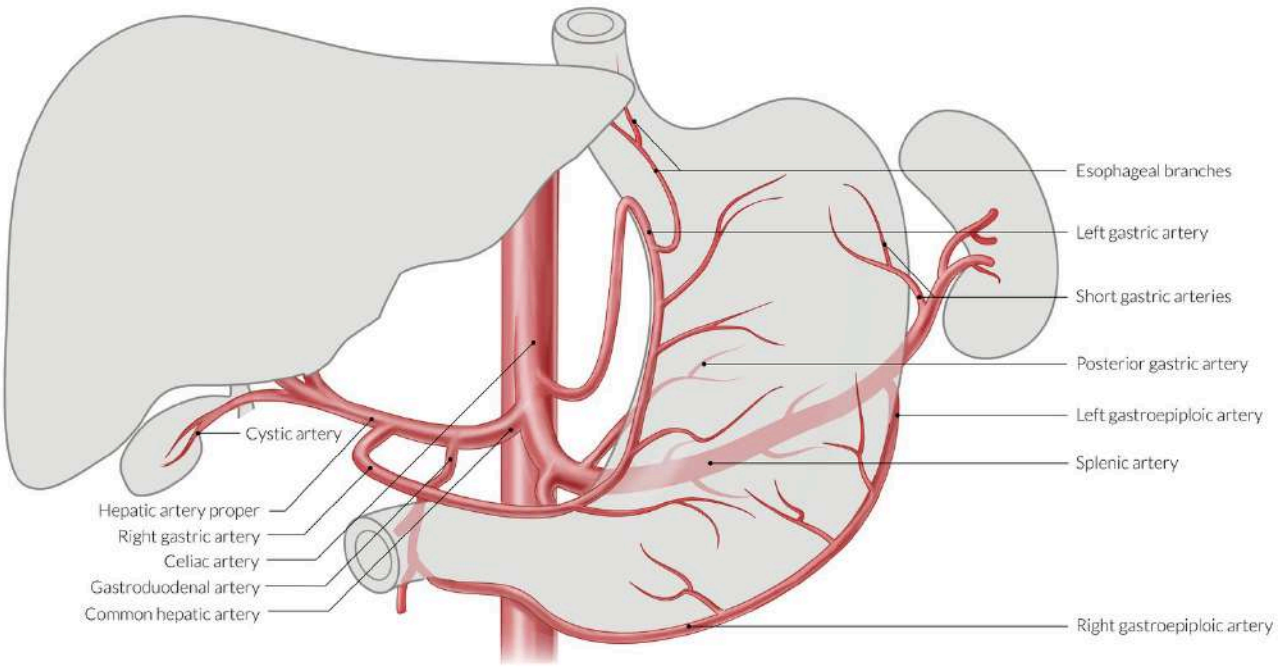
D - Greater curvature of the stomach

Explanation Why

The greater curvature of the stomach is supplied by the right gastroepiploic artery and left gastroepiploic artery. An ulcer in this location could penetrate into those arteries and cause hemorrhage. However, erosion of the right gastric artery, as found in this patient, would not be expected.

E - Lesser curvature of the stomach

Image



Explanation Why

The lesser curvature of the stomach is supplied by the right and left gastric artery. The right gastric artery arises from the common hepatic artery, while the left gastric artery arises from the celiac trunk. Since this patient's ulcer has eroded the right gastric artery, it likely originated from the lower

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lesser curvature, which is a common location for peptic ulcers.

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Question # 25

A 38-year-old man comes to the physician because of an 8-month history of upper abdominal pain. During this period, he has also had nausea, heartburn, and multiple episodes of diarrhea with no blood or mucus. He has smoked one pack of cigarettes daily for the past 18 years. He does not use alcohol or illicit drugs. Current medications include an antacid. The abdomen is soft and there is tenderness to palpation in the epigastric and umbilical areas. Upper endoscopy shows several ulcers in the duodenum and the upper jejunum as well as thick gastric folds. Gastric pH is < 2. Biopsies from the ulcers show no organisms. Which of the following tests is most likely to confirm the diagnosis?

	Answer	Image
A	24-hour esophageal pH monitoring	
B	Fasting serum gastrin level	
C	Urine metanephrine levels	
D	Urea breath test	
E	Serum vasoactive intestinal polypeptide level	

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Hint

Several peptic ulcers, ulcers in unusual locations (i.e., jejunum), and thick gastric folds should raise suspicion for Zollinger-Ellison syndrome.

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Correct Answer

A - 24-hour esophageal pH monitoring

Explanation Why

24-hour esophageal pH monitoring is used to confirm the diagnosis of gastroesophageal reflux disease (GERD). While this patient certainly has GERD given his history of heartburn and low gastric pH, GERD alone would not explain his endoscopic findings (e.g., thick gastric folds, several peptic ulcers). These findings are more suggestive of Zollinger-Ellison syndrome and 24-hour esophageal pH monitoring would not be of any further diagnostic value.

B - Fasting serum gastrin level

Explanation Why

Determining the fasting serum gastrin level is the best initial test for diagnosing gastrinoma (Zollinger-Ellison syndrome), which this patient likely has. A 10-fold increase in gastrin levels is conclusive evidence of a gastrinoma, especially in combination with a gastric pH < 2. A secretin stimulation test (SST) may also be used in the diagnosis of ZES. However, it must be performed without acid suppression therapy and is not recommended in patients with severe manifestations of ZES.

C - Urine metanephrine levels

Explanation Why

Measurement of urine metanephrine levels (e.g., catecholamine metabolites) is indicated if the diagnosis of pheochromocytoma is suspected. While pheochromocytoma can cause episodic diarrhea, this patient is missing other characteristic features, such as headache, palpitations, and hypertension, making this diagnosis unlikely. ZES, which this patient has, is associated with MEN-1, while pheochromocytoma is associated with MEN-2A and MEN-2B.

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D - Urea breath test

Explanation Why

A urea breath test is a good screening test for *Helicobacter pylori* (HP). However, the gold standard for detecting HP is the histopathologic evaluation of endoscopic biopsies, which were already performed in this patient and came back negative (e.g., no organisms seen). There is no point in performing a screening test after already conducting the confirmation test.

E - Serum vasoactive intestinal polypeptide level

Explanation Why

Measurement of serum VIP levels would be indicated if there were suspicion of a VIPoma, a rare neuroendocrine tumor associated with MEN-1 that typically manifests with high-volume, watery diarrhea. In addition, ZES, which this patient has, is also associated with MEN-1. However, abdominal tenderness, heartburn, and this patient's upper endoscopic findings are not consistent with a VIPoma.

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Question # 26

A 43-year-old man is brought to the emergency department 30 minutes after falling from the roof of a construction site. He reports abdominal and right-sided flank pain. His temperature is 37.1°C (98.8°F), pulse is 114/min, and blood pressure is 100/68 mm Hg. Physical examination shows numerous ecchymoses over the trunk and flanks and a tender right abdomen without a palpable mass. Focused assessment with sonography for trauma (FAST) shows no intraperitoneal fluid collections. His hemoglobin concentration is 7.6 g/dL. The most likely cause of his presentation is injury to which of the following organs?

	Answer	Image
A	Liver	
B	Spleen	
C	Kidney	
D	Stomach	
E	Small bowel	

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Hint

This patient is hemorrhaging (tachycardia, hypotension, low hemoglobin). His FAST findings suggest that the source of the bleeding does not lie intraperitoneal.

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Correct Answer

A - Liver

Explanation Why

Injury to the liver, an intraperitoneal organ, could explain this patient's abdominal pain and signs of hemorrhage. However, traumatic liver bleeds should result in free intraperitoneal fluid on a FAST exam.

B - Spleen

Explanation Why

The spleen is an intraperitoneal organ that is the most common source of hemorrhage after blunt force trauma. Splenic rupture would explain this patient's abdominal pain and signs of hemorrhage. However, a FAST exam would likely show intraperitoneal fluid accumulations.

C - Kidney

Explanation Why

Since the FAST exam is negative for intraperitoneal fluid collections, it is likely that this patient is experiencing a retroperitoneal bleed. The retroperitoneal localization along with his right-sided flank pain are consistent with injury to the kidney.

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D - Stomach

Explanation But

If perforation of the small bowel, a hollow viscus, is present, an upright abdominal x-ray would show free peritoneal air.

Explanation Why

Injury to the stomach could explain this patient's abdominal pain and signs of hemorrhage. However, because the stomach is intraperitoneal, fluid would likely be visualized on a FAST exam.

E - Small bowel

Explanation But

If perforation of the small bowel, a hollow viscus, is present, an upright abdominal x-ray would show free peritoneal air.

Explanation Why

Injury to the small bowel could explain this patient's abdominal pain and signs of hemorrhage. However, because the small bowel is intraperitoneal, fluid would likely be visualized on a FAST exam.

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Question # 27

A 69-year-old man comes to the physician because of progressive difficulty swallowing and a 5-kg (11-lb) weight loss over the past 3 months. He first had trouble swallowing solid foods and then also developed difficulty swallowing liquids over the past week. Endoscopy shows a large mass 3 cm proximal to the esophagogastric junction. Biopsy of the mass shows significant distortion of glandular architecture. Which of the following is the strongest predisposing factor for this patient's condition?

	Answer	Image
A	Atrophic gastritis	
B	Consumption of hot liquids	
C	Chronic alcohol use	
D	Visceral obesity	
E	Chewing of betel nuts	
F	Consumption of cured meats	

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Hint

Visualization of a mass in the distal third of the esophagus with histopathologic examination that shows distorted glandular architecture confirms a diagnosis of esophageal adenocarcinoma.

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Correct Answer

A - Atrophic gastritis

Explanation Why

Atrophic gastritis increases the risk of esophageal squamous cell carcinoma (eSCC). Bacterial overgrowth in the achlorhydric stomach generates reactive carcinogenic nitrogen products that can induce eSCC transformation. Although eSCC manifests with dysphagia and weight loss, as seen in this patient, a biopsy would show pathognomonic circular areas of keratinization. Atrophic gastritis is not associated with an increased risk of esophageal adenocarcinoma.

B - Consumption of hot liquids

Explanation Why

Chronic consumption of hot liquids and food increases the risk of esophageal squamous cell carcinoma due to thermal damage of the esophageal mucosa. The resulting inflammation stimulates the production of reactive nitrogen species, which are carcinogenic. Although eSCC manifests with dysphagia and weight loss, as seen in this patient, a biopsy would show pathognomonic circular areas of keratinization. Consumption of hot liquids is not associated with an increased risk of esophageal adenocarcinoma.

C - Chronic alcohol use

Explanation Why

Chronic and excessive alcohol consumption increases the risk of esophageal squamous cell carcinoma (eSCC). Although eSCC manifests with dysphagia and weight loss, as seen in this patient, a biopsy would show pathognomonic circular areas of keratinization. Chronic alcohol use is not associated with an increased risk of esophageal adenocarcinoma.

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D - Visceral obesity

Explanation But

Other risk factors for esophageal adenocarcinoma include smoking, achalasia, and certain diets (high animal protein, high cholesterol, low-fiber). Smoking and achalasia furthermore increase the risk of esophageal squamous cell carcinoma.

Explanation Why

Obesity is an important risk factor for esophageal adenocarcinoma. Although the exact mechanism is unknown, it is hypothesized that obesity increases the risk of GERD, which induces metaplasia (Barrett esophagus) that can progress to adenocarcinoma. In addition, excessive visceral fat increases the risk of inflammation, the production of cytokines and growth factors, and insulin resistance, all of which are risk factors for carcinoma.

E - Chewing of betel nuts

Explanation Why

Betel nut or areca nut chewing is strongly associated with an increased risk for esophageal squamous cell carcinoma (eSCC). The exact mechanism of this is unknown, but it has been hypothesized to be a combination of mechanical irritation and the release of carcinogenic reactive oxygen species. Although eSCC manifests with dysphagia and weight loss, as seen in this patient, a biopsy would show pathognomonic circular areas of keratinization. Chewing of betel nuts is not associated with an increased risk of esophageal adenocarcinoma.

F - Consumption of cured meats

Explanation Why

Chronic consumption of nitrosamine-rich foods (e.g., bacon, other cured meats, pickles, alcohol) is associated with an increased risk of esophageal squamous cell carcinoma (eSCC). Although eSCC

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manifests with dysphagia and weight loss, as seen in this patient, a biopsy would show pathognomonic circular areas of keratinization. Consumption of cured meats is not associated with an increased risk of esophageal adenocarcinoma.

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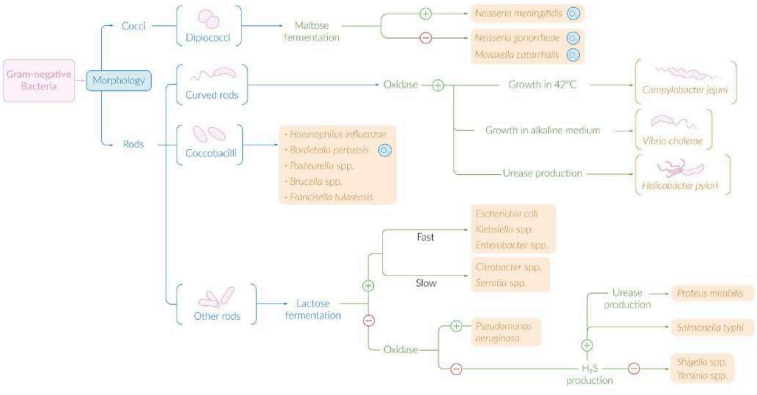
Question # 28

A 10-year-old girl is brought to the emergency department because of a 2-day history of bloody diarrhea and abdominal pain. Four days ago, she visited a petting zoo with her family. Her temperature is 39.4°C (102.9°F). Abdominal examination shows tenderness to palpation of the right lower quadrant. Stool cultures at 42°C grow colonies that turn black after adding phenylenediamine. Which of the following best describes the most likely causal organism?

	Answer	Image
A	Gram-negative, flagellated bacteria that ferment lactose	
B	Gram-negative, non-flagellated bacteria that do not ferment lactose	
C	Gram-positive, anaerobic, rod-shaped bacteria that form spores	
D	Gram-negative, flagellated bacteria that do not ferment lactose	
E	Gram-positive, aerobic, rod-shaped bacteria that produce catalase	

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	Answer	Image
F	Gram-positive, aerobic, rod-shaped bacteria that form spores	

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Hint

This girl presents with right lower quadrant pain, bloody diarrhea, and fever after exposure to animals. Many pathogens can cause this presentation, but stool cultures that grow oxidase-positive organisms (colonies that turn black with phenylenediamine) at 42°C suggests infection with *Campylobacter* species.

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Correct Answer

A - Gram-negative, flagellated bacteria that ferment lactose

Explanation Why

Enterohemorrhagic *E. coli* are Shiga-toxin producing, gram-negative bacteria that fit the above description. Infection with these bacteria causes bloody diarrhea, abdominal pain, and fever. Cows, which the patient is likely to have been exposed to at the petting zoo, are a common carrier of the pathogen. Transmission occurs through a fecal-oral route. However, *E. coli* tests negative for oxidase.

B - Gram-negative, non-flagellated bacteria that do not ferment lactose

Explanation Why

Both *Yersinia* and *Shigella* spp. fit the above description. Upon infection, both species can cause bloody diarrhea, abdominal pain, and fever. Moreover, *Yersinia enterocolitica* infections are associated with animal exposure (deer, cattle, and pigs). However, *Yersinia* and *Shigella* spp test negative for oxidase.

C - Gram-positive, anaerobic, rod-shaped bacteria that form spores

Explanation Why

Clostridium spp. fit this description. *C. perfringens* causes watery diarrhea and is associated with the ingestion of undercooked food. *C. difficile* is a nosocomial infection associated with antibiotic use. *C. botulinum* causes diarrhea with neurological dysfunctions (cranial neuropathies and descending weakness). However, *Clostridium* spp test negative for oxidase.

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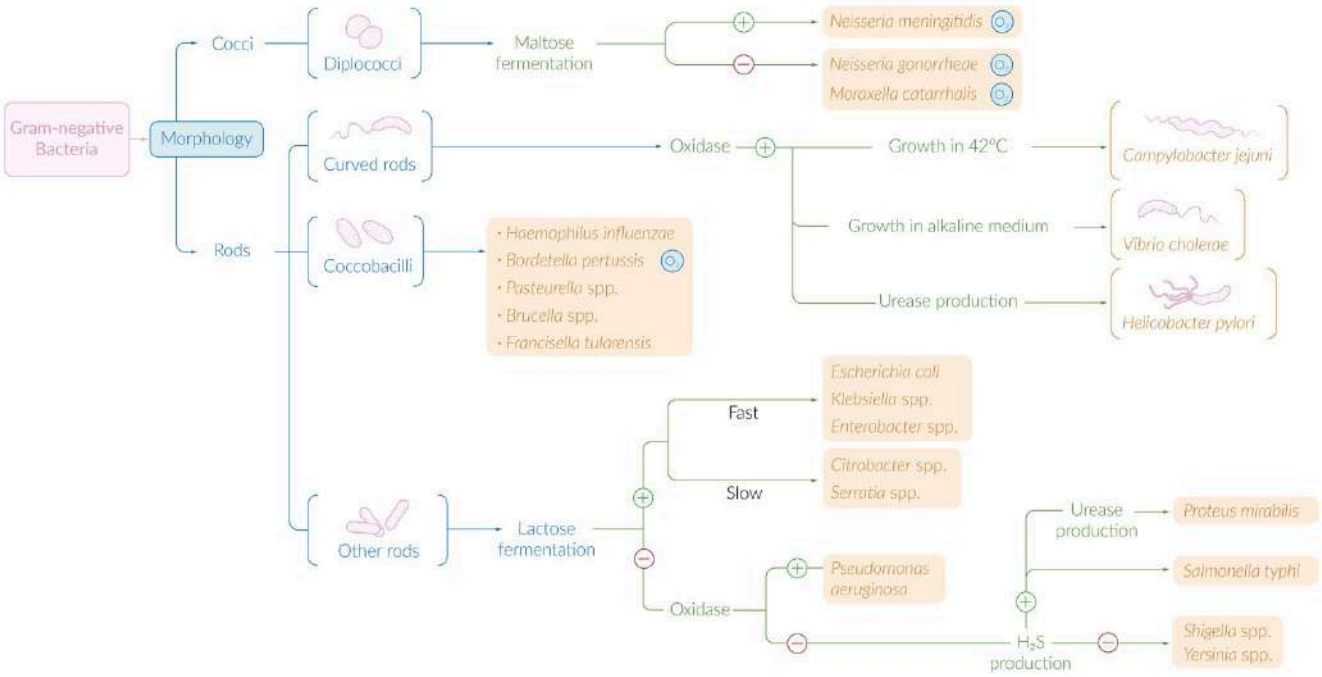
D - Gram-negative, flagellated bacteria that do not ferment lactose

Image



Explanation Why

Campylobacter jejuni is a species of comma-shaped, non-lactose fermenting bacteria with polar flagella. It is a leading cause of bloody diarrhea in children. The infection is transmitted fecal-orally by ingestion of undercooked, contaminated poultry/meat, unpasteurized milk, or fomites containing the pathogen. Direct contact with infected animals (dogs, cats, pigs) at petting zoos is a risk factor. *Campylobacter* infection can lead to Guillain-Barré syndrome and reactive arthritis. *Salmonella* spp. are also gram-negative, flagellated bacteria that do not ferment lactose and infection with *Salmonella* can cause fever, abdominal pain, and bloody diarrhea in younger children. Exposure to reptiles and live poultry is also a potential risk factor for transmission. However, *Salmonella* spp. test negative for oxidase.

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E - Gram-positive, aerobic, rod-shaped bacteria that produce catalase

Explanation Why

Listeria monocytogenes fits this description. This pathogen can cause fever, diarrhea, and abdominal pain due to gastroenteritis but diarrhea caused by Listeria is typically non-bloody. Moreover, Listeria tests negative for oxidase and *Listeria* infection is typically acquired by ingestion of unpasteurized dairy products.

F - Gram-positive, aerobic, rod-shaped bacteria that form spores

Explanation Why

Bacillus cereus fits this description. This pathogen can cause copious diarrhea, fever, and abdominal pain. However, diarrhea caused by *B. cereus* is typically non-bloody and *B. cereus* tests negative for oxidase. Moreover, *B. cereus* diarrheal syndrome usually involves the ingestion of foods that have been left at room temperature, allowing the bacteria to grow (a problem commonly encountered with fried rice, hence the common name “fried rice syndrome”).

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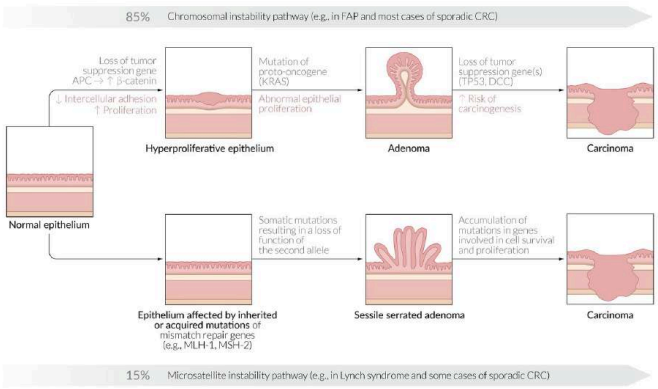
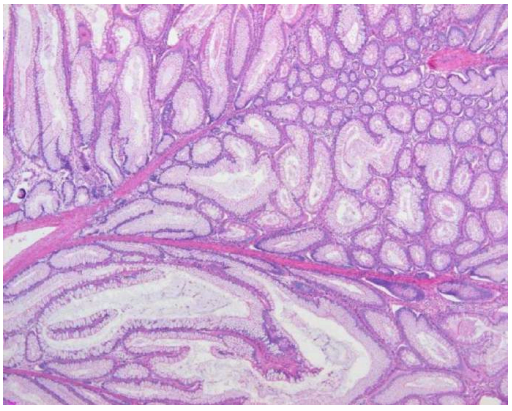
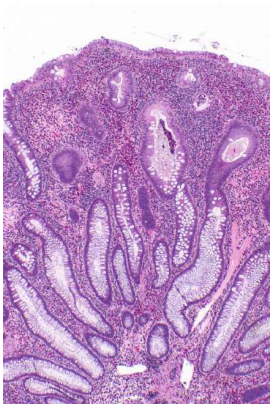
Question # 29

A 65-year-old man comes to the physician for a routine health maintenance examination. He has a strong family history of colon cancer. A screening colonoscopy shows a 4 mm polyp in the upper sigmoid colon. Which of the following findings on biopsy is associated with the lowest potential for malignant transformation into colorectal carcinoma?

	Answer	Image
A	Branching tubules embedded in lamina propria	
B	Tree-like branching of muscularis mucosa	
C	Regenerating epithelium with inflammatory infiltrate	

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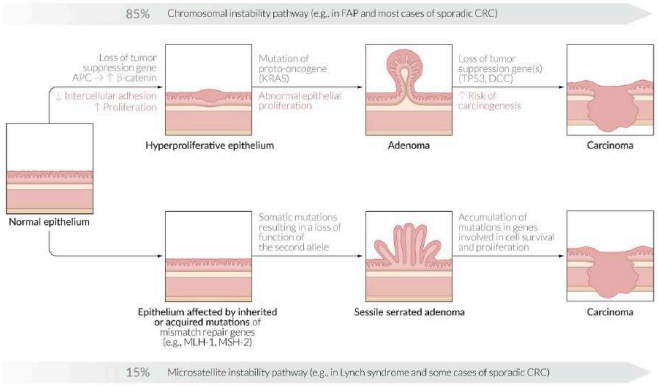
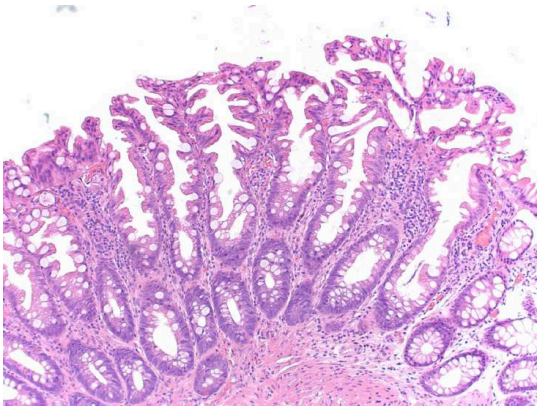
	Answer	Image
D	Finger-like projections with a fibrovascular core	
E	Hyperplastic epithelium at the base of crypts	

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Hint

Small epithelial proliferation in the rectosigmoid colon has the lowest potential for malignant transformation.

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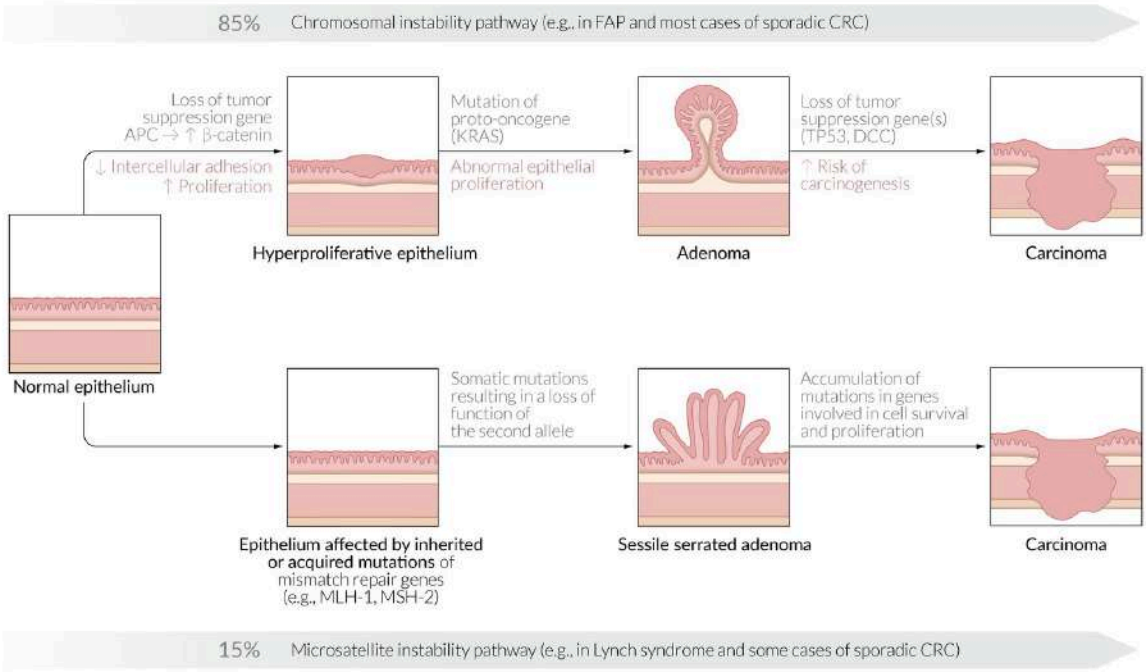
Correct Answer

A - Branching tubules embedded in lamina propria

Image



Explanation Why

Tubular adenomas consist of branching tubules embedded in the lamina propria. These common polyps carry a smaller risk of malignant transformation (approx. 5%) compared to other types of adenomatous polyps but still carry a greater risk of malignant transformation when compared to a different type of polyp.

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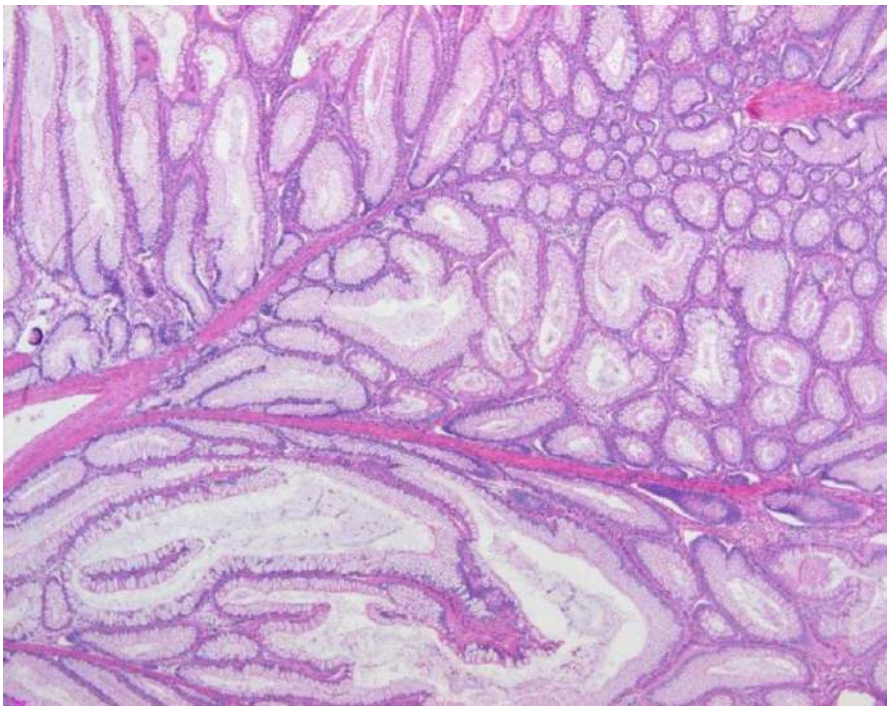
B - Tree-like branching of muscularis mucosa

Image



Explanation Why

Peutz-Jeghers syndrome (PJS) is associated with multiple non-neoplastic hamartomatous polyps, which typically show tree-like branching of the muscularis mucosa. PJS is associated with an increased risk of colorectal, gastric, breast, and ovarian cancers. The lifetime risk of colorectal cancer is approx. 40%.

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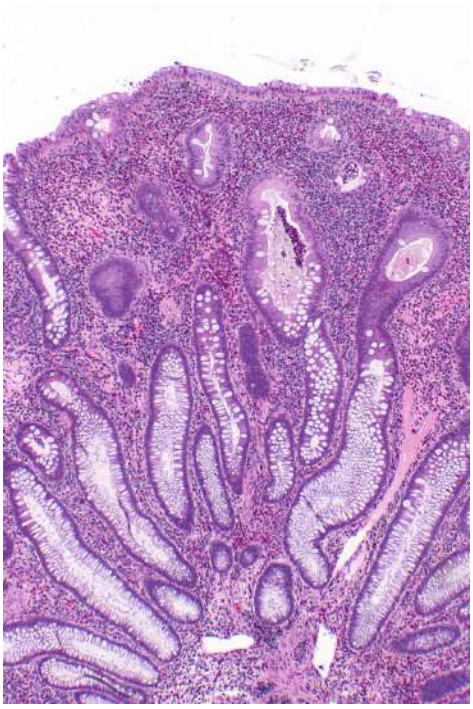
C - Regenerating epithelium with inflammatory infiltrate

Image



Explanation Why

Regenerating epithelium with inflammatory infiltrate is found in patients with inflammatory bowel disease (e.g., ulcerative colitis) and can manifest as pseudopolyps. While pseudopolyps only carry a low risk of malignant transformation, patients with chronic inflammatory bowel disease generally have an increased risk of colorectal cancer because of persistent cell damage from recurrent inflammation.

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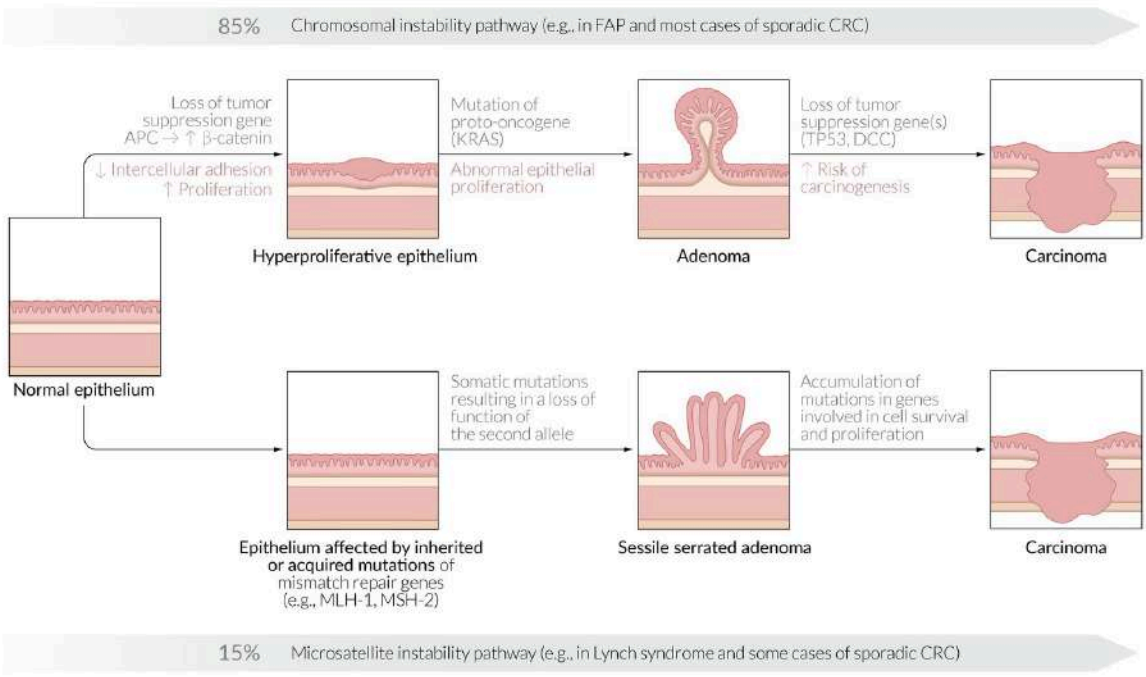
D - Finger-like projections with a fibrovascular core

Image



Explanation Why

Villous adenomas consist of finger-like projections with a fibrovascular core. They have the highest risk (approx. 50%) of malignant transformation of the three types of adenomatous polyps (i.e., tubular adenoma, tubulovillous adenoma, or villous adenoma).

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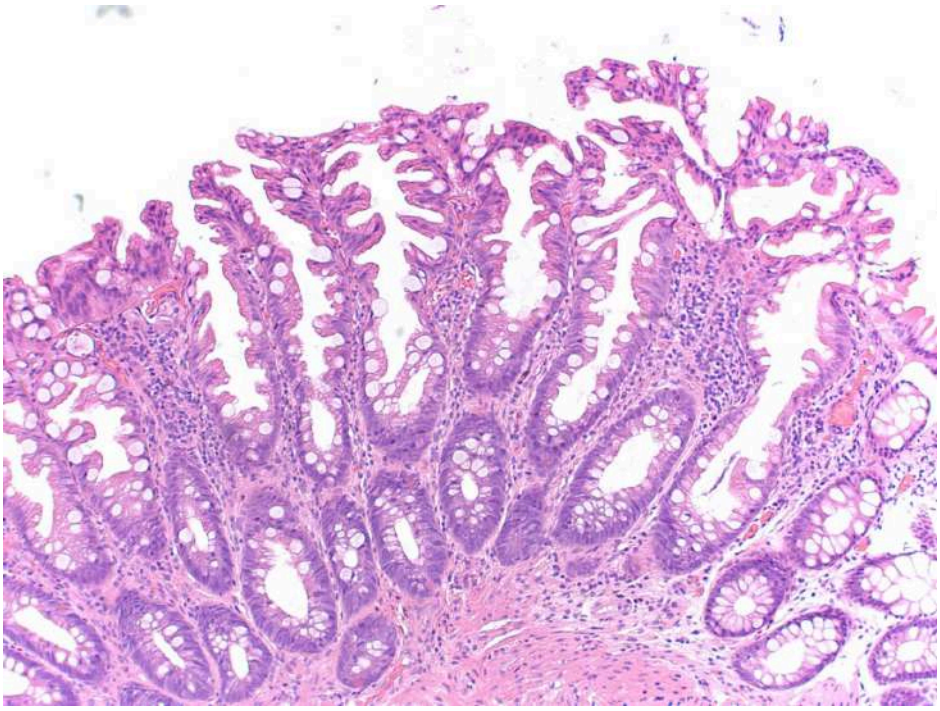
E - Hyperplastic epithelium at the base of crypts

Image



Explanation Why

Hyperplastic polyps consist of hyperplastic epithelium at the base of the crypts of Lieberkuhn. They are a common type of polyp and most frequently occur in the rectosigmoid and left colon. Hyperplastic polyps are benign and carry a very low risk of transforming into malignancy because there is no dysplasia present. Other examples of polyps that are benign include mucosal polyps and submucosal polyps.

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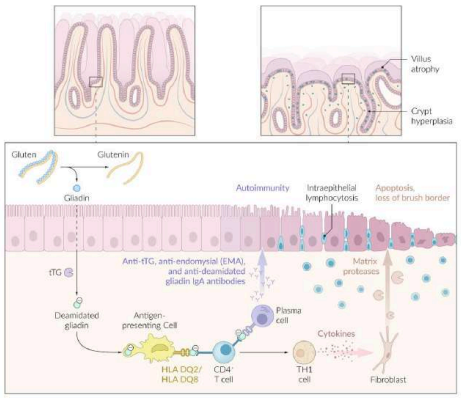
Question # 30

A 50-year-old man comes to the physician because of an 8-month history of intermittent watery diarrhea and abdominal pain. He has had a 12-kg (26-lb) weight loss during this period. He has also had episodic pain of the ankle, wrist, and knee joints during the past 5 years. An endoscopy with small bowel biopsy is performed. Histopathologic examination of a tissue specimen shows foamy macrophages in the lamina propria with periodic acid-Schiff (PAS)-positive inclusions. Further evaluation is most likely to show which of the following?

	Answer	Image
A	Multinucleated trophozoites	
B	Anti-tissue transglutaminase antibodies	
C	Anti-cyclic citrullinated peptide antibody	
D	Anti-saccharomyces cerevisiae antibodies	

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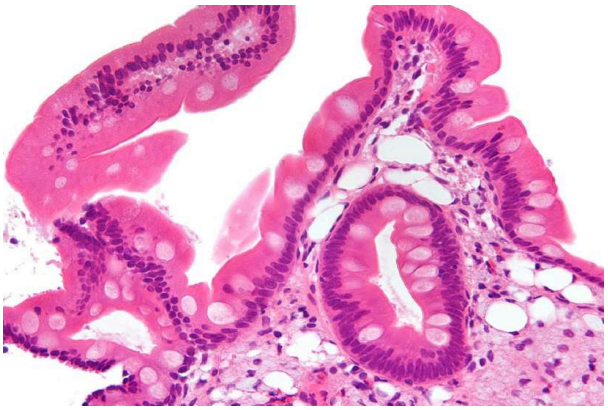
	Answer	Image
E	Intracellular, gram-positive bacilli	
F	Low serum TSH and high free T4 concentrations	

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Hint

Chronic polyarthritis that precedes the development of diarrhea, abdominal pain, and weight loss raises suspicion for Whipple disease. Small bowel biopsy showing PAS-positive, foamy macrophages in the lamina propria confirms the diagnosis.

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Correct Answer

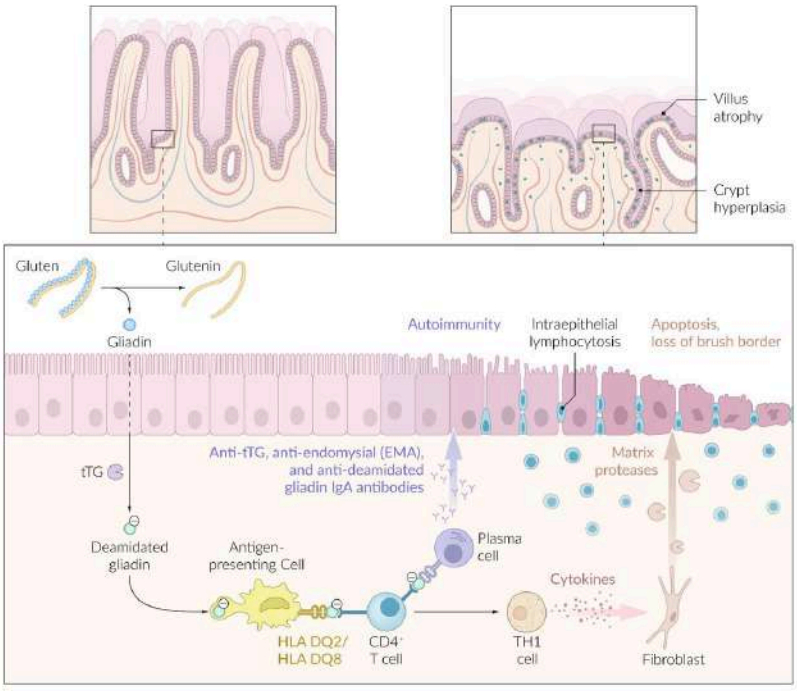
A - Multinucleated trophozoites

Explanation Why

Multinucleated trophozoites would be found in the stool sample of a patient with severe diarrhea of protozoan etiology (e.g., *Entamoeba histolytica* or *Giardia lamblia*). Although this patient presents with abdominal pain, weight loss, and diarrhea, the presence of PAS-positive foamy macrophages is highly indicative of another infection not caused by protozoan species.

B - Anti-tissue transglutaminase antibodies

Image



Explanation Why

Anti-tissue transglutaminase antibodies (most common), anti-endomysial antibodies, and anti-

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deamidated gliadin peptide antibodies are all serological markers seen in celiac disease. This patient's weight loss, diarrhea, and abdominal pain are concerning for a pathology involving the small bowel. Histological findings in celiac disease would, however, include villous atrophy, crypt hyperplasia, and intraepithelial lymphocytic infiltration. This patient's biopsy shows PAS-positive foamy macrophages, which is not consistent with celiac disease, but rather, is the histological hallmark of a specific infectious condition.

C - Anti-cyclic citrullinated peptide antibody

Explanation Why

Anti-cyclic citrullinated peptide antibodies (ACPA) are serological markers used in the diagnosis of rheumatoid arthritis. The presence of long-standing arthralgia would be consistent with this diagnosis, but this patient's recurrent diarrhea, weight loss, abdominal pain, and small bowel biopsy findings are not. These findings are more indicative of an infectious pathology of the small bowel.

D - Anti-saccharomyces cerevisiae antibodies

Explanation Why

Anti-Saccharomyces cerevisiae antibodies (ASCA) are serological markers that help distinguish between Crohn disease and ulcerative colitis, as they are more prevalent in the former. Although patients with inflammatory bowel diseases may present with some of the extraintestinal manifestations (e.g., arthralgia) seen in this patient, these disorders also cause chronic, bloody diarrhea. Additionally, the presence of PAS-positive inclusions in this patient's biopsy is highly indicative of a specific infectious pathology.

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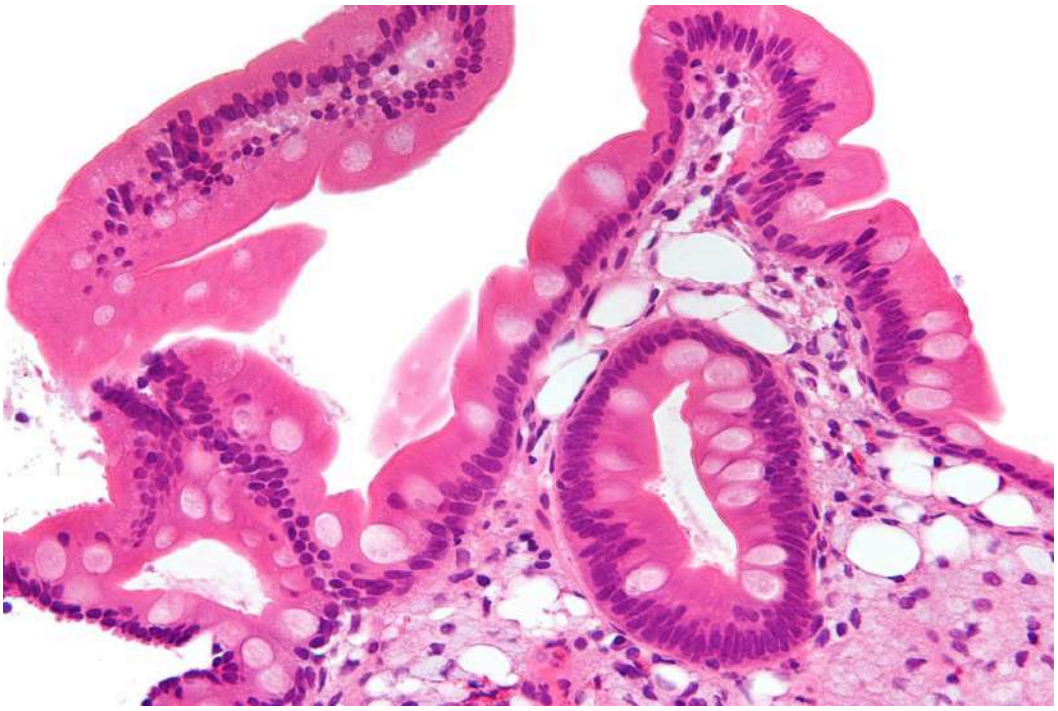
E - Intracellular, gram-positive bacilli

Image



Explanation Why

The causative organism in Whipple disease is *Tropheryma whipplei*, an intracellular, gram-positive bacillus. Frequently missed in staining, the histological hallmark of classical Whipple disease is periodic acid-Schiff (PAS) reactive vacuoles in macrophages found within the lamina propria of the small bowel, as seen in this patient. Whipple disease is lethal if left untreated. Intravenous antibiotics (ceftriaxone or penicillin plus streptomycin) for 14 days is the recommended induction therapy for Whipple disease, followed by maintenance therapy with trimethoprim-sulfamethoxazole (TMP-SMX) for 1 year.

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F - Low serum TSH and high free T4 concentrations

Explanation Why

Low serum TSH and high free T4 concentrations would be suggestive of hyperthyroidism. Weight loss and diarrhea are clinical features of hyperthyroidism, but this patient's abdominal pains, joint pains, and PAS-positive foamy macrophages on biopsy are hallmarks of an infectious pathology of the small bowel.

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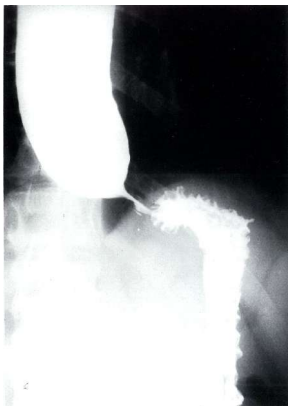
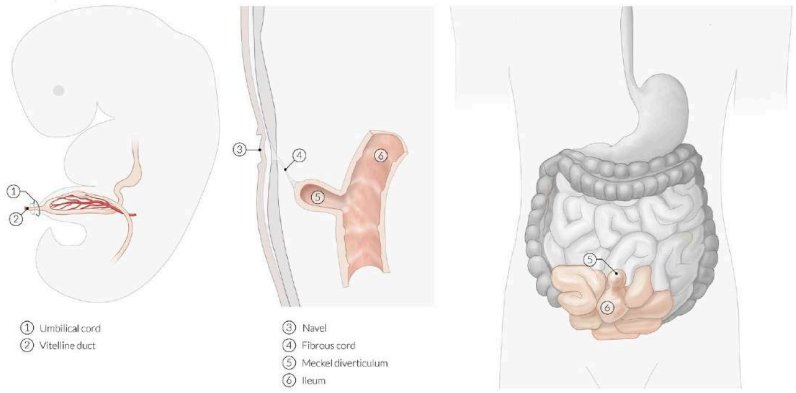
Question # 31

A 68-year-old man comes to the physician because of a 6-month history of difficulty swallowing pieces of meat and choking frequently during meal times. He also sometimes regurgitates foul-smelling, undigested food particles. Examination shows no abnormalities. A barium swallow shows an accumulation of contrast in an outpouching of the posterior pharyngeal wall at the C5 level. Which of the following is the most likely underlying cause of this patient's condition?

	Answer	Image
A	Inadequate relaxation of lower esophageal sphincter	
B	Remnant of the embryological omphalomesenteric duct	

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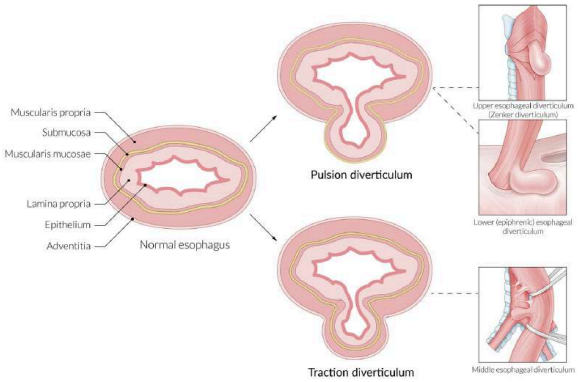
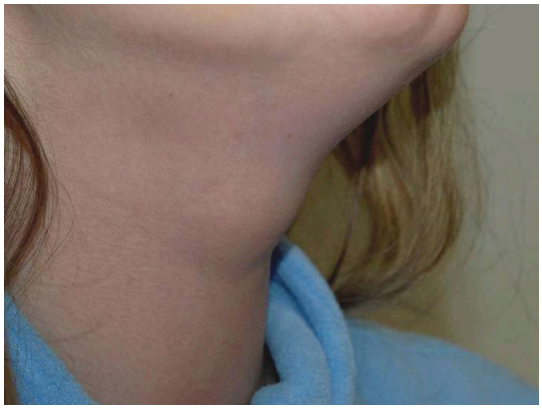
	Answer	Image
C	Increased intrapharyngeal pressure	
D	Scar fibrosis and traction of the esophagus	
E	Remnant of the thyroglossal duct	
F	Remnant of the second branchial cleft	

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Hint

This patient's clinical features and barium swallow are diagnostic of Zenker diverticulum, a pharyngoesophageal false diverticulum.

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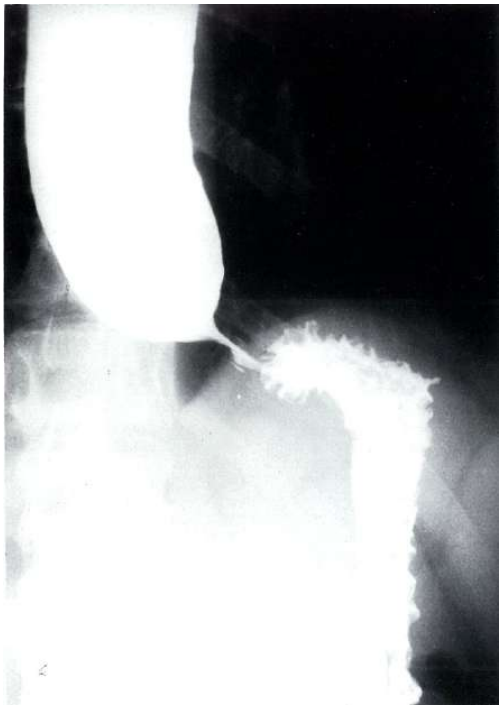
Correct Answer

A - Inadequate relaxation of lower esophageal sphincter

Image



Explanation But

Achalasia may predispose individuals to Zenker diverticulum.

Explanation Why

Inadequate relaxation of the lower esophageal sphincter due to degeneration of inhibitory neurons within the myenteric plexus causes achalasia. This condition manifests with dysphagia, halitosis, and regurgitation of undigested food, similar to what is seen in this patient. However, it is not associated with the accumulation of contrast on barium swallow. Instead, barium swallow shows a classic "bird's beak" appearance of the gastroesophageal junction. Manometry may be used to confirm the impaired sphincter relaxation.

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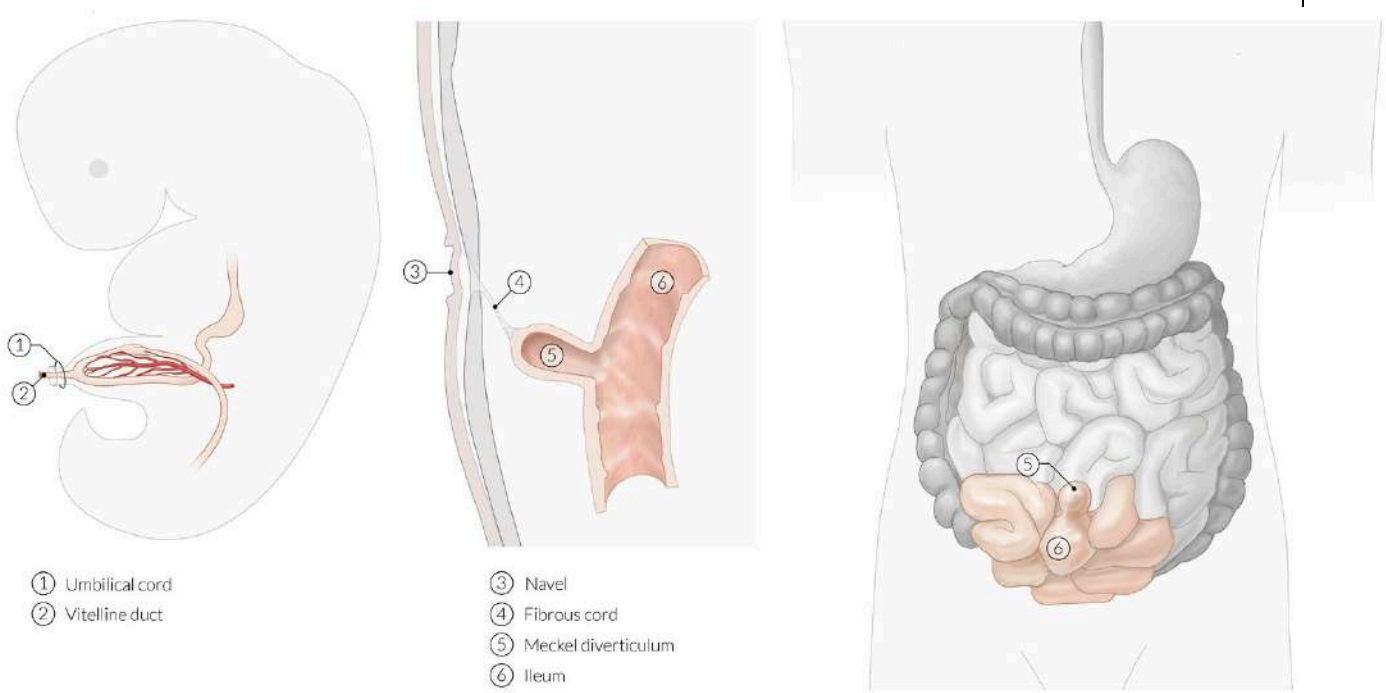
B - Remnant of the embryological omphalomesenteric duct

Image



Explanation Why

A Meckel diverticulum is a remnant of the embryological omphalomesenteric duct and it is a true diverticulum involving all layers of the ileal wall. In most cases, Meckel diverticulum is asymptomatic. In symptomatic patients (mostly children < 2 years of age), painless lower gastrointestinal bleeding is the most common presentation. Merkel diverticulum does not manifest with dysphagia, regurgitation, or accumulation of contrast in an outpouching of the posterior pharyngeal wall, all of which are seen here.

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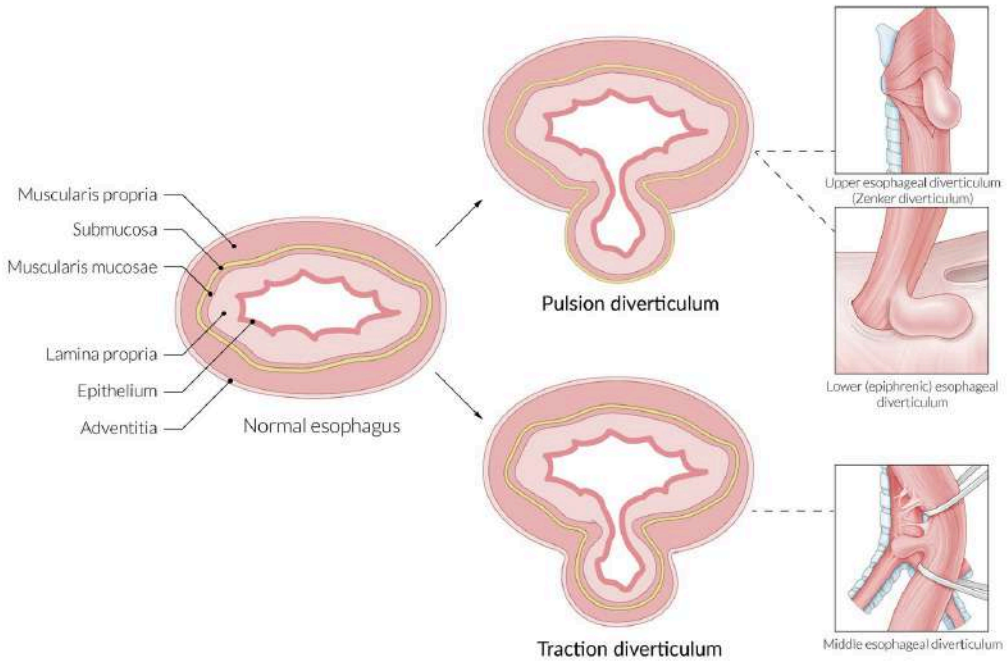
C - Increased intrapharyngeal pressure

Image



Explanation Why

Increased intrapharyngeal pressure on a physiologically weakened area of the hypopharynx (Killian triangle) causes the local mucosa and submucosa to bulge through the muscularis propria, creating a Zenker diverticulum. Pressure increase is usually due to esophageal dysmotility (e.g., inadequate relaxation of the upper esophageal sphincter). Pulsion diverticula (due to increased intraluminal pressure), such as Zenker diverticulum or colonic diverticula in diverticulosis, are typically false diverticula, whereas traction diverticula (due to inflammatory processes) are true diverticula.

D - Scar fibrosis and traction of the esophagus

Explanation Why

Scar fibrosis and traction of the esophagus can cause a traction diverticulum, a true diverticulum of

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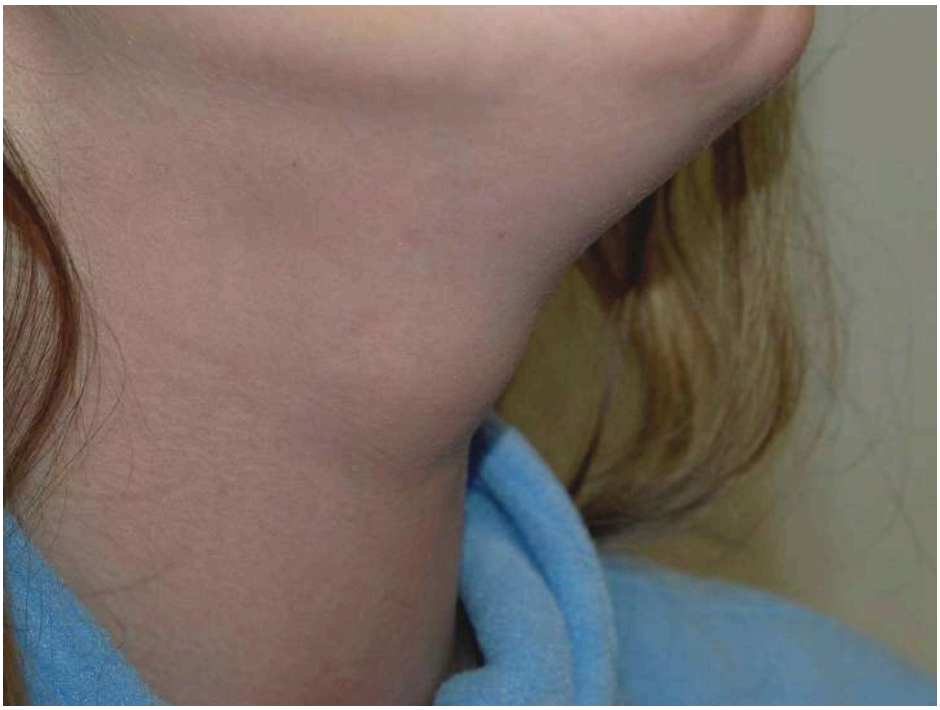
all esophageal layers. Traction diverticula manifest with dysphagia, regurgitation, and halitosis, all of which are seen in this patient. However, barium swallow typically shows a pointed, triangular bulge in the midesophagus rather than an accumulation of contrast in an outpouching of the posterior pharyngeal wall, which is seen here. A true esophageal diverticulum is rare and is likely preceded by an inflammatory condition of the esophagus (e.g., tuberculosis or fungal infection).

E - Remnant of the thyroglossal duct

Image



Explanation Why

A thyroglossal duct cyst is a remnant of the thyroglossal duct, formed during thyroid gland development. This condition may cause dysphagia, which is seen in this patient. However, cystic masses are typically located in the anterior midline near the hyoid bone, which is not seen here. Moreover, it would not manifest with regurgitation or halitosis, nor cause abnormal findings in barium swallow. Finally, thyroglossal duct cysts are most commonly diagnosed in early childhood.

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F - Remnant of the second branchial cleft

Explanation Why

A branchial cleft cyst is a remnant of the second branchial cleft. Branchial cleft cysts manifest as a painless neck mass lateral to the midline and anterior to the sternocleidomastoid; this patient's physical examination is unremarkable. In addition, this condition is not associated with regurgitation or halitosis, both of which are seen here. Furthermore, a branchial cleft cyst is usually diagnosed in late childhood or adulthood, and barium swallow is typically unremarkable.

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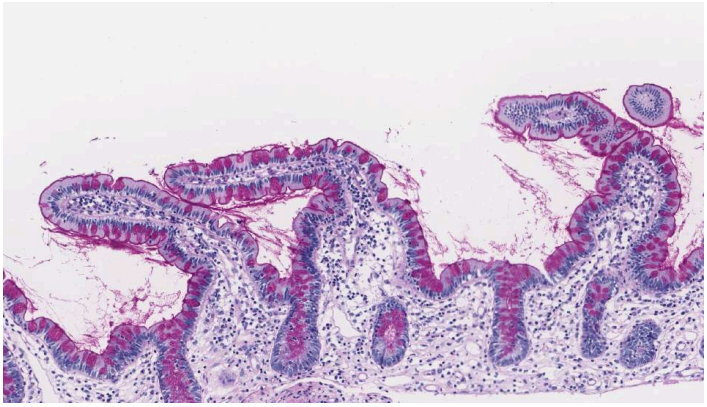
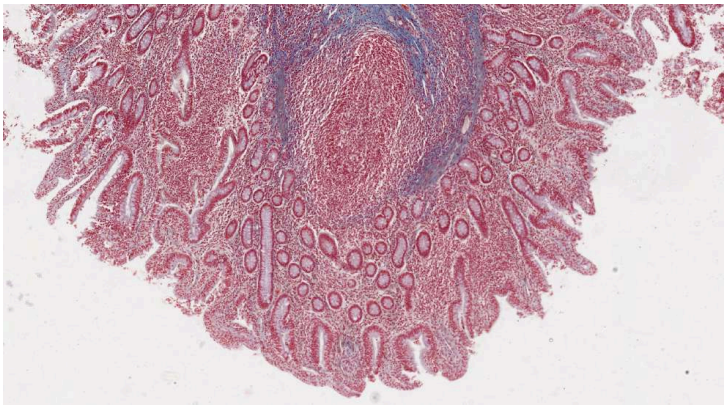
Question # 32

A 56-year-old woman comes to the physician because of a 2-year-history of intermittent upper abdominal pain that occurs a few hours after meals and occasionally wakes her up in the middle of the night. She reports that the pain is relieved with food intake. Physical examination shows no abnormalities. Endoscopy shows a 0.5 x 0.5 cm ulcer on the posterior wall of the duodenal bulb. A biopsy specimen obtained from the edge of the ulcer shows hyperplasia of submucosal glandular structures. Hyperplasia of these cells most likely results in an increase of which of the following?

	Answer	Image
A	Glycoprotein synthesis	
B	Antigen presentation	

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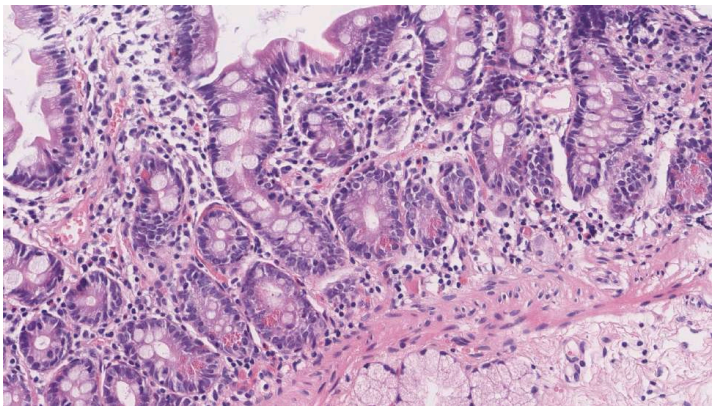
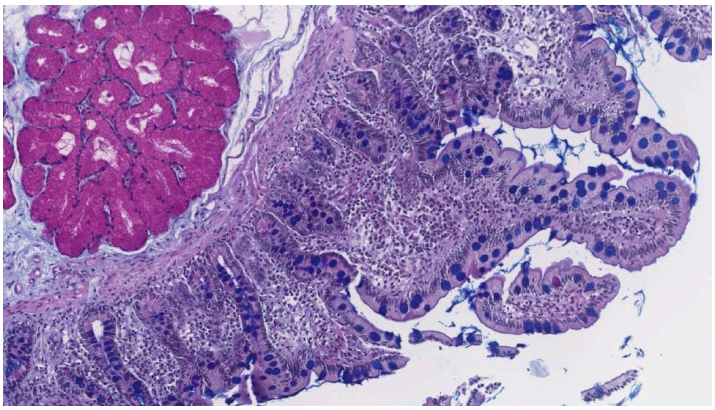
	Answer	Image
C	Lysozyme secretion	
D	Cholecystokinin secretion	
E	Nutrient absorption	
F	Hydrochloric acid secretion	
G	Bicarbonate secretion	

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Hint

Brunner glands are located in the submucosa of the duodenum and undergo hyperplasia as a protective mechanism in patients with peptic ulcer disease.

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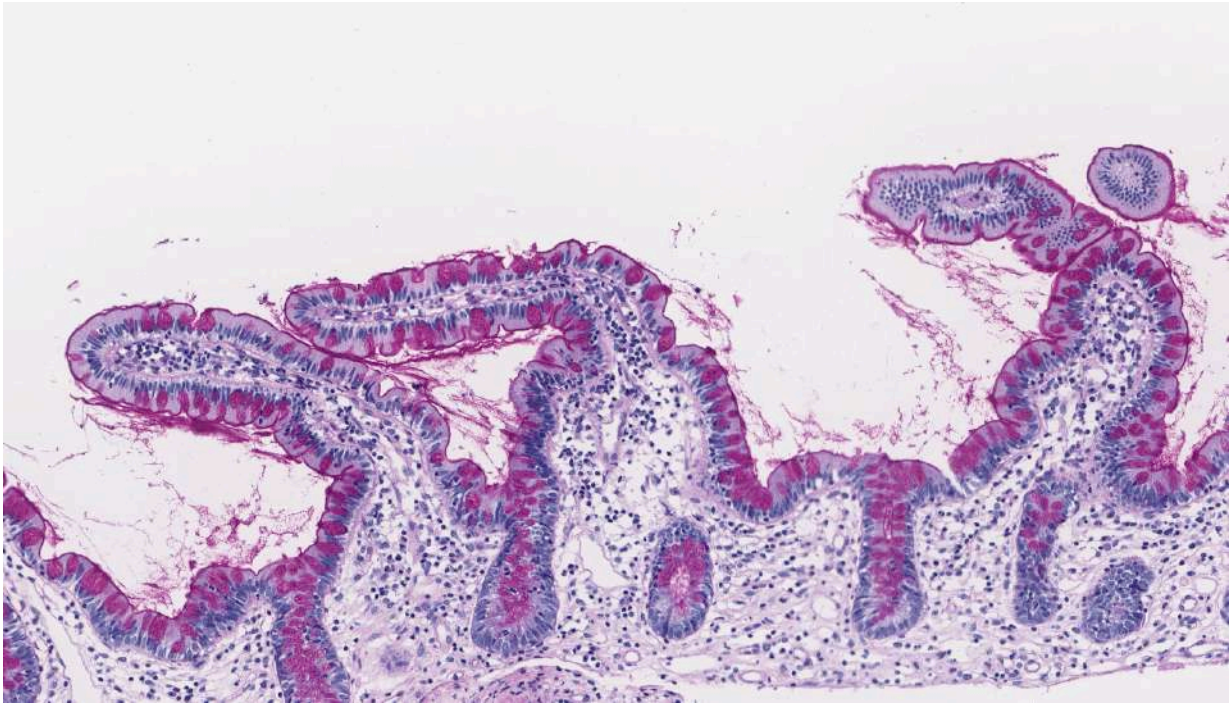
Correct Answer

A - Glycoprotein synthesis

Image



Explanation Why

Glycoproteins form the mucosal barrier of the intestine and are synthesized by goblet cells, which are located in the mucosa, not the submucosa. Moreover, goblet cells are found in the lowest concentration in the duodenum. Their number increases in jejunum and ileum.

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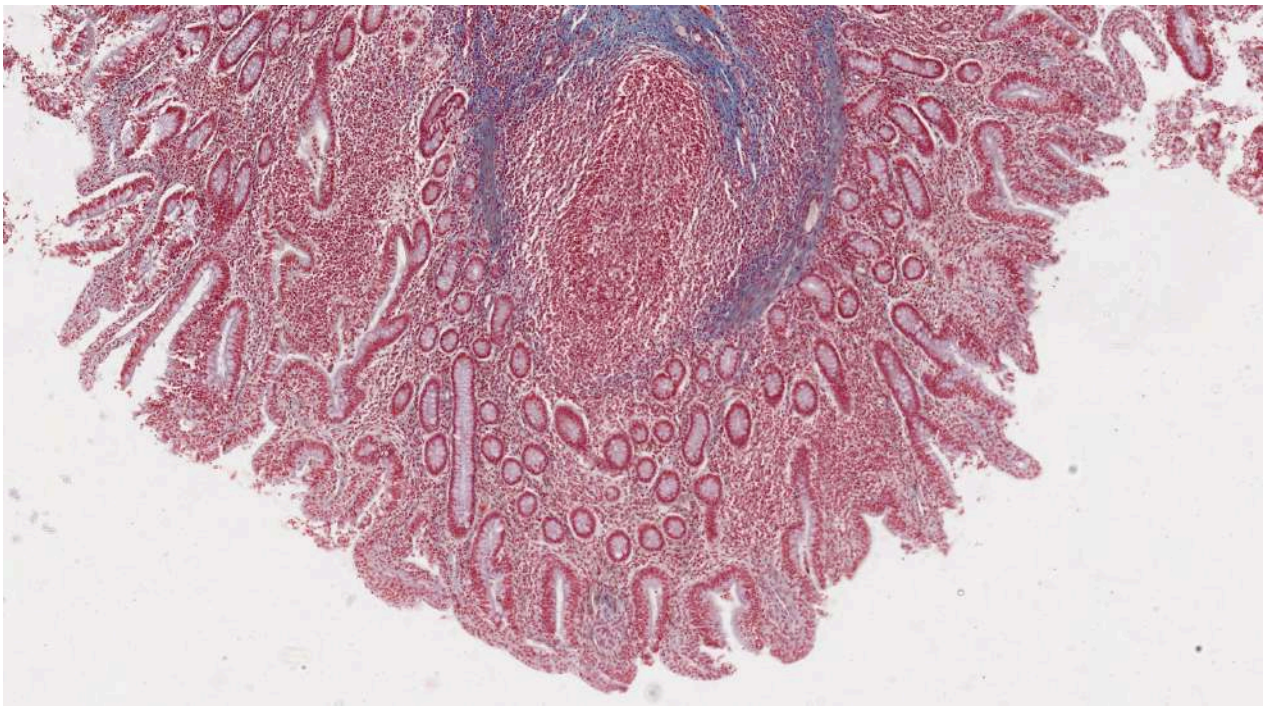
B - Antigen presentation

Image



Explanation Why

Presentation of ingested antigens occurs in lymphocyte aggregates called Peyer patches, which are found in the lamina propria and submucosa of the ileum, not the duodenum.

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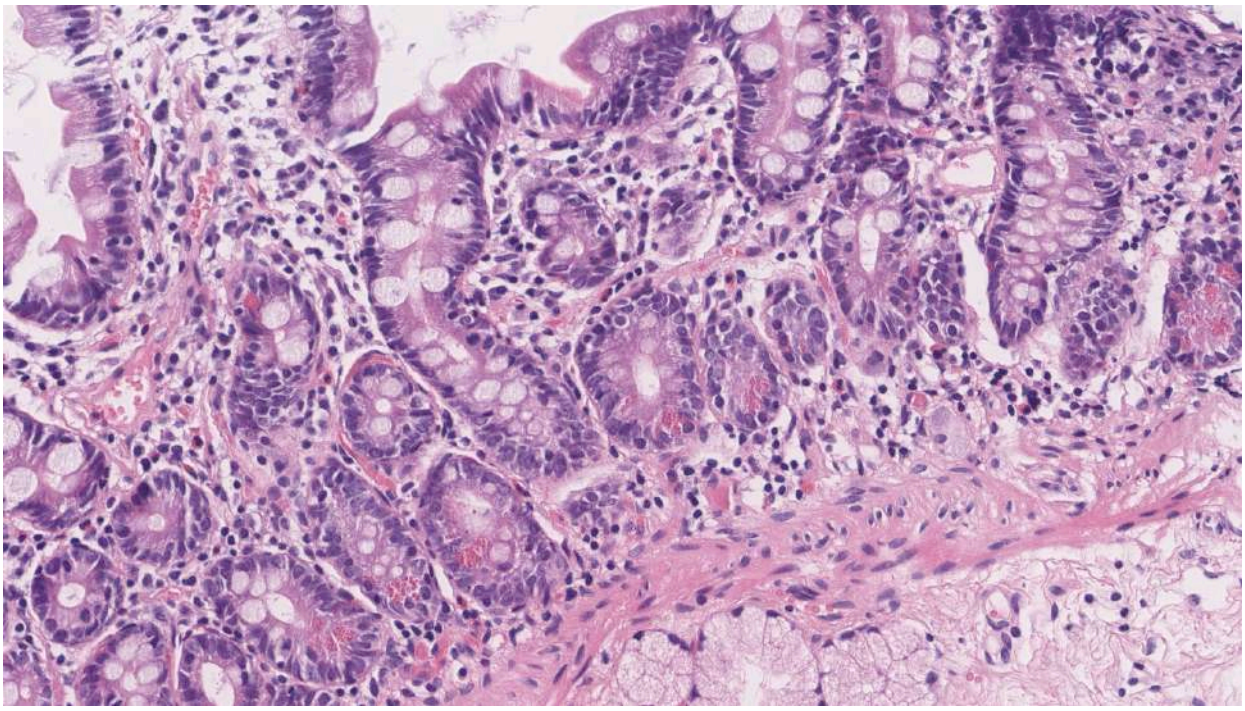
C - Lysozyme secretion

Image



Explanation Why

Lysozyme is secreted by Paneth cells, which occupy the base of the crypts of Lieberkuhn in the mucosa of duodenum, jejunum, and ileum. Lysozymes act as antibacterial agents and are not involved in the pathogenesis of peptic ulcer disease.

D - Cholecystokinin secretion

Explanation Why

Cholecystokinin (CCK) is produced by a type of enteroendocrine cell called I cells, which are located in the duodenal and jejunal mucosa, not submucosa. CCK stimulates gallbladder contraction, sphincter of Oddi relaxation, and secretion of enzymes and bicarbonate by the pancreas. In addition, CCK slows gastric emptying.

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E - Nutrient absorption

Explanation Why

Absorption of certain nutrients such as iron occurs in the duodenum via the surface columnar epithelial cells of the duodenal mucosa, not the duodenal submucosa.

F - Hydrochloric acid secretion

Explanation Why

Hydrochloric acid is secreted by parietal cells in the gastric mucosa to maintain the acidic environment of the stomach. Increased secretion of HCl can lead to peptic ulcer disease in the stomach or duodenum. Parietal cells are not present in the duodenum.

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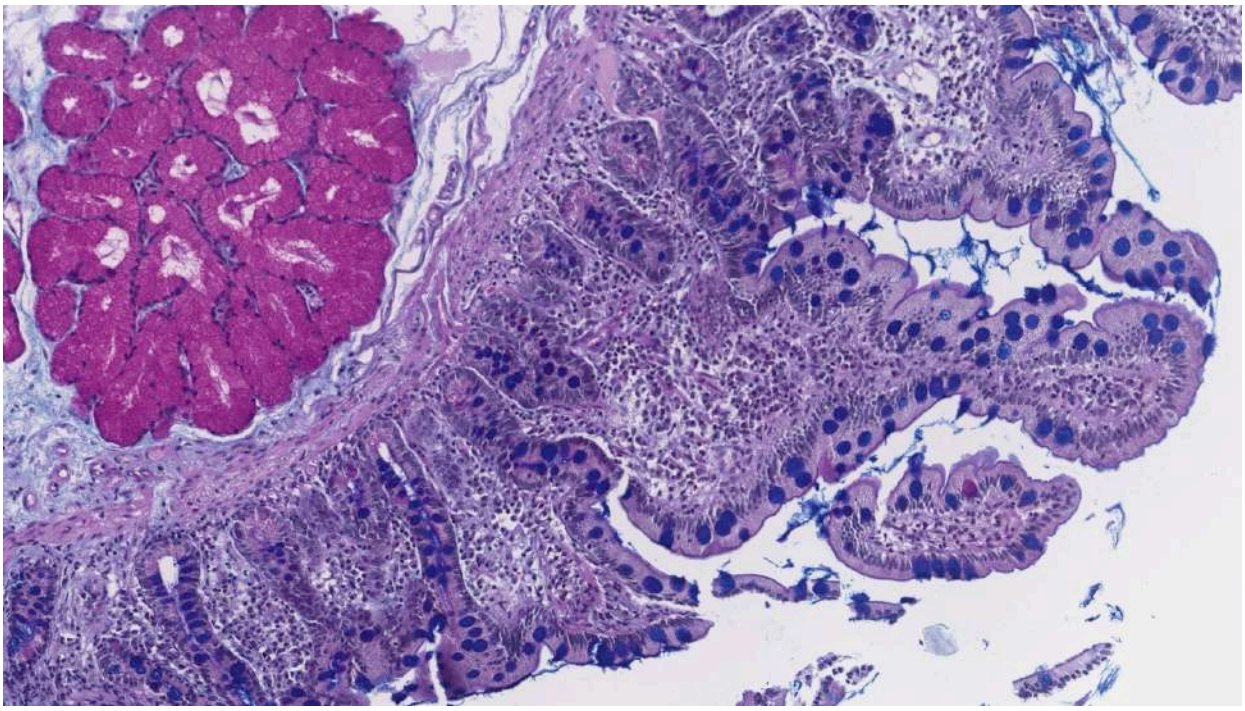
G - Bicarbonate secretion

Image



Explanation Why

Brunner glands are located in the submucosa of the duodenum and secrete an alkaline, bicarbonate-rich fluid to neutralize stomach acid. The duct openings deliver the secretions into the base of the crypts of Lieberkuhn. Peptic ulcer disease can lead to compensatory hyperplasia of Brunner glands.

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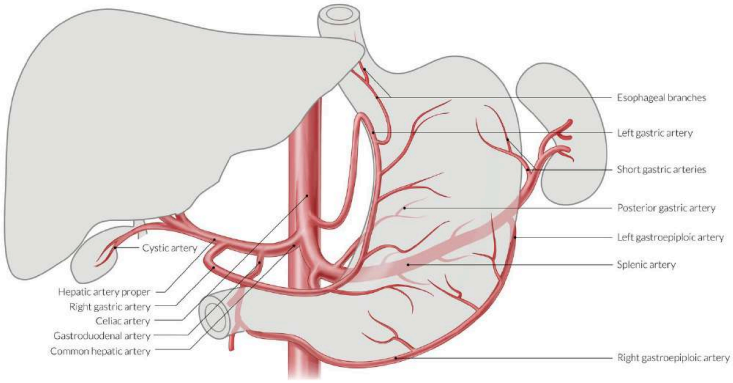
Question # 33

A 57-year-old woman comes to the physician because of a 2-week history of worsening epigastric pain that improves with meals. She has had similar pain of lesser intensity for the past 4 years. Physical examination shows no abnormalities. Upper endoscopy shows a 0.5-cm mucosal breach in the anterior duodenal bulb that extends into the submucosa. A biopsy specimen of the lesion shows hypertrophy of the Brunner glands. This patient is at the greatest risk for which of the following complications?

	Answer	Image
A	Perforation	
B	Hematemesis	
C	MALT lymphoma	
D	Gastric outlet obstruction	
E	Adenocarcinoma	

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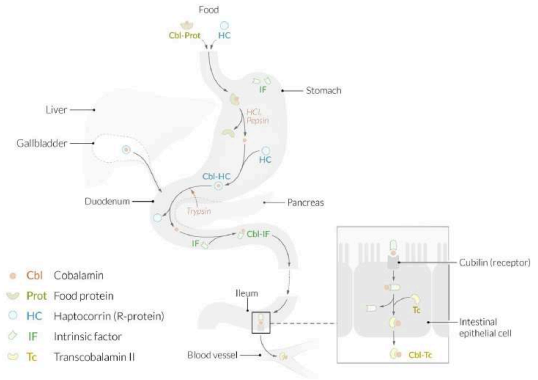
	Answer	Image
F	Pernicious anemia	

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Hint

This patient has epigastric pain that improves with food intake, which suggests a duodenal ulcer. The diagnosis of duodenal ulcer is confirmed by endoscopic findings, including a mucosal breach in the anterior duodenum, and by the hypertrophic Brunner glands in the biopsy specimen. The location of a peptic ulcer partly determines its most likely complications.

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Correct Answer

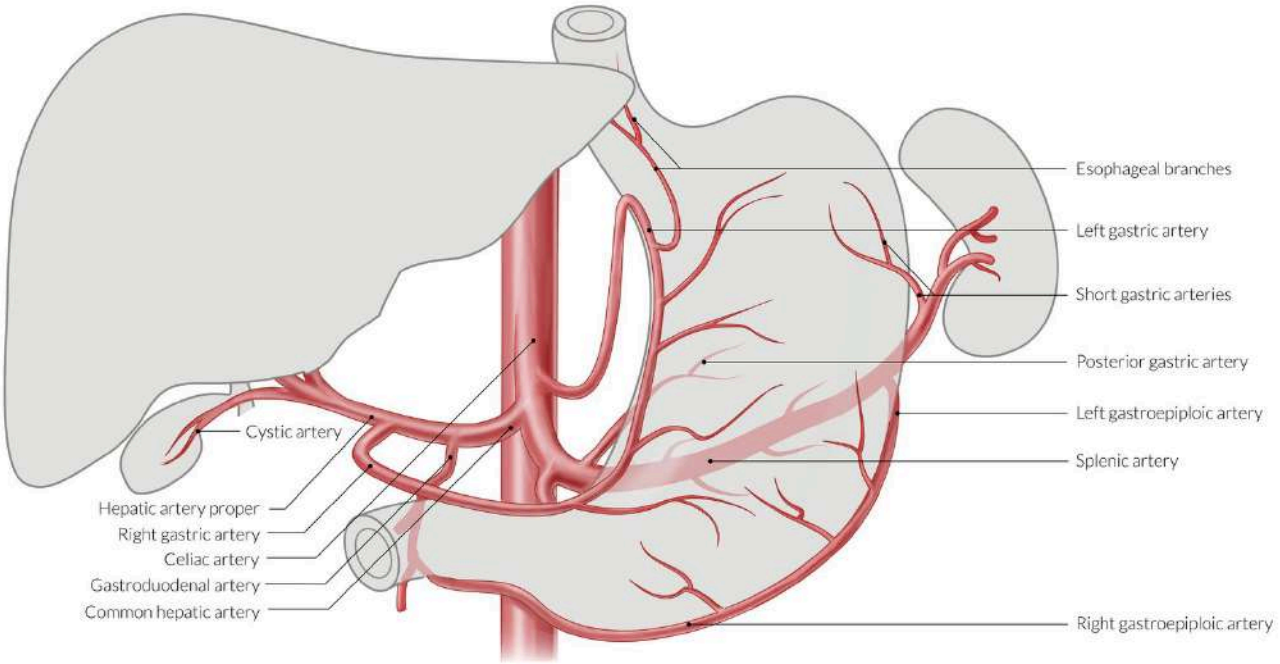
A - Perforation

Explanation Why

Peptic ulcer perforation occurs when an ulcer erodes through all the layers of the bowel, allowing spillage of gastric or duodenal contents into surrounding structures. It is the second most common complication of chronic PUD, bleeding being the first. The most common location for peptic ulcer perforation is the anterior duodenum. Ulcers of the anterior duodenum usually perforate into the peritoneal cavity, in contrast to ulcers of the posterior duodenum, which tend to cause massive bleeding (e.g., hematemesis) from the adjacent gastroduodenal artery.

B - Hematemesis

Image



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Explanation Why

GI bleeding is the most common complication of all peptic ulcers, regardless of location. However, a massive upper GI bleed, manifesting with hematemesis and hemodynamic changes, is most commonly caused by posterior duodenal ulcers because of the proximity of the gastroduodenal artery to the posterior wall of the duodenal bulb. Although this patient's anterior duodenal ulcer might be complicated by anemia due to chronic GI bleeding, it is less likely to be complicated by a massive GI bleed.

C - MALT lymphoma

Explanation Why

MALT lymphoma is a complication of chronic *H. pylori* infection of the stomach. It develops due to accumulation and persistent activation of T cells and B cells in response to chronic infection of the gastric mucosa. Although *H. pylori* accounts for most duodenal ulcers, MALT lymphomas are typically localized to the stomach and are very rare in the duodenum.

D - Gastric outlet obstruction

Explanation Why

Gastric outlet obstruction (GOO) is most commonly caused by a malignancy. A duodenal peptic ulcer can cause acute GOO (due to inflammation and edema) or chronic GOO (due to scarring and fibrosis) but a different complication is much more likely to occur than GOO.

E - Adenocarcinoma

Explanation Why

Adenocarcinoma of the stomach is a rare complication of chronic gastric ulcers. For reasons yet unknown, duodenal ulcers are generally benign and do not undergo malignant transformation. This patient is therefore unlikely to develop adenocarcinoma as a complication.

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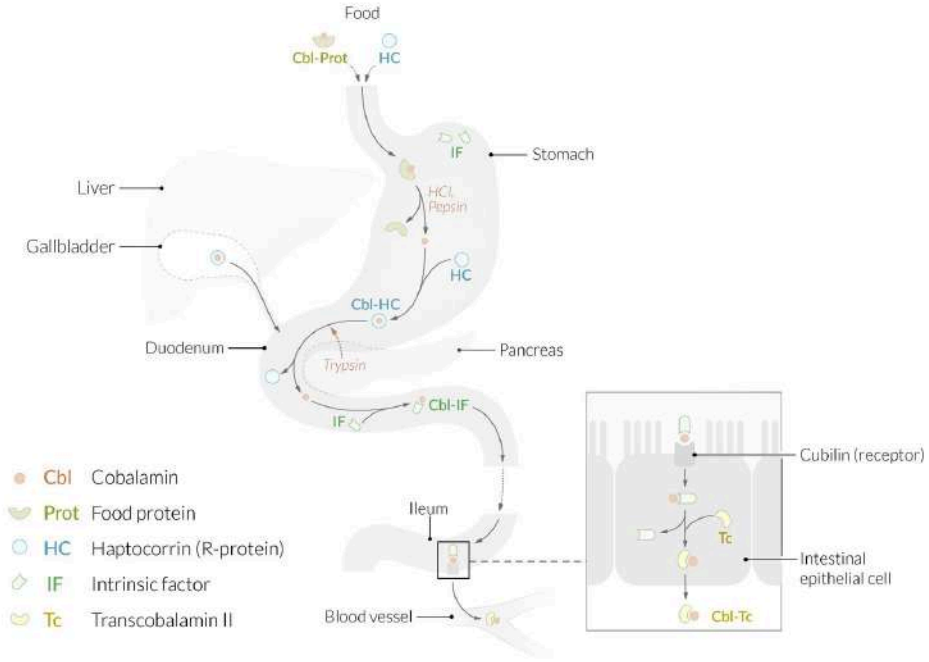
F - Pernicious anemia

Image



Explanation Why

Pernicious anemia is a complication of autoimmune gastritis, which affects the body and fundus of the stomach and is characterized by glandular atrophy with lymphocytic infiltrates in the lamina propria. This patient with a duodenal peptic ulcer is likely to develop microcytic anemia (due to chronic GI bleeding), not pernicious anemia.

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Question # 34

A 71-year-old woman comes to the physician because of an 8-month history of fatigue. Laboratory studies show a hemoglobin concentration of 13.3 g/dL, a serum creatinine concentration of 0.9 mg/dL, and a serum alkaline phosphatase concentration of 130 U/L. Laboratory evaluation of which of the following parameters would be most helpful in determining the cause of this patient's symptoms?

	Answer	Image
A	Cancer antigen 27-29	
B	Lactate dehydrogenase	
C	Ferritin	
D	Gamma-glutamyl transpeptidase	
E	Calcitriol	

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Hint

The patient has nonspecific symptoms and an elevation of serum alkaline phosphatase that may be associated with liver disease or bone pathology. To determine the underlying disease a specific laboratory marker is needed.

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Correct Answer

A - Cancer antigen 27-29

Explanation Why

Cancer antigen 27-29 (CA 27-29) is a marker used in the follow up of advanced breast cancer. Although high levels of CA 27-29 can indicate liver or bone metastases, which may also cause elevated ALP, CA 27-29 is a nonspecific parameter that can also be elevated in various other cancers and noncancerous conditions. Therefore, CA 27-29 cannot be used to determine the cause of this patient's symptoms.

B - Lactate dehydrogenase

Explanation Why

Lactate dehydrogenase (LDH) is an enzyme that catalyzes the reversible conversion of lactate to pyruvate and is elevated in any case of cell damage or disease with increased cell turnover. LDH would not help in determining the underlying cause of this patient's symptoms because it is a rather nonspecific marker that can be elevated in various conditions, including malignancies, hemolytic anemia, hepatocyte injury, and infarction.

C - Ferritin

Explanation Why

Ferritin is responsible for iron storage and acts as an acute phase reactant. Ferritin would not help in determining the underlying cause of this patient's symptoms because it is a rather nonspecific marker that can be elevated in various conditions, including systemic inflammation, malignant disease, anemia of chronic disease, and sideroblastic anemia. A different investigation is more appropriate in this patient with normal hemoglobin and increased ALP.

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D - Gamma-glutamyl transpeptidase

Explanation Why

In a patient with increased ALP, gamma-glutamyl transpeptidase (GGT) would be the most appropriate test to differentiate a disease of the hepatobiliary system from a disease of the bone. Simultaneous elevation in both ALP and GGT would signify a liver or biliary tract pathology. If ALP is elevated as a result of increased bone turnover, GGT levels would be normal. Increased GGT with normal ALP is characteristic of heavy alcohol use.

E - Calcitriol

Explanation Why

Calcitriol assays are indicated to diagnose vitamin D deficiency (osteomalacia/rickets), which can present with fatigue and increased ALP (due to secondary hyperparathyroidism). However, hepatic disorders are also associated with fatigue and increased ALP. Therefore, a different test is more appropriate to determine the tissue of origin of ALP before investigations pertinent to bone disorders are considered.

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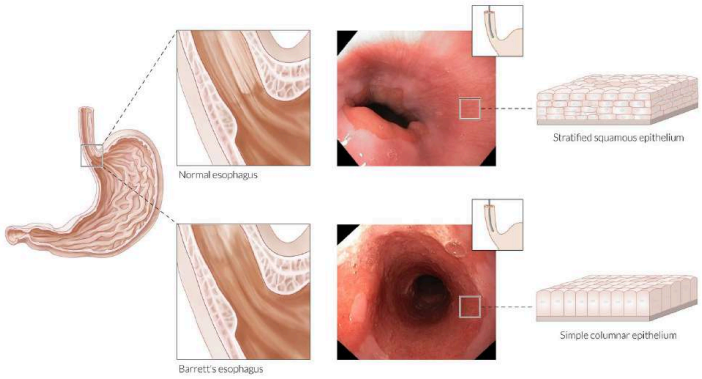
Question # 35

A 56-year-old man comes to the physician because of intermittent retrosternal chest pain. Physical examination shows no abnormalities. Endoscopy shows salmon pink mucosa extending 5 cm proximal to the gastroesophageal junction. Biopsy specimens from the distal esophagus show nonciliated columnar epithelium with numerous goblet cells. Which of the following is the most likely cause of this patient's condition?

	Answer	Image
A	Neoplastic proliferation of esophageal epithelium	
B	Esophageal exposure to gastric acid	
C	Atopic inflammation of the esophagus	
D	Hypermotile esophageal contractions	
E	Fungal infection of the lower esophagus	

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	Answer	Image
F	Incomplete relaxation of lower esophageal sphincter	

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Hint

Esophageal mucosa is normally whitish-pink and composed of stratified squamous epithelium. Intestinal mucosa is normally composed of columnar epithelium with goblet cells.

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Correct Answer

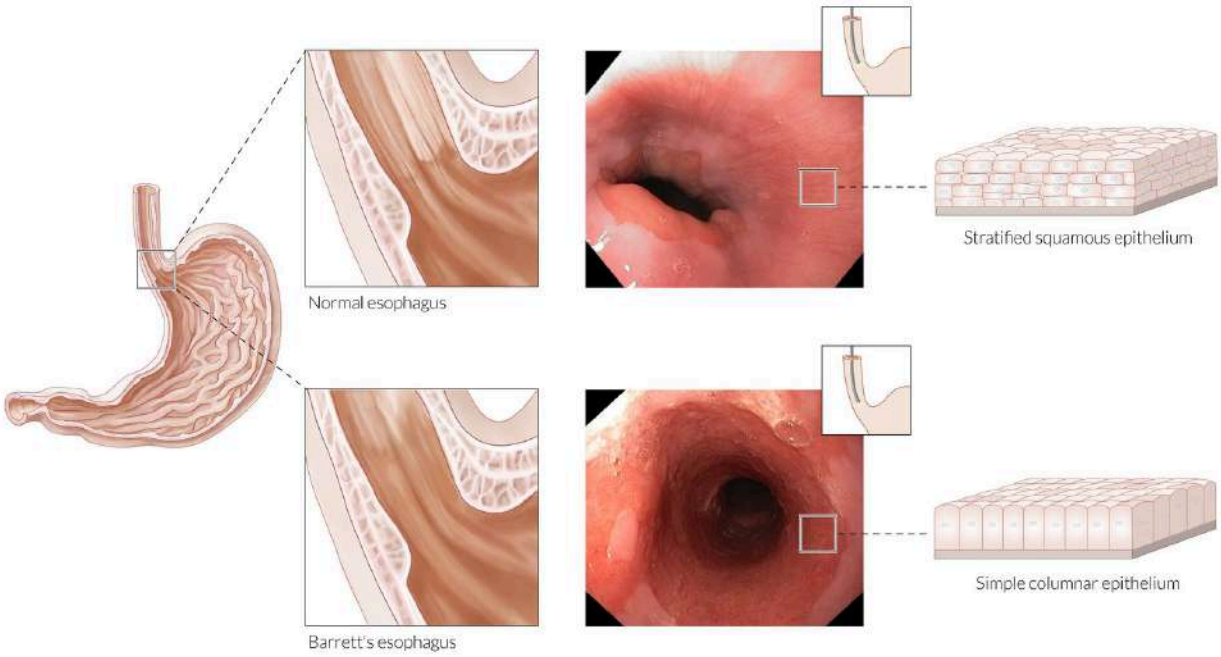
A - Neoplastic proliferation of esophageal epithelium

Explanation Why

Neoplastic proliferation of esophageal epithelium is seen in esophageal cancer. This patient is at increased risk to develop esophageal adenocarcinoma. However, he lacks typical features of an esophageal malignancy such as weight loss, dysphagia, and an ulcerative mass on endoscopy.

B - Esophageal exposure to gastric acid

Image



Explanation Why

Chronic exposure of the esophagus to gastric acid promotes transformation of the stratified squamous epithelium of the esophagus to metaplastic columnar epithelium with goblet cells (Barrett

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esophagus). Barrett esophagus classically occurs in patients with GERD, which commonly presents with intermittent retrosternal pain, as seen in this patient. Adequate diagnosis of Barrett esophagus requires histologic confirmation of intestinal metaplasia.

C - Atopic inflammation of the esophagus

Explanation Why

Atopic inflammation of the esophagus is seen in eosinophilic esophagitis, which is thought to be caused by an abnormal response of the immune system to an antigenic stimulus. Affected individuals commonly present with retrosternal pain, dysphagia to solids, and food impaction. Although this patient presents with retrosternal pain, biopsy would likely show numerous eosinophils within multiple layers of the esophagus rather than metaplastic changes.

D - Hypermotile esophageal contractions

Explanation Why

Hypermotile esophageal contractions are seen in spastic disorders of the esophagus (e.g., nutcracker esophagus, diffuse esophageal spasms). Hypermotile esophagus may present with sudden, retrosternal chest pain and a distinctive pattern on barium swallow and manometry. Although this patient does have intermittent retrosternal pain, those conditions would not usually present with mucosal abnormalities.

E - Fungal infection of the lower esophagus

Explanation Why

Fungal infection of the esophagus can be caused by pathogens such as *Candida albicans* (esophageal candidiasis). Although it may cause retrosternal pain, as seen here, the absence of risk factors (e.g., immunosuppression) and fungal patches on endoscopy make this diagnosis unlikely.

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F - Incomplete relaxation of lower esophageal sphincter

Explanation Why

Incomplete relaxation of the lower esophageal sphincter occurs in patients with achalasia due to absent or decreased myenteric neurons. Although achalasia can manifest with retrosternal pain, as seen in this patient, it would classically also present with regurgitation and dysphagia of solids and liquids. Endoscopy could possibly show inflammation in case of retained food, but intestinal metaplasia would not be expected.

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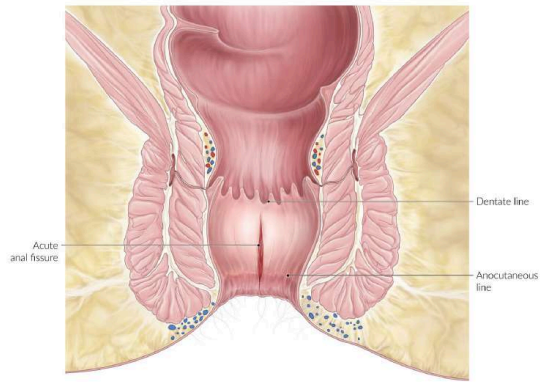
Question # 36

A 40-year-old woman comes to the physician because of a 2-week history of anal pain that occurs during defecation and lasts for several hours. She reports that she often strains during defecation and sees bright red blood on toilet paper after wiping. She typically has 3 bowel movements per week. Physical examination shows a longitudinal, perianal tear. This patient's symptoms are most likely caused by tissue injury in which of the following locations?

	Answer	Image
A	Posterior midline of the anal canal, distal to the pectinate line	
B	Anterior midline of the anal canal, proximal to the pectinate line	
C	Anterior midline of the anal canal, distal to the pectinate line	
D	Posterior midline of the anal canal, proximal to the pectinate line	
E	Lateral aspect of the anal canal, distal to the pectinate line	

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Hint

The region of tissue injury in this patient receives innervation from the inferior rectal branch of the pudendal nerve.

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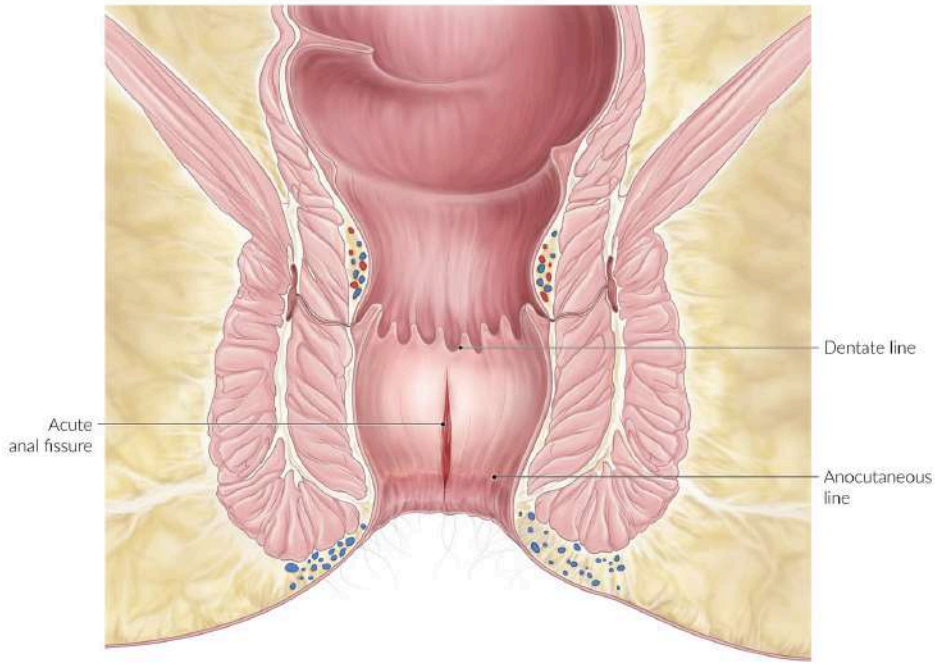
Correct Answer

A - Posterior midline of the anal canal, distal to the pectinate line

Image



Explanation But

Other pathologies that could occur arise below the pectinate line include external hemorrhoids (typically at the left lateral, right anterior, and right posterior positions) and squamous cell carcinoma. Pathologies that arise from below the pectinate line receive somatic innervation from the inferior rectal nerve and are therefore often painful.

Explanation Why

Approximately 90% of anal fissures occur at the posterior midline of the anal canal, distal to the pectinate line (dentate line). The etiology is usually benign and primary in nature, with the most common cause being local trauma (e.g., passing of hard stools due to constipation), persistent diarrhea, vaginal delivery, or anal sex. This predilection for the posterior midline is likely due to poor perfusion to this area. Often, a skin tag (sentinel pile) formed by hypertrophied papillae would be visible in the perianal region at the site of the fissure.

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B - Anterior midline of the anal canal, proximal to the pectinate line

Explanation Why

The region of the anal canal proximal to the pectinate line is a common location for internal hemorrhoids and adenocarcinoma of the anal canal, whereas anal fissures occur distal to the pectinate line. Internal hemorrhoids are characterized by the passage of bright red blood per rectum with a bowel movement. However, defecation is usually painless.

C - Anterior midline of the anal canal, distal to the pectinate line

Explanation Why

Only 10% of anal fissures occur at the anterior midline of the anal canal, distal to the pectinate line. Anal fissures at this location are usually secondary to anal surgery, IBD (e.g., Crohn disease), infections (e.g., syphilis) or malignancy (leukemia). There is no evidence of an underlying condition in this patient that would make an anal fissure at an atypical location likely.

D - Posterior midline of the anal canal, proximal to the pectinate line

Explanation Why

The region of the anal canal proximal to the pectinate line is a common location for internal hemorrhoids, whereas anal fissures occur distal to the pectinate line. Internal hemorrhoids are characterized by passage of bright red blood per rectum with a bowel movement. However, defecation is usually painless.

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E - Lateral aspect of the anal canal, distal to the pectinate line

Explanation Why

External hemorrhoids arise below the pectinate, often occur at the left lateral aspect of the anal canal (3 o' clock position), are typically painful, and can cause per rectal bleeding. However, external hemorrhoids would be visible as perianal swellings on physical examination. Less than 1% of anal fissures occur at the lateral aspect of the anal canal. Anal fissures that occur at this location are usually secondary to anal surgery, IBD (e.g., Crohn disease), infections (e.g., syphilis) or malignancy (leukemia). There is no evidence of an underlying condition in this patient that would that would make an anal fissure at an atypical location likely.

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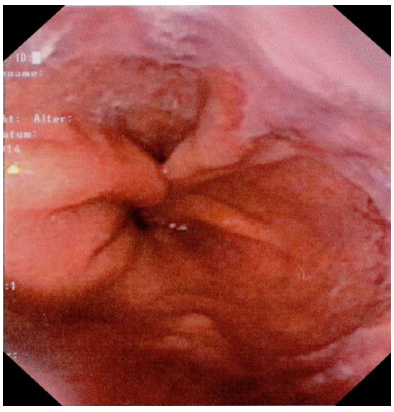
Question # 37

A 45-year-old woman comes to the physician because of a 5-month history of recurrent retrosternal chest pain that often wakes her up at night. Physical examination shows no abnormalities. Upper endoscopy shows hyperemia in the distal third of the esophagus. A biopsy specimen from this area shows nonkeratinized stratified squamous epithelium with hyperplasia of the basal cell layer and neutrophilic inflammatory infiltrates. Which of the following is the most likely underlying cause of this patient's findings?

	Answer	Image
A	Increased lower esophageal sphincter tone	
B	Increased collagen production and fibrosis	
C	Chronic gastrointestinal iron loss	
D	Dysfunction of the gastroesophageal junction	
E	Spread of neoplastic cells	

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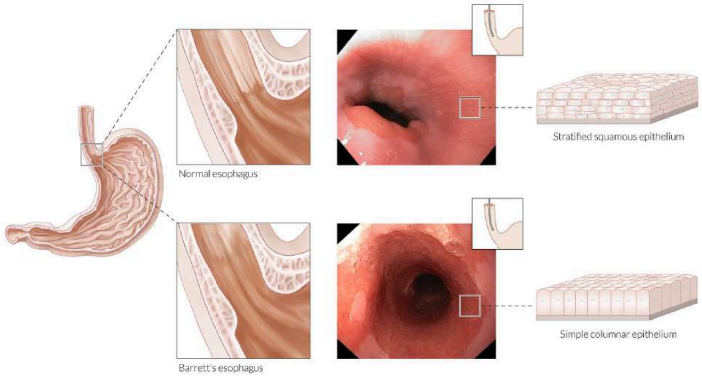
	Answer	Image
F	Metaplastic transformation of the esophageal epithelium	

Hint

This patient's clinical features and endoscopy and biopsy findings suggest gastroesophageal reflux disease (GERD).

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Correct Answer

A - Increased lower esophageal sphincter tone

Explanation Why

Increased lower esophageal sphincter (LES) tone, as seen in achalasia, typically presents with dysphagia to both solids and liquids, although symptoms of esophageal reflux may also be present. Other features include retrosternal pain and weight loss. This patient does not present with symptoms of dysphagia, making achalasia an unlikely diagnosis.

B - Increased collagen production and fibrosis

Explanation Why

Increased collagen production and fibrosis can be seen in CREST syndrome, which may be associated with esophageal dysmotility and reflux esophagitis. However, CREST syndrome is an uncommon condition and unlikely to manifest solely with reflux esophagitis; other features of CREST syndrome, such as calcinosis cutis, Raynaud phenomenon, sclerodactyly, and telangiectasia, are not seen in this patient.

C - Chronic gastrointestinal iron loss

Explanation Why

Chronic gastrointestinal iron loss is seen in Plummer-Vinson syndrome. The syndrome manifests with a triad of dysphagia, upper esophageal webs, and iron deficiency anemia, none of which are seen in this patient.

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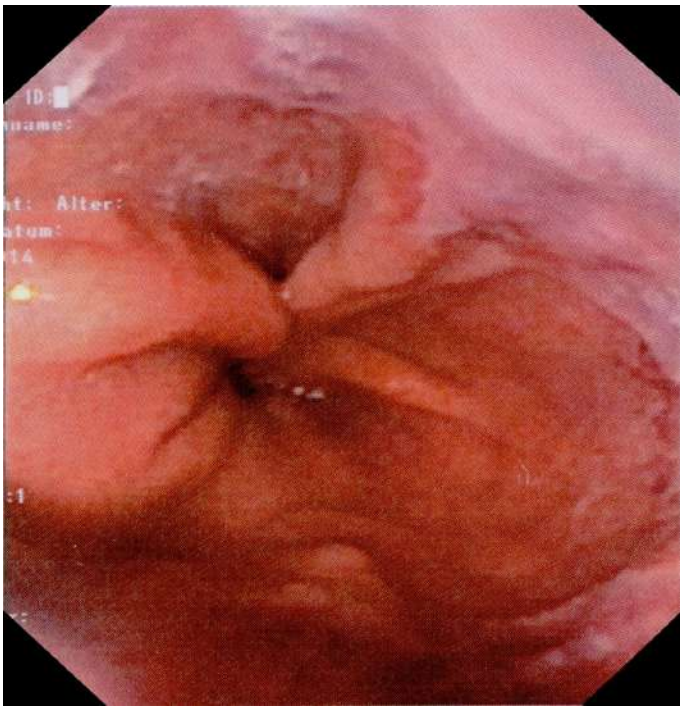
D - Dysfunction of the gastroesophageal junction

Image



Explanation Why

This patient's history of intermittent retrosternal chest pain that worsens at night, in conjunction with the hyperemia of the distal third of the esophagus and the biopsy showing nonkeratinized stratified squamous epithelium with hyperplasia of the basal cell layer and neutrophilic inflammatory infiltrates, is consistent with GERD. Dysfunction of the gastroesophageal junction allows stomach contents to flow back into the esophagus, causing inflammation of the esophageal epithelium. Risk factors for GERD include dysfunction of the lower esophageal sphincter due to anatomical disruption (e.g., due to hiatal hernia), decreased tension (e.g., due to smoking), and transient relaxation (e.g., due to obesity).

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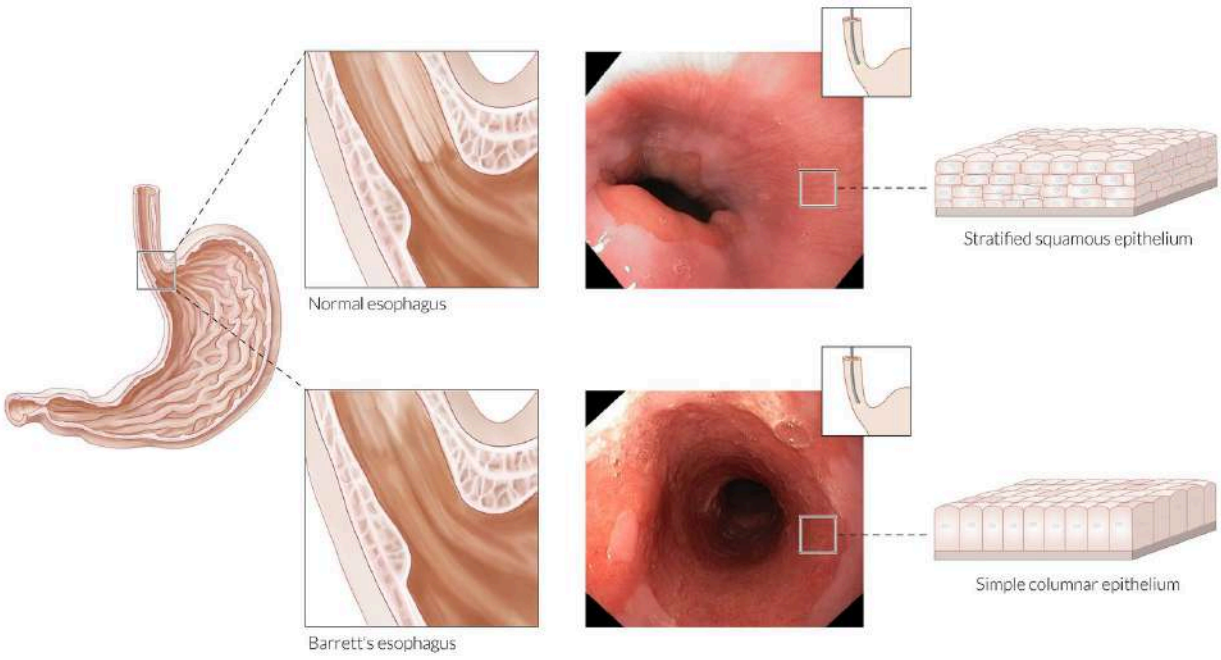
E - Spread of neoplastic cells

Explanation Why

Spread of neoplastic cells, as seen in esophageal cancer, would be unlikely to cause this patient's findings. Nonkeratinizing squamous epithelium is a nonmalignant pathologic finding and does not occur as a result of the malignant spread of cells.

F - Metaplastic transformation of the esophageal epithelium

Image



Explanation Why

Metaplastic transformation of the esophageal epithelium is the hallmark of Barrett esophagus, in which normal squamous epithelium is replaced by metaplastic columnar epithelium. Long-standing reflux esophagitis can lead to Barrett esophagus, which is a precursor lesion for esophageal cancer. This patient's biopsy findings show nonkeratinized stratified squamous epithelium with hyperplasia

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of the basal cell layer rather than metaplasia, making Barrett esophagus an unlikely diagnosis.

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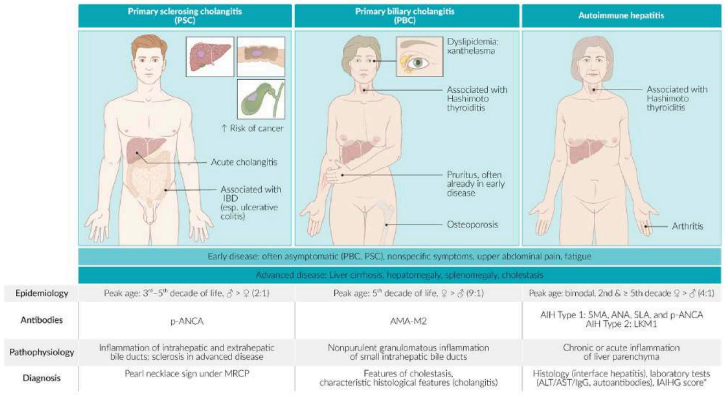
Question # 38

A 46-year-old man comes to the physician with a 1-week history of yellowish discoloration of his eyes, generalized fatigue, and pruritus. He was diagnosed with ulcerative colitis 7 years ago. At the time of diagnosis, a pANCA test was also positive. Physical examination shows scleral icterus and multiple scratch marks on the trunk and extremities. Abdominal examination is unremarkable. Serum studies show a total bilirubin concentration of 3.2 mg/dL, direct bilirubin concentration of 2.5 mg/dL, and alkaline phosphatase level of 450 U/L. Magnetic resonance cholangiopancreatography shows focal areas of intrahepatic bile duct strictures alternating with areas of dilation. Histologic examination of a liver biopsy specimen is most likely to show which of the following findings?

	Answer	Image
A	Periductal concentric scarring and fibrosis	
B	Periportal lymphocytic infiltration and piecemeal necrosis	
C	Diffuse fibrosis with PAS-staining globules	
D	Irregular ductal glands lined by atypical and pleomorphic cells	

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	Answer	Image
E	Ductopenia and fibrotic degeneration of periportal hepatocytes	

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Hint

This patient with ulcerative colitis has pruritus, icterus, elevated parameters of cholestasis, and alternating strictures and dilation on MRCP (beading pattern). A well-known cause of cholestatic jaundice in patients with autoimmune diseases, particularly ulcerative colitis, is primary sclerosing cholangitis.

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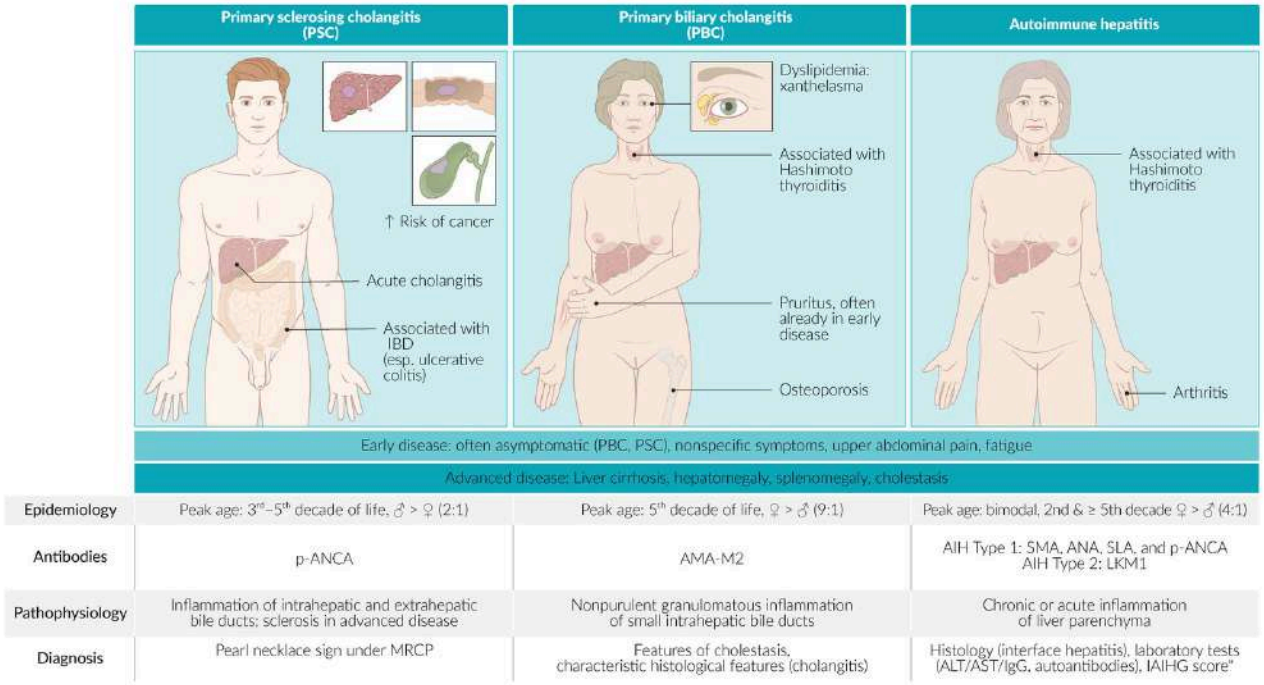
Correct Answer

A - Periductal concentric scarring and fibrosis

Image



Explanation Why

This patient's symptoms, laboratory, and imaging studies are consistent with the diagnosis of primary sclerosing cholangitis (PSC). In 90% of cases, this condition is associated with inflammatory bowel disease (IBD), usually ulcerative colitis, which this patient has. Histopathological examination of bile ducts would typically show periductal concentric scarring and fibrosis that are consistent with the characteristic onion-skin appearance. PSC, which is classically seen in middle-aged men, increases the risk of development of cancer of the gallbladder and cholangiocarcinoma (10–15% of cases). Perinuclear anti-neutrophil cytoplasmic antibodies (pANCA) are not specific to PSC but can be present in up to 80% of cases.

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B - Periportal lymphocytic infiltration and piecemeal necrosis

Explanation Why

Periportal lymphocytic infiltration and piecemeal necrosis can be seen in various conditions that cause fulminant liver failure, e.g., autoimmune hepatitis. Although fulminant liver failure can cause hyperbilirubinemia and jaundice, as seen here, coagulopathy, hepatic encephalopathy, and elevated serum ALT and AST levels (usually in the 1000 U/L range) would also be expected. Moreover, this would not explain alternating intrahepatic bile duct strictures, which is a characteristic finding of PSC.

C - Diffuse fibrosis with PAS-staining globules

Explanation Why

Alpha-1 antitrypsin deficiency can cause an accumulation of misfolded PAS-positive globules and fibrosis within the hepatocytes. Elevated parameters of cholestasis, hyperbilirubinemia, and elevated alkaline phosphatase are not common features of α1-antitrypsin deficiency-mediated hepatic cirrhosis.

D - Irregular ductal glands lined by atypical and pleomorphic cells

Explanation But

While PSC can increase the risk of cholangiocarcinoma, the finding of alternating intrahepatic bile duct strictures on MRCP is uncommon.

Explanation Why

Irregular ductal glands lined by atypical and pleomorphic cells on histologic examination is consistent with intrahepatic cholangiocarcinoma, a rare type of cancer of the bile ducts. Although this condition can also cause obstructive jaundice and elevated ALP, as seen here, patients with cholangiocarcinoma are more likely asymptomatic. Other symptoms that would suggest this

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diagnosis, such as hepatomegaly, a painless palpable gallbladder (Courvoisier's sign), and nonspecific B symptoms (e.g., weight loss, nausea), are also lacking.

E - Ductopenia and fibrotic degeneration of periportal hepatocytes

Explanation Why

Fibrotic degeneration of periportal hepatocytes and ductopenia are characteristic late histopathologic findings of primary biliary cholangitis (PBC). In the early stages, lymphocytic infiltration of portal areas and periductal granulomas would be expected. PBC may present with pruritus, hyperbilirubinemia, and elevated alkaline phosphatase, just like this patient. However, PBC does not cause alternating intrahepatic bile duct strictures. Moreover, PBC would be associated with the development of antimitochondrial autoantibodies, not pANCA.

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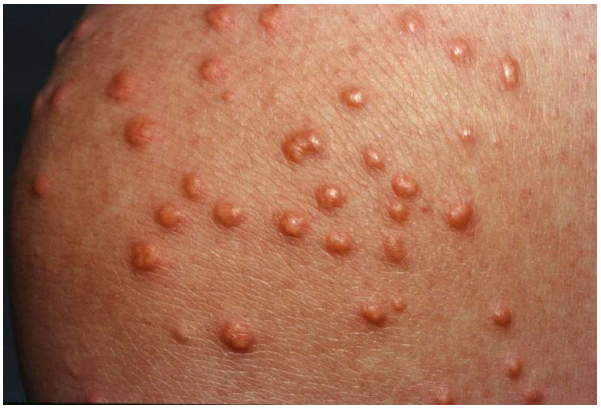
Question # 39

A 36-year-old man is brought to the emergency department 3 hours after the onset of progressively worsening upper abdominal pain and 4 episodes of vomiting. His father had a myocardial infarction at the age of 40 years. Physical examination shows tenderness and guarding in the epigastrium. Bowel sounds are decreased. His serum amylase is 400 U/L. Symptomatic treatment and therapy with fenofibrate are initiated. Further evaluation of this patient is most likely to show which of the following findings?

	Answer	Image
A	Salt and pepper skull	
B	Bilateral parotid gland enlargement	
C	Decreased serum ACTH levels	
D	Eruptive xanthomas	
E	Separate dorsal and ventral pancreatic ducts	
F	Elevated serum IgG4 levels	

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Hint

This findings of worsening epigastric pain with tenderness and guarding in the setting of elevated amylase levels are highly indicative of pancreatitis. The fact that this patient was prescribed fenofibrate indicates that severe hypertriglyceridemia was diagnosed as the underlying cause of his pancreatitis.

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Correct Answer

A - Salt and pepper skull

Explanation Why

Salt and pepper skull refers to a characteristic pattern of tiny, radiolucent areas within the calvaria, which classically occurs in the setting of hyperparathyroidism. High calcium levels can lead to premature activation of pancreatic enzymes and therefore pancreatitis. However, as this patient has no mentioned history of hypercalcemic symptoms (e.g., fatigue, polyuria, constipation, neuropsychiatric disturbances), salt and pepper skull would be unlikely.

B - Bilateral parotid gland enlargement

Explanation Why

Bilateral parotid gland enlargement is the hallmark of mumps, of which acute pancreatitis is a rare complication. This patient, however, has not had any classic prodromal findings of mumps, e.g., low-grade fever or malaise. Moreover, fenofibrate would be of no use in mumps-associated pancreatitis, as this complication typically resolves with symptomatic therapy alone.

C - Decreased serum ACTH levels

Explanation Why

Decreased serum ACTH levels can be found in patients with prolonged steroid use, which can lead to exogenous hypercortisolism. Although steroid use is associated with the development of pancreatitis, this patient does not exhibit additional features linked to chronic steroid intake (e.g., truncal obesity, striae, moon facies). In addition, decreased serum ACTH levels due to steroid use would be treated by slowly tapering steroids, not by prescribing fenofibrate.

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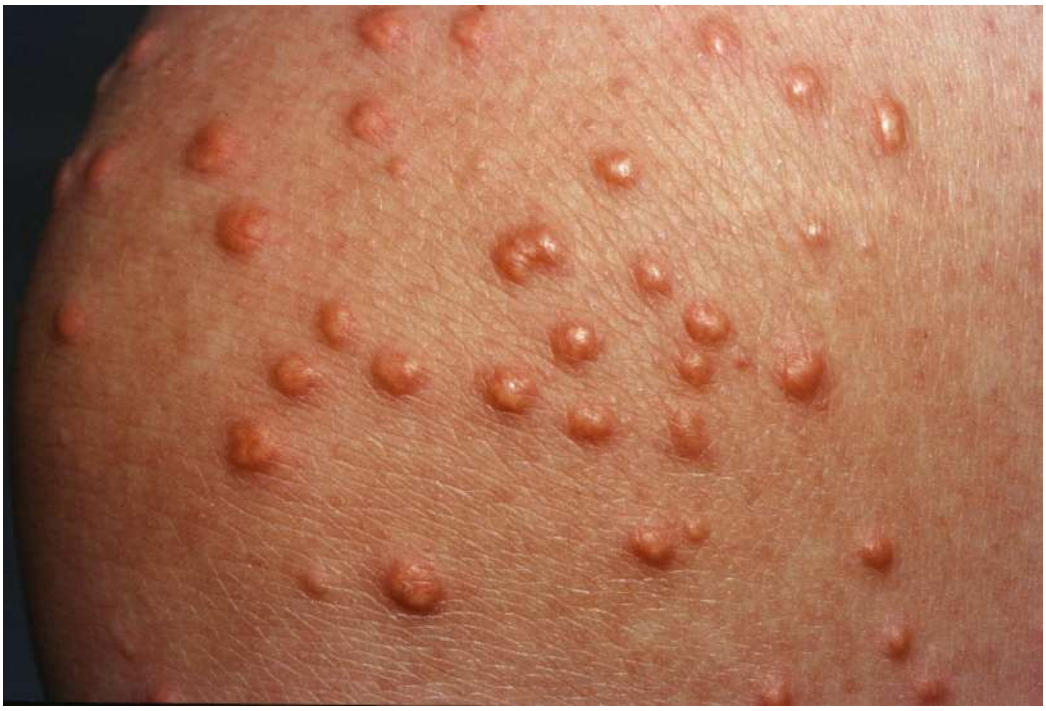
D - Eruptive xanthomas

Image



Explanation Why

Eruptive xanthomas occur due to lipid deposition in the dermis and are associated with hypertriglyceridemia. This patient's family history of premature MI further supports hypertriglyceridemia as the underlying cause of his pancreatitis. Treatment generally focuses on dietary restrictions and initiation of fibric acid derivatives, such as fenofibrate.

E - Separate dorsal and ventral pancreatic ducts

Explanation Why

Separate dorsal and ventral pancreatic ducts are characteristic of pancreas divisum, a mostly asymptomatic congenital malformation, in which the dorsal and ventral pancreatic buds fail to fuse. Pancreas divisum can occasionally cause pancreatitis but the fact that this patient was treated with

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fenofibrate suggests a different cause for the patient's symptoms.

F - Elevated serum IgG4 levels

Explanation Why

Elevated serum IgG4 levels occur in the setting of autoimmune pancreatitis, which is associated with other autoimmune disorders such as retroperitoneal fibrosis, Riedel thyroiditis, and non-infectious aortitis. This patient does not have a personal or family history of any of these conditions. Also, autoimmune pancreatitis would be treated with steroids, not fenofibrate.

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Question # 40

A 1-week-old male newborn is brought to the physician for a follow-up examination after the results of newborn screening showed an increased serum concentration of phenylalanine. Genetic analysis confirms a diagnosis of phenylketonuria. The physician counsels the patient's family on the recommended dietary restrictions, including avoidance of artificial sweeteners that contain aspartame. Aspartame is a molecule composed of aspartate and phenylalanine and its digestion can lead to hyperphenylalaninemia in patients with phenylketonuria. Which of the following enzymes is primarily responsible for the breakdown of aspartame?

	Answer	Image
A	Pepsin	
B	Dipeptidase	
C	Chymotrypsin	
D	Trypsin	
E	Carboxypeptidase A	

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Hint

Aspartame is primarily cleaved by a brush border enzyme on the villi of the intestinal mucosa.

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Correct Answer

A - Pepsin

Explanation Why

Pepsin, a gastric endopeptidase, cleaves peptide bonds within protein molecules and targets specific peptide bonds between hydrophobic and aromatic amino acids (e.g., phenylalanine-tryptophan). Pepsin does not target peptide bonds involving hydrophilic amino acids such as aspartate. Moreover, aspartame has two terminal amino acids and can only be broken down by an enzyme with exopeptidase activity.

B - Dipeptidase

Explanation Why

Dipeptidase is a brush border enzyme in the human duodenum, jejunum, and ileum. It is a type of exopeptidase that hydrolyzes dipeptides such as aspartame.

C - Chymotrypsin

Explanation Why

Chymotrypsin, a pancreatic endopeptidase, cleaves peptide bonds within protein molecules and targets specific peptide bonds between hydrophobic and aromatic amino acids (e.g., phenylalanine-tryptophan). Chymotrypsin does not target peptide bonds involving hydrophilic amino acids such as aspartate. Moreover, aspartame has two terminal amino acids and can only be broken down by an enzyme with exopeptidase activity.

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D - Trypsin

Explanation Why

Trypsin, a pancreatic endopeptidase, cleaves peptide bonds within protein molecules and targets specific peptide bonds that contain the positively charged amino acids arginine or lysine. Trypsin does not target peptide bonds involving the hydrophobic amino acid phenylalanine or the negatively charged aspartate. Moreover, aspartame has two terminal amino acids and can only be broken down by an enzyme with exopeptidase activity.

E - Carboxypeptidase A

Explanation Why

Carboxypeptidase A, a pancreatic exopeptidase, cleaves peptide bonds at the carboxyterminal end and preferentially targets peptide bonds with aromatic amino acids such as phenylalanine. Aspartame, a dipeptide, has a carboxyterminal phenylalanine residue. However, in dipeptides the rate of peptide bond hydrolysis by carboxypeptidase A is very slow; a different type of exopeptidase is primarily responsible for their breakdown.

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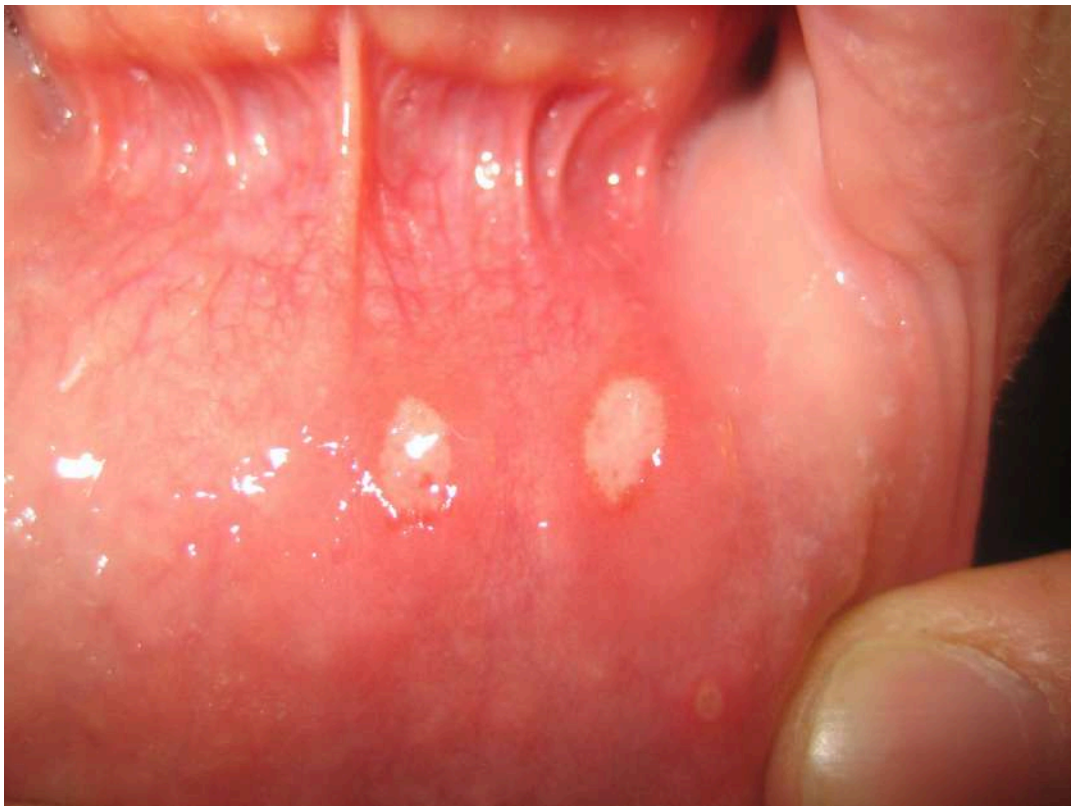
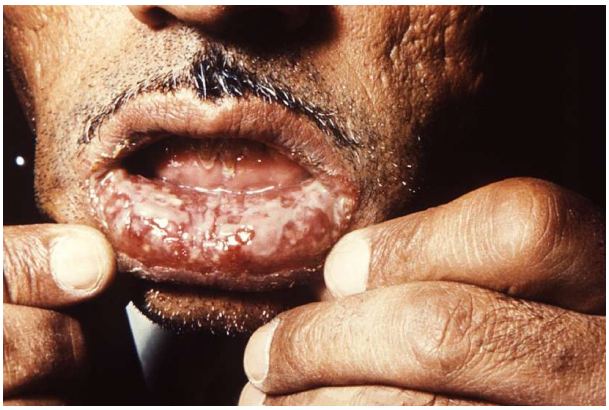
Question # 1

A 16-year-old boy is brought to the physician by his mother because of a 4-day history of painful lesions in the mouth. During the past year, he has twice had similar lesions that resolved without treatment after approximately 10 days. He has never had any genital or anal lesions. His mother reports that he has been very stressed over the past month because he is approaching his senior year in high school. He is otherwise healthy and takes no medications. He appears thin. His temperature is 37.6°C (99.7°F). A photograph of the oral cavity is shown. The remainder of the examination shows no abnormalities. Which of the following is the most likely diagnosis?



	Answer	Image
A	Pemphigus vulgaris	

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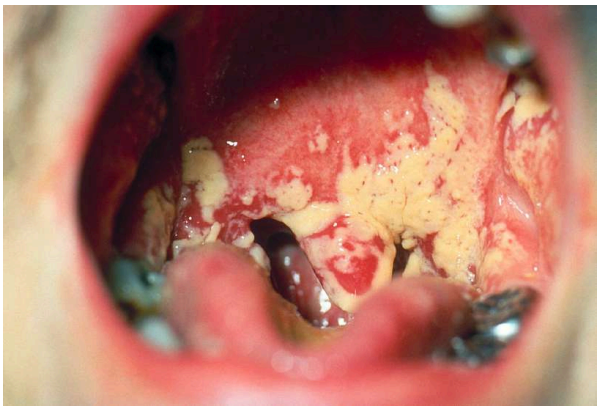
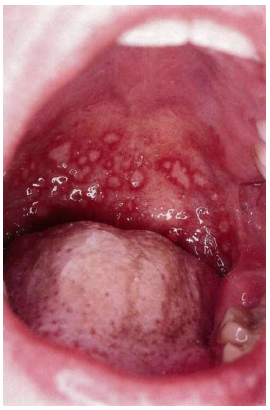
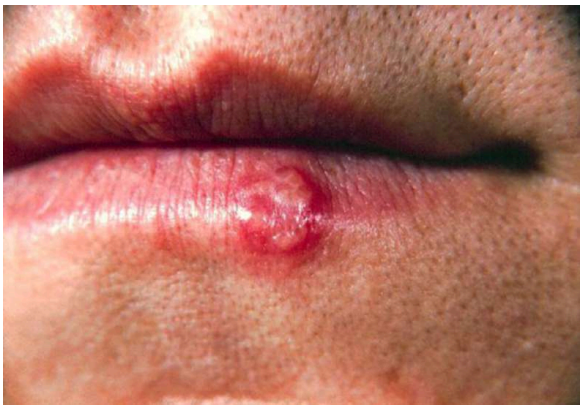
	Answer	Image
B	Oral thrush	
C	Herpangina	
D	Labial herpes	
E	Aphthous stomatitis	

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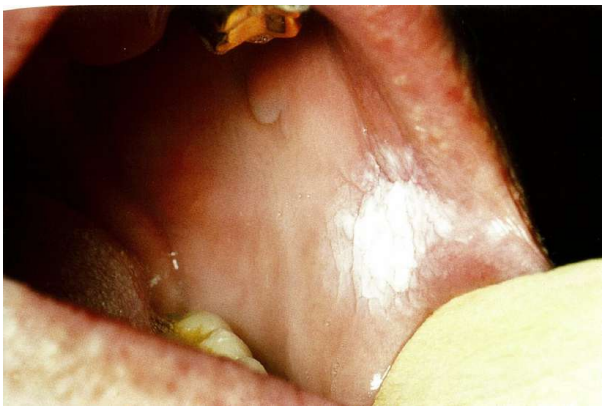
	Answer	Image
F	Oral leukoplakia	

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Hint

The image shows two ovoid erosions with regular margins and surrounding erythema on the labial mucosa.

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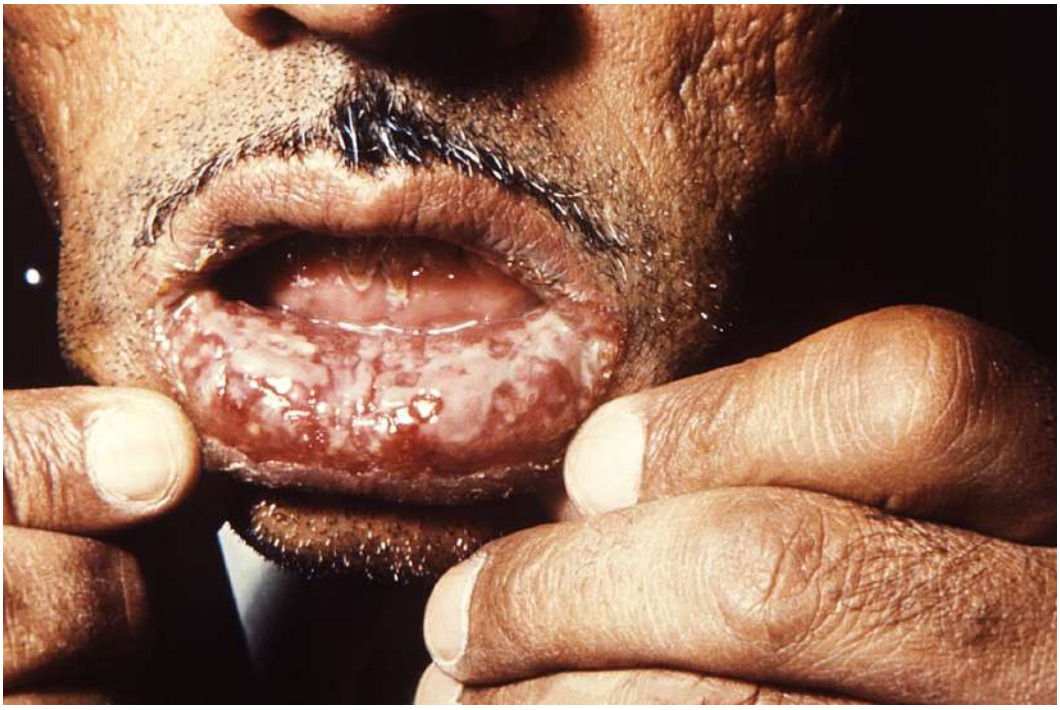
Correct Answer

A - Pemphigus vulgaris

Image



Explanation Why

A common initial manifestation of pemphigus vulgaris is painful oral blisters that eventually ulcerate. Most patients also develop blisters on other body parts, but recurrent episodes of pemphigus vulgaris can occur without any associated cutaneous lesions (mucosal pemphigus vulgaris). However, the oral ulcers of pemphigus vulgaris typically have irregular margins, unlike the well-defined ovoid lesions seen here. Moreover, pemphigus vulgaris most commonly develops in older patients (40–60 years of age), and the lesions typically do not resolve without treatment.

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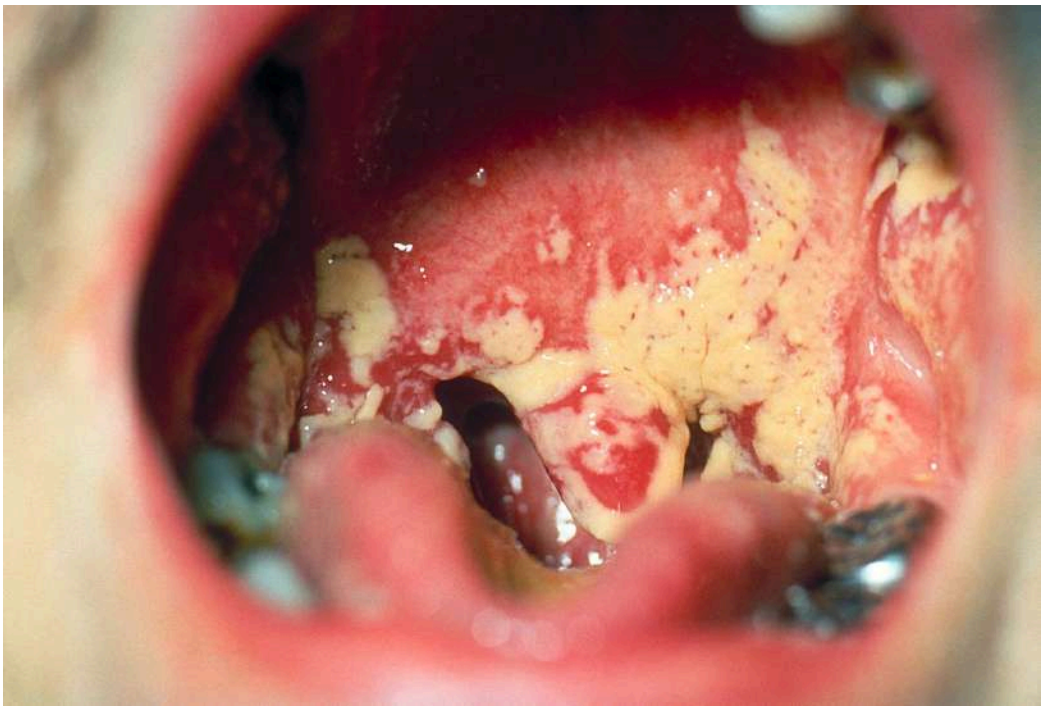
B - Oral thrush

Image



Explanation Why

Oral thrush (oral candidiasis) typically manifests as painless, cream-white lesions of the tongue, buccal mucosa, or palate and occurs in individuals with risk factors such as immunosuppression (e.g., HIV infection), antibiotic therapy, corticosteroid use, xerostomia, and diabetes mellitus. Painful erosions of the labial mucosa in an otherwise healthy adolescent suggest a different diagnosis.

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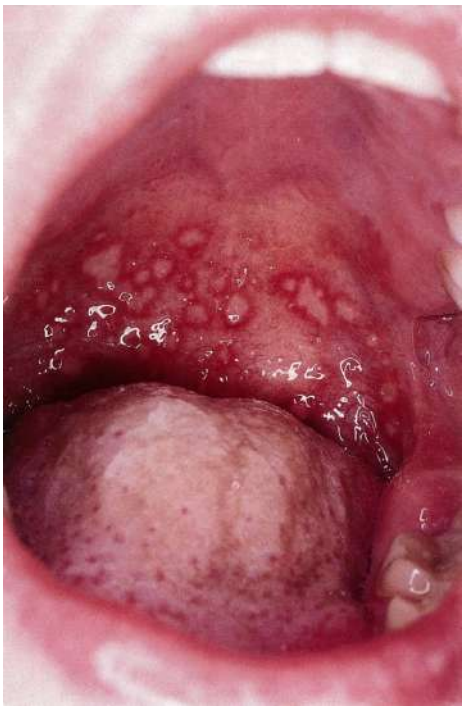
C - Herpangina

Image



Explanation Why

Herpangina typically affects children and adolescents and can manifest as painful oral erosions surrounded by an erythematous halo, which is seen here. However, the lesions typically occur on the palate and posterior pharyngeal wall, not the labial mucosa. Moreover, patients with herpangina are typically febrile and present with throat pain. Following an episode of herpangina, individuals become immune to the infecting group A coxsackievirus strain but can develop a recurrent attack of herpangina as a result of infection by a different virus strain.

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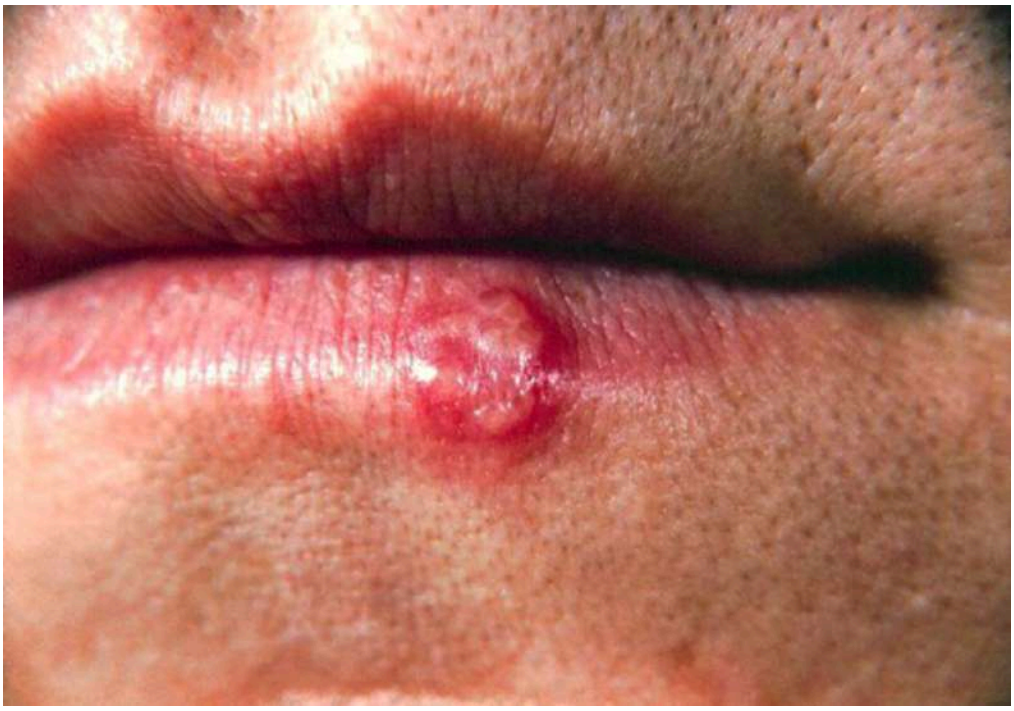
D - Labial herpes

Image



Explanation Why

Herpes of the lips or oral mucosa manifests with painful blisters that eventually ulcerate. Following the primary infection, herpes stomatitis can recur during periods of stress, which is seen here. However, the lesions of recurrent herpes stomatitis typically occur on keratinized parts of the mouth and oral cavity, such as attached gingiva, the hard palate, and the vermillion border of the lip. The location of this patient's lesions on nonkeratinized areas such as the labial mucosa suggests a different diagnosis.

E - Aphthous stomatitis

Explanation But

Systemic disorders associated with recurrent oral ulcerations include Behçet syndrome, systemic

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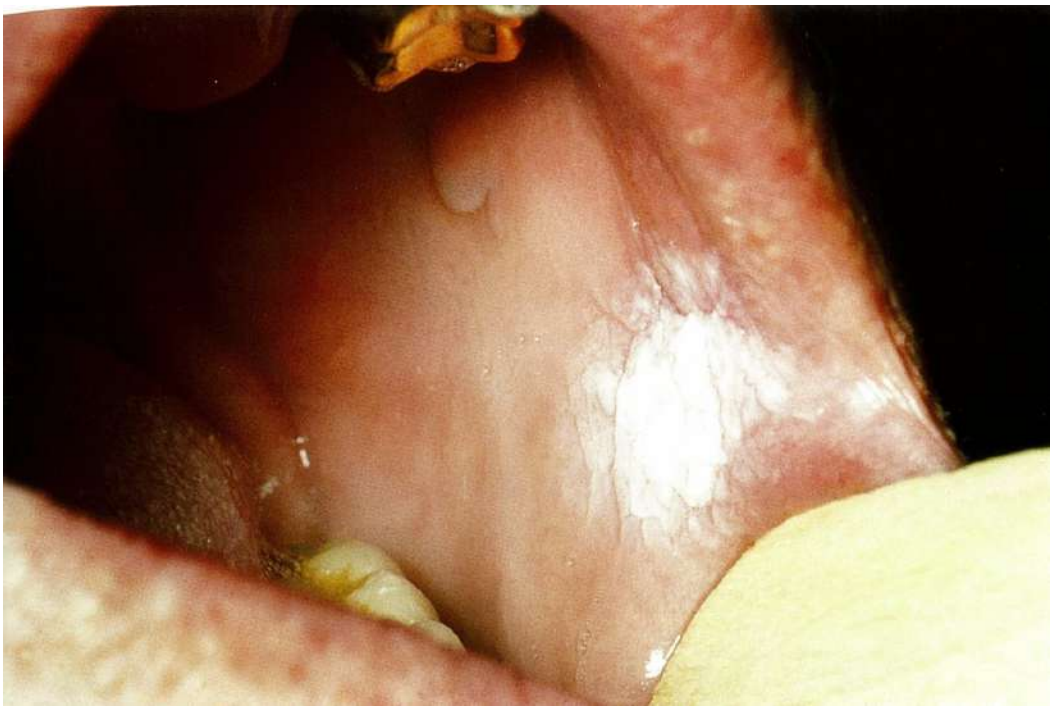
lupus erythematosus, HIV infection, and Crohn disease. While these are important differential diagnoses of recurrent aphthous stomatitis, this patient lacks signs and symptoms of systemic disease.

Explanation Why

Aphthous stomatitis is a common condition that manifests as painful, oral mucosal ulcers with regular margins, a yellow fibrinous base, and a surrounding erythematous halo. The lesions occur in parts of the oral cavity with nonkeratinized mucosa, such as the buccal and labial mucosae, the floor of the mouth, and the ventral surface of the tongue. The lesions typically disappear without treatment within 10–14 days but can recur during periods of acute stress.

F - Oral leukoplakia

Image



Explanation Why

Oral leukoplakia manifests as a white adherent plaque on the oral mucosa. It is a slowly growing, painless premalignant lesion and is usually seen in middle-aged or elderly patients with a history of tobacco use disorder.

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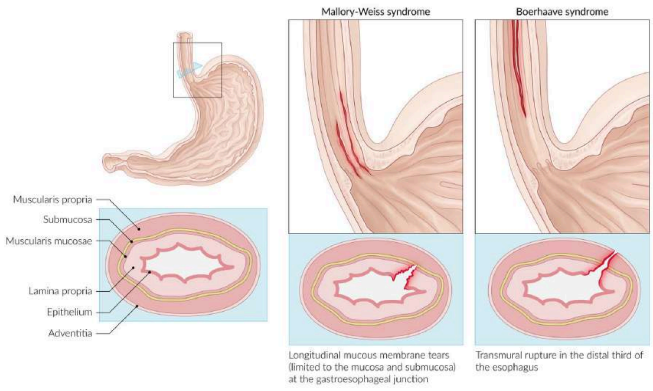
Question # 2

A 22-year-old woman comes to the emergency department because of chest and epigastric pain that started just after vomiting 30 minutes ago. She does not take any medications and does not drink alcohol or smoke cigarettes. While in the emergency department, the patient experiences two episodes of forceful, bloody emesis. Her temperature is 99.1°F (37.3°C), pulse is 110/minute, and blood pressure is 105/60 mm Hg. Physical examination shows dental enamel erosion and calluses on the dorsal aspect of her right hand. There is tenderness to palpation in the epigastrium. An x-ray of the chest is normal. Further evaluation of this patient is most likely to show which of the following findings?

	Answer	Image
A	Dilated veins in the esophageal submucosa	
B	Rupture of the distal esophagus	
C	Clean-based gastric ulcer	
D	Mucosal lacerations at the gastroesophageal junction	
E	Friable mass in the distal esophagus	

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Hint

This patient has findings suggestive of bulimia nervosa (poor dentition, Russell sign), which is a common cause of this patient's presenting condition.

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Correct Answer

A - Dilated veins in the esophageal submucosa

Explanation Why

Dilated veins in the esophageal submucosa result from esophageal varices secondary to cirrhosis or Dieulafoy's lesion. Both conditions can also cause hemorrhage, hematemesis, retrosternal or epigastric pain, and shock, as seen in this patient. However, neither condition is associated with bulimia nervosa, and given a lack of signs of cirrhosis (e.g., jaundice, ascites) and the rarity of Dieulafoy's lesions, another diagnosis is more likely.

B - Rupture of the distal esophagus

Explanation Why

Transmural rupture of the distal esophagus, or Boerhaave syndrome, can present with hematemesis, severe retrosternal or epigastric pain, and can lead to shock, as in this patient. However, patients classically have crepitus of the chest due to subcutaneous emphysema and a pneumomediastinum on CXR.

C - Clean-based gastric ulcer

Explanation Why

A clean-based gastric ulcer, suggestive of peptic ulcer disease (PUD), can also present with hematemesis and epigastric pain. However, given the acute nature of this patient's pain and forceful vomiting, as well as a history negative for PUD risk factors (e.g., NSAID or corticosteroid use, smoking, no previous heartburn), this diagnosis is unlikely.

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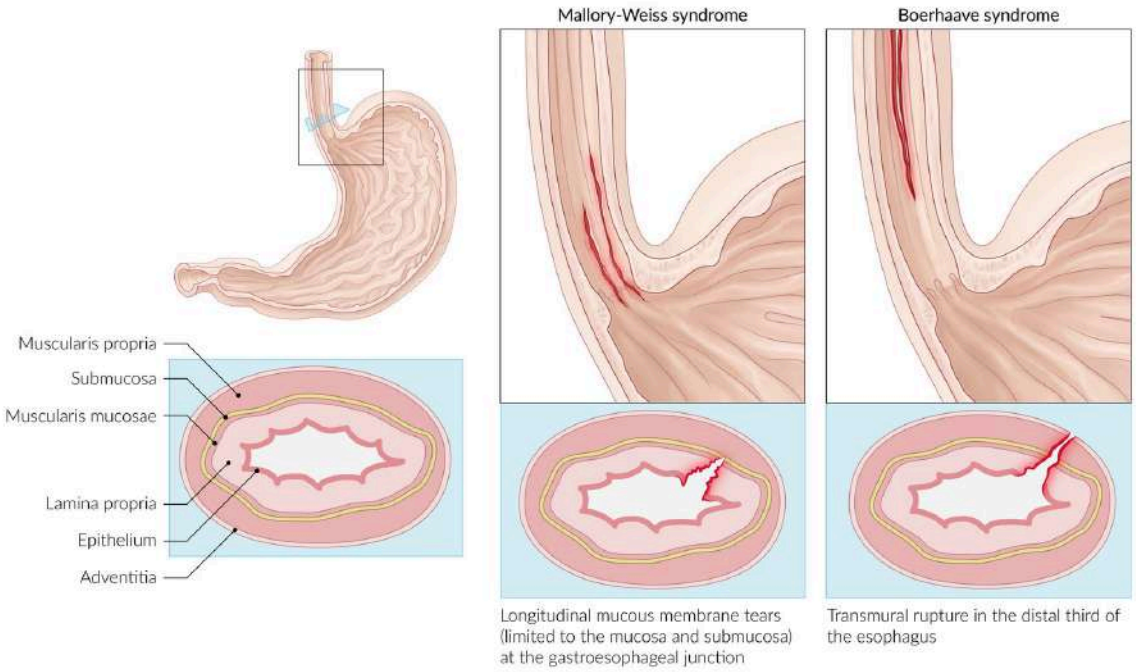
D - Mucosal lacerations at the gastroesophageal junction

Image



Explanation Why

Mucosal lacerations at the gastroesophageal junction are found in Mallory-Weiss syndrome, which is the cause of this patient's epigastric pain, forceful hematemesis, and unstable vitals (indicating hypovolemic shock). Conditions associated with frequent forceful vomiting, such as this patient's presumed bulimia nervosa, predispose to Mallory-Weiss syndrome. Other predisposing conditions include alcohol abuse disorder, hiatal hernia, and GERD.

E - Friable mass in the distal esophagus

Explanation Why

A friable mass in the distal esophagus indicates an adenocarcinoma. Although esophageal carcinomas can present with retrosternal or epigastric pain, this patient's hematemesis is atypical.

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Additionally, previous dysphagia, odynophagia, and/or weight loss would be expected. Lastly, given the patient's lack of risk factors (i.e., older age, male gender, history of GERD, obesity, smoking history), adenocarcinoma is unlikely.

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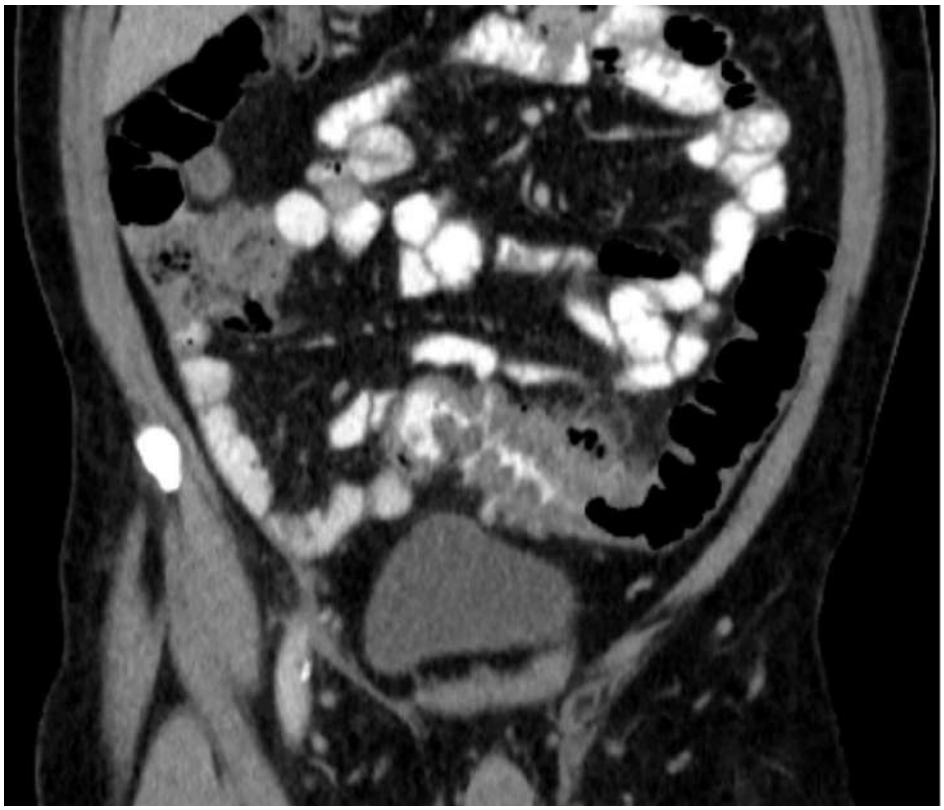
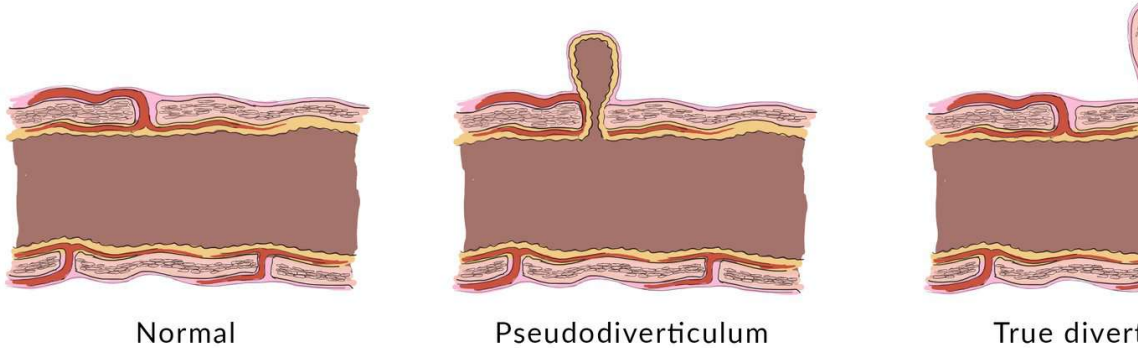
Question # 3

A 65-year-old man comes to the physician because of abdominal pain and bloody, mucoid diarrhea for 3 days. He has been taking over-the-counter supplements for constipation over the past 6 months. He was diagnosed with type 2 diabetes mellitus 15 years ago. He has smoked one pack of cigarettes daily for 35 years. His current medications include metformin. His temperature is 38.4°C (101.1°F), pulse is 92/min, and blood pressure is 134/82 mm Hg. Examination of the abdomen shows no masses. Palpation of the left lower abdomen elicits tenderness. A CT scan of the abdomen is shown. Which of the following is the most likely underlying cause of the patient's condition?



	Answer	Image
A	Focal weakness of the colonic muscularis layer	

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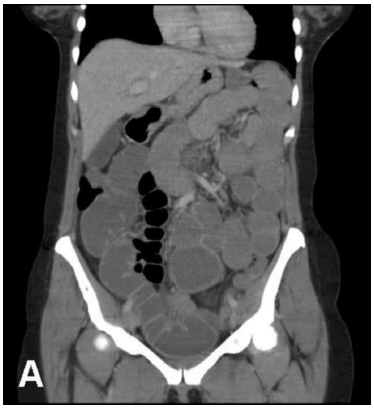
	Answer	Image
B	Infiltrative growth in the descending colon	
C	Transmural inflammation of the terminal ileum	
D	Twisting of the sigmoid colon around its mesentery	
E	Decreased perfusion to mesenteric blood vessel	
F	Mucosal ulcerations of the rectum	

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Hint

The patient's CT shows segmental thickening and enhancement of the colonic wall with air-filled pouches in the surrounding segments.

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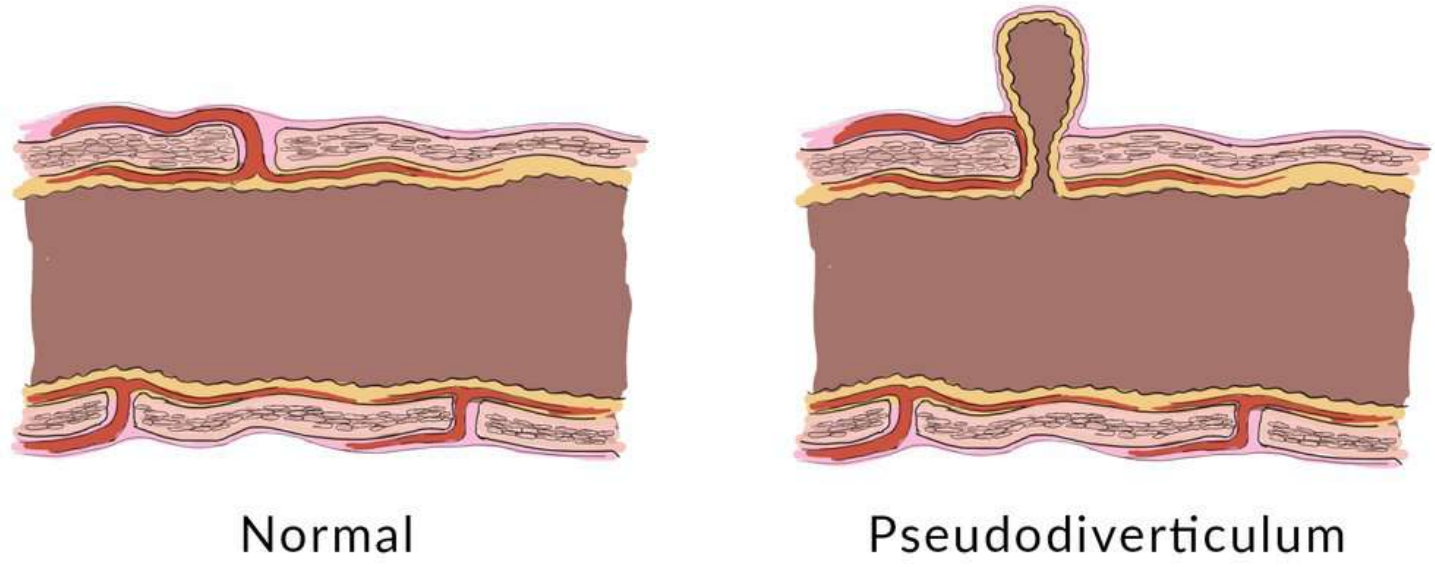
Correct Answer

A - Focal weakness of the colonic muscularis layer

Image



Explanation But

The prevalence of diverticulosis increases with age, which is thought to be because of structural changes in collagen associated with aging. Patients with connective tissue disorders such as Ehlers-Danlos, Marfan syndrome, and autosomal dominant polycystic kidney disease may present with diverticula prematurely because they develop these structural changes earlier in life.

Explanation Why

Focal weakness of the colonic muscularis layer, typically at points where the vasa recta traverse the intestinal wall, allows for the formation of protrusions of mucosal and submucosal layers in response to increased intraluminal pressure (e.g., from chronic constipation). These protrusions (i.e., diverticula) are referred to as "pseudodiverticula" because not all layers of the intestinal wall are affected. Diverticulosis is the asymptomatic presence of these protrusions (identified as air-filled pouches on CT). Diverticulitis is an acute inflammation of diverticula that typically manifests with bowel wall thickening on CT, fever, left-sided lower abdominal pain, and bloody, mucoid diarrhea,

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all of which are seen in this patient. Risk factors for diverticular disease include diet (low in fiber, high in red meat and fat), BMI ≥ 25 kg/m^2, lack of physical activity, and smoking (≥ 40 pack-years).

B - Infiltrative growth in the descending colon

Explanation Why

An infiltrative growth in the descending colon is consistent with left-sided colorectal cancer (CRC). CRC can manifest with changes in bowel habits (e.g., diarrhea), rectal bleeding, and abdominal pain. However, as opposed to this patient's acute presentation, symptoms usually develop over a long period of time. Moreover, nonspecific symptoms (e.g., weight loss, night sweats, fatigue) would be expected at that point. Also, a CT scan typically shows a soft tissue density mass causing narrowing of the bowel lumen; adjacent air-filled pouches are not found in this condition.

C - Transmural inflammation of the terminal ileum

Explanation Why

Transmural inflammation of the terminal ileum is consistent with Crohn disease (CD). CD may manifest with low-grade fever, abdominal pain, and bloody diarrhea, as seen in this patient. However, he lacks other typical features of CD such as signs of malabsorption (e.g., weight loss, anemia) and extraintestinal symptoms (e.g., arthritis, erythema nodosum). A CT scan of a patient with CD may show bowel wall thickening, fat stranding, and strictures or fistulas; air-filled pouches are not typically seen in this condition.

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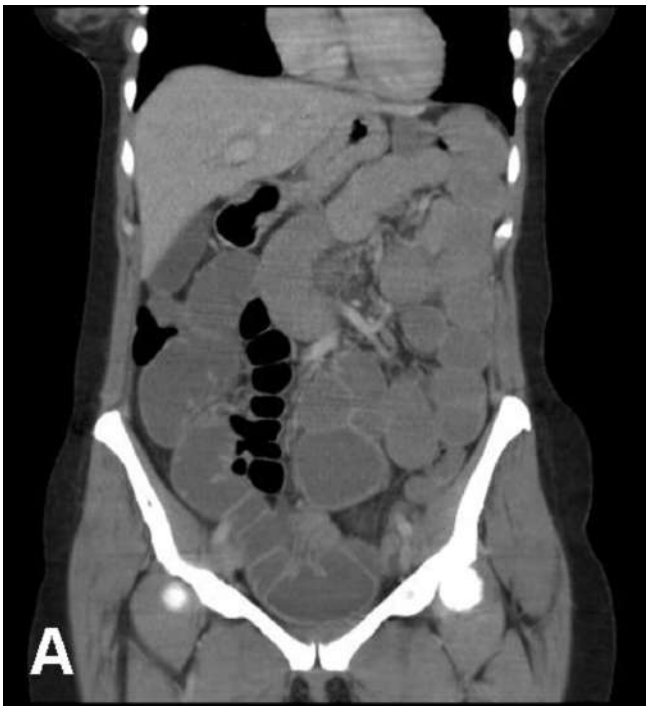
D - Twisting of the sigmoid colon around its mesentery

Image



Explanation Why

Twisting of the sigmoid colon around its mesentery is consistent with sigmoid volvulus, which can lead to bowel obstruction, infarction, and/or perforation. Sigmoid volvulus typically manifests with episodic abdominal pain, asymmetric abdominal distention, and progressive signs of bowel obstruction. In severe cases, rectal bleeding, hematemesis, and peritonitis may also be present. CT scan typically shows gas-filled loops of bowel, twisting of the mesentery and mesenteric vessels (whirl sign), and gradual narrowing or tapering of the sigmoid colon up to the level of obstruction (bird beak sign), none of which are seen here.

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E - Decreased perfusion to mesenteric blood vessel

Explanation Why

Decreased perfusion to the mesenteric blood vessels can lead to acute mesenteric ischemia (AMI) and can be caused by an arterial embolism (most common), arterial thrombus, low cardiac output, and/or venous thrombosis. AMI characteristically manifests with severe acute periumbilical pain out of proportion to physical examination findings and, in later stages, bloody diarrhea and rectal bleeding, which is not consistent with this patient's presentation. CT findings include intestinal pneumatosis, mesenteric stranding, and bowel wall thickening and distension; air-filled pouches are not typically seen in this condition.

F - Mucosal ulcerations of the rectum

Explanation Why

Mucosal (and submucosal) ulcerations of the rectum are consistent with ulcerative colitis (UC). UC commonly manifests with low-grade fever, abdominal pain, and bloody diarrhea, as seen in this patient. Although a CT scan of a patient with UC usually shows bowel wall thickening, which is also seen here, adjacent air-filled pouches are not typical. In addition, patients with UC regularly have extraintestinal symptoms (e.g., ankylosing spondylitis, migratory monoarticular arthritis, erythema nodosum), none of which are present in this patient.

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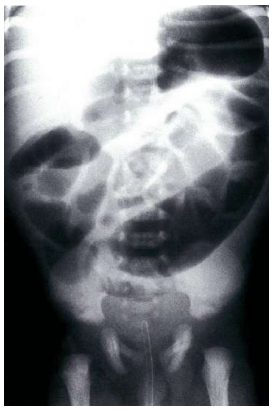
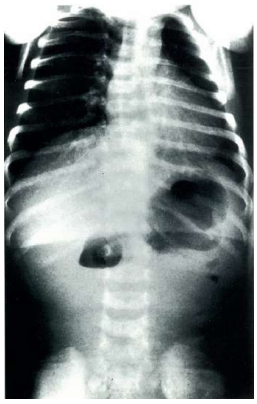
Question # 4

A 5-week-old male infant is brought to the physician by his mother because of a 4-day history of recurrent nonbilious vomiting after feeding. He was born at 36 weeks' gestation via spontaneous vaginal delivery. Vital signs are within normal limits. Physical examination shows a 2-cm epigastric mass. Further diagnostic evaluation of this patient is most likely to show which of the following?

	Answer	Image
A	High serum 17-hydroxyprogesterone concentration	
B	Dilated colon segment on abdominal x-ray	
C	Double bubble sign on abdominal x-ray	

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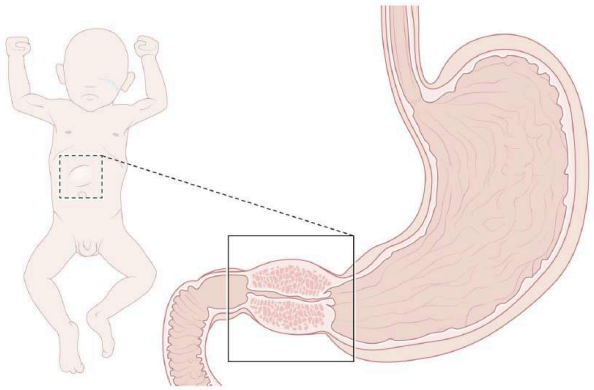
	Answer	Image
D	Elongated and thickened pylorus on abdominal ultrasound	
E	Corkscrew sign on upper gastrointestinal contrast series	

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Hint

This patient has a condition associated with macrolide antibiotic treatment that is predominantly seen in male infants.

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Correct Answer

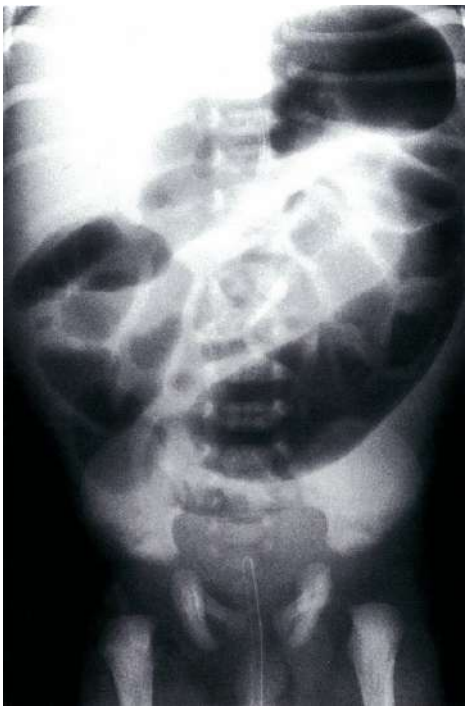
A - High serum 17-hydroxyprogesterone concentration

Explanation Why

A high serum 17-hydroxyprogesterone concentration is seen in patients with congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency. Patients with CAH may develop adrenal crisis and develop recurrent vomiting. However, additional symptoms of CAH include hypotension, hyponatremia, hyperkalemia, metabolic acidosis, and, possibly, ambiguous genitalia, none of which are seen here. This patient's presentation with nonbilious vomiting and an epigastric mass 5 weeks after birth suggests a different diagnosis.

B - Dilated colon segment on abdominal x-ray

Image



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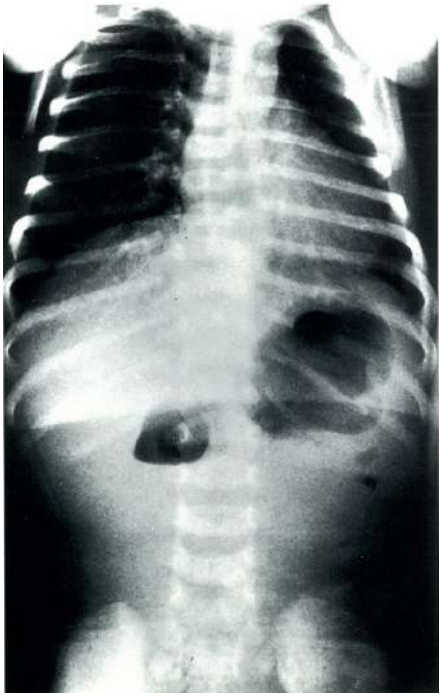
Explanation Why

A dilated colon segment on abdominal x-ray is seen in patients with Hirschsprung disease, which often initially manifests with failure to pass meconium within 48 hours of birth and/or symptoms of gastrointestinal obstruction (e.g., bilious vomiting and abdominal distention). This patient's presentation with nonbilious vomiting and an epigastric mass 5 weeks after birth suggests a different diagnosis.

C - Double bubble sign on abdominal x-ray

Image



Explanation Why

A double bubble sign on abdominal x-ray is seen in patients with duodenal atresia or annular pancreas. Although both conditions can manifest with recurrent vomiting (usually bilious in duodenal atresia and nonbilious in annular pancreas), other signs of duodenal obstruction, including a distended upper abdomen and delayed meconium passage would also be expected. Moreover, both duodenal atresia and annular pancreas classically manifest within the first days of life. This patient's presentation of epigastric mass 5 weeks after birth suggests a different diagnosis.

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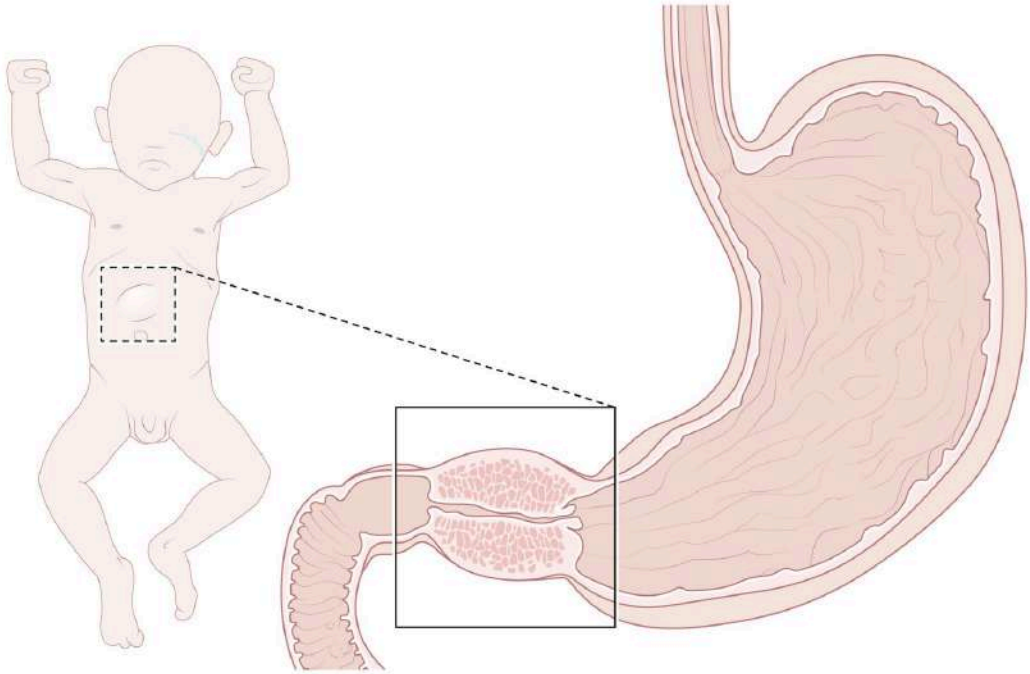
D - Elongated and thickened pylorus on abdominal ultrasound

Image



Explanation But

Treatment of hypertrophic pyloric stenosis condition includes conservative measures and surgical incision (Ramstedt pyloromyotomy).

Explanation Why

Postprandial nonbilious vomiting in conjunction with a palpable epigastric mass (often described as olive-shaped) in a male infant is highly suggestive of hypertrophic pyloric stenosis (IHPS). IHPS predominantly affects firstborn, male infants, and classically manifests within the first 3–6 weeks of life. Other symptoms include visible gastric peristalsis, early satiety, weight loss, and/or hypokalemic, hypochloremic metabolic alkalosis. Abdominal ultrasound typically shows an elongated and thickened pylorus, which confirms the diagnosis.

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E - Corkscrew sign on upper gastrointestinal contrast series

Explanation Why

A corkscrew sign on an upper gastrointestinal contrast series is seen in patients with volvulus due to twisting of the distal duodenum and proximal jejunum around the mesentery. Volvulus usually manifests during the first two months of life with bilious vomiting and feeding intolerance. This patient's presentation with nonbilious vomiting and an epigastric mass 5 weeks after birth suggests a different diagnosis.

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Question # 5

During a study on gastrointestinal hormones, a volunteer is administered the hormone secreted by S cells. Which of the following changes most likely represent the effect of this hormone on gastric and duodenal secretions?

	Gastric H^+	**Duodenal HCO_3^-**	**Duodenal Cl^-**
A	↑	↑	↓
B	↓	↓	↓
C	↓	no change	no change
D	↓	↑	↓
E	↑	↓	no change
F	No change	no change	no change

	Answer	**Image**
A	A	
B	B	
C	C	
D	D	
E	E	

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	Answer	Image
F	F	

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Hint

S-cells secrete secretin, whose primary function is to dilute or neutralize the effect of gastric acid in the duodenum.

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Correct Answer

A - A

Explanation Why

This combination describes the effects of gastrin. Gastrin is the primary mediator of gastric acid secretion and, through binding cholecystokinin receptors, contributes to pancreatic HCO_3^- secretion and Cl^- uptake as well as gallbladder contraction. Although secretin mirrors gastrin's effects on duodenal HCO_3^- and Cl^-, it has a different effect on gastric acid.

B - B

Explanation Why

This combination describes the effects of somatostatin, a hormone that inhibits gastric and pancreatic secretions, decreases gastric motility, and reduces gastrointestinal blood flow. Although secretin inhibits gastric acid secretions, it does not inhibit pancreatic secretions and thus would not cause a decrease in duodenal HCO_3^-.

C - C

Explanation Why

This combination describes the effects of gastric inhibitory peptide (GIP). While GIP mainly functions to stimulate insulin secretion from pancreatic beta cells, it also inhibits gastric emptying and has a minor inhibitory effect on gastric acid secretion. Secretin also inhibits gastric acid secretion, but it alters concentrations of duodenal HCO_3^- and Cl^- via modulation of pancreatic secretions.

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D - D

Explanation But

Other gastrointestinal hormones such as cholecystokinin and vasoactive intestinal peptide achieve the same effect as secretin on ion concentrations via inhibition of gastric acid and stimulation of pancreatic secretions.

Explanation Why

This combination describes an alkalization of gastrointestinal secretions along with a drop in duodenal Cl. Secretin inhibits parietal cells of the stomach, decreasing their secretion of gastric H^+. Secretin also binds epithelial cells that line pancreatic ducts, resulting in HCO_3^- export in exchange for Cl^- import. Thus, pancreatic secretions that reach the duodenum are high in HCO_3^- but low in Cl^-.

E - E

Explanation Why

This combination of an increase in gastric H^+ and a decrease in duodenal HCO_3^- does not represent the effect of any gastrointestinal hormone. Secretin instead decreases gastric H^+ and increases duodenal HCO_3^- as a coordinated response to gastric acid or fatty acids in the duodenum.

F - F

Explanation Why

This combination describes a zero effect on the concentration of all three ions. This could represent the effect of a hormone such as motilin, which contributes to gut motility and gallbladder contraction but does not alter secretions. However, this does not describe secretin, which is instead highly involved in modulating gastric secretions.

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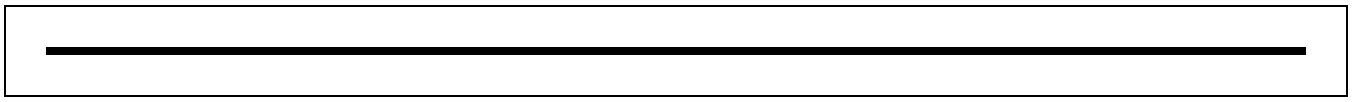

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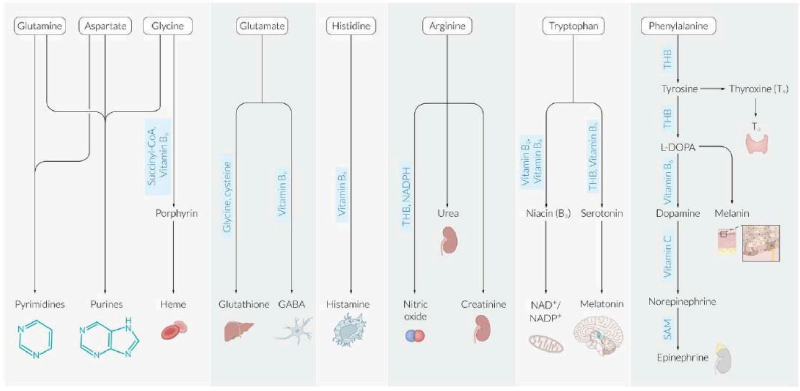
Question # 6

A 34-year-old man comes to the physician because of palpitations, shortness of breath, diarrhea, and abdominal cramps for 2 months. Physical examination shows cutaneous flushing of the face. Auscultation of the chest shows bilateral wheezing. A 24-hour urine collection shows increased 5-hydroxyindoleacetic acid (5-HIAA) concentration. A contrast-enhanced CT scan of the abdomen shows an intestinal tumor with extensive metastasis to the liver. A diagnosis of an inoperable disease is made and the patient is started on treatment with octreotide. Six weeks later, the patient's symptoms have improved except for his abdominal pain and frequent loose stools. The physician suggests enrolling the patient in a trial to test additional treatment with a new drug that has been shown to improve symptoms in other patients with the same condition. The expected beneficial effect of this new drug is most likely caused by inhibition of which of the following?

	Answer	Image
A	Dopamine β-hydroxylase	
B	Vasoactive intestinal peptide	
C	Plasma kallikrein	
D	Histidine decarboxylase	
E	Tryptophan hydroxylase	

Hint

Palpitations, dyspnea with wheezing, flushing, and diarrhea in a patient with a metastatic intestinal tumor and increased urinary 5-HIAA is suggestive of carcinoid syndrome. Telotristat is used as adjunctive therapy in patients with carcinoid tumors.

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Correct Answer

A - Dopamine β-hydroxylase

Explanation Why

Dopamine β-hydroxylase is an enzyme of catecholamine synthesis (dopamine → norepinephrine). Excess catecholamines can lead to palpitations, facial flushing, and shortness of breath, which are seen in this patient. However, carcinoid tumors are not associated with elevated catecholamine levels, so inhibition of dopamine β-hydroxylase is unlikely to improve this patient's symptoms of carcinoid syndrome. Dopamine β-hydroxylase inhibitors could potentially be used to treat pheochromocytoma.

B - Vasoactive intestinal peptide

Explanation Why

Vasoactive intestinal peptide (VIP) is a hormone that can cause abdominal pain, diarrhea, and flushing, all of which are seen in this patient. However, carcinoid tumors are not associated with elevated VIP levels, so VIP inhibition is unlikely to improve symptoms of carcinoid syndrome. Abnormally increased VIP is seen in patients with VIPomas, which can also be treated with octreotide.

C - Plasma kallikrein

Explanation Why

Plasma kallikrein is part of the kinin cascade, which releases bradykinin from high-molecular-weight kininogen. Bradykinin excess can cause dyspnea, abdominal pain, and diarrhea, which are seen in this patient. Although an increased production of kallikrein is associated with carcinoid tumors, kallikrein inhibitors (e.g., ecallantide) are not approved for use in these patients. They are, however, used in the treatment of bradykinin excess due to hereditary angioedema.

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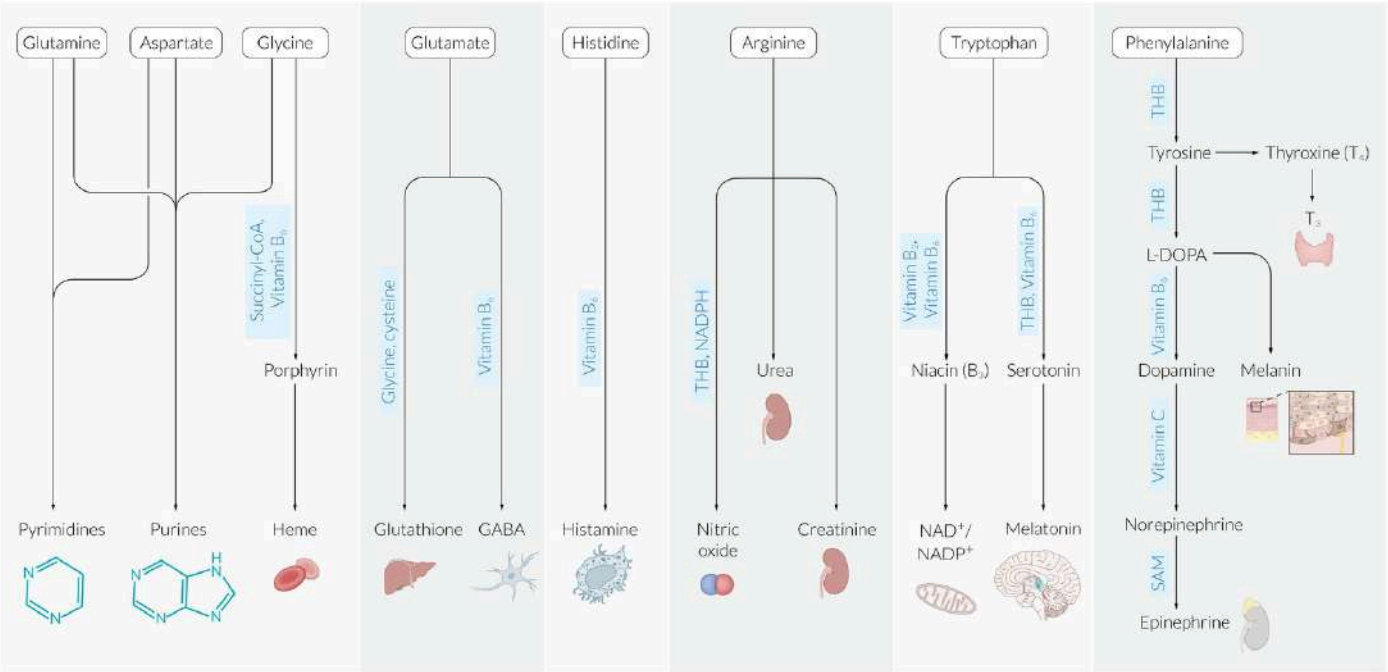
D - Histidine decarboxylase

Explanation Why

Histidine decarboxylase converts histidine to histamine, which can cause anaphylactic symptoms such as dyspnea, wheezing, cutaneous flushing, abdominal cramps and diarrhea, all of which are seen in this patient. Carcinoid tumors are known to produce histamine, so reducing histamine levels could potentially be beneficial, but there are no histidine decarboxylase inhibitors currently approved for clinical use.

E - Tryptophan hydroxylase

Image



Explanation Why

Tryptophan hydroxylase is an enzyme that converts tryptophan to serotonin. The hallmark of carcinoid tumors is the excess production of serotonin, which is primarily responsible for the

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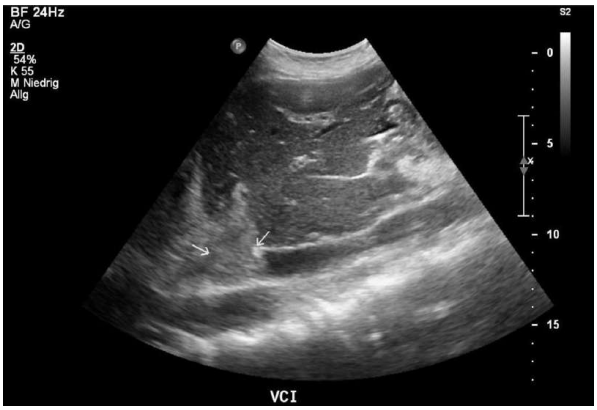
gastrointestinal symptoms (e.g., diarrhea) in carcinoid syndrome. Telotristat, an inhibitor of tryptophan hydroxylase, has recently been approved as adjunctive therapy for patients with carcinoid tumors whose diarrhea is not controlled with somatostatin analogs (e.g., octreotide).

Question # 7

A 38-year-old woman comes to the physician because of a 3-month history of moderate abdominal pain that is unresponsive to medication. She has a history of two spontaneous abortions at 11 and 12 weeks' gestation. Ultrasound examination of the abdomen shows normal liver parenchyma, a dilated portal vein, and splenic enlargement. Upper endoscopy shows dilated submucosal veins in the lower esophagus. Further evaluation of this patient is most likely to show which of the following findings?

	Answer	Image
A	Increased prothrombin time	
B	Palmar erythema	
C	Hepatic venous congestion	
D	Increased serum bilirubin levels	

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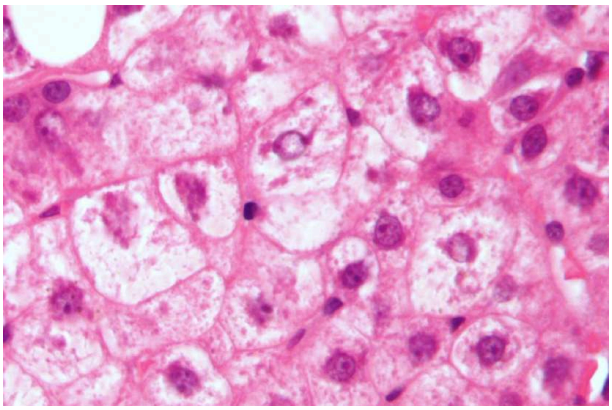
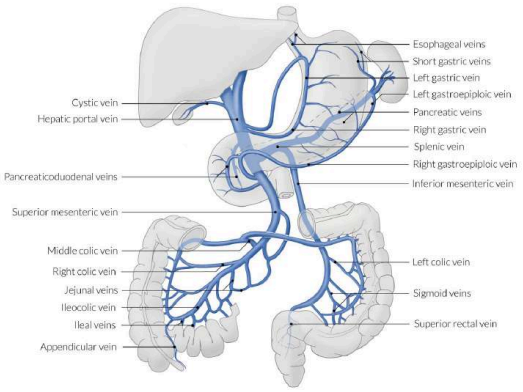
	Answer	Image
E	Councilman bodies	
F	Thrombocytopenia	

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Hint

A dilated portal vein, splenic enlargement, and dilated lower esophageal submucosal veins with an ultrasound showing normal liver parenchyma suggests portal hypertension due to portal vein thrombosis.

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Correct Answer

A - Increased prothrombin time

Explanation Why

Increased prothrombin time is seen in cirrhosis, which can result in portal hypertension. However, additional findings of cirrhotic portal hypertension such as ascites and features of cirrhosis (e.g., increased surface nodularity, coarse or heterogeneous echotexture) on hepatic ultrasound are absent in this patient. Although the repeated spontaneous miscarriages and current portal vein thrombosis seen here suggest antiphospholipid syndrome (APS), partial thromboplastin time is usually prolonged while prothrombin time would be normal in patients with APS.

B - Palmar erythema

Explanation Why

Palmar erythema can occur in hyperestrogenic states, e.g., due to cirrhosis, which could explain this patient's portal hypertension. However, additional findings of cirrhotic portal hypertension (e.g., ascites) and features of cirrhosis on hepatic ultrasound (e.g., increased surface nodularity, coarse or heterogeneous echotexture) are absent here.

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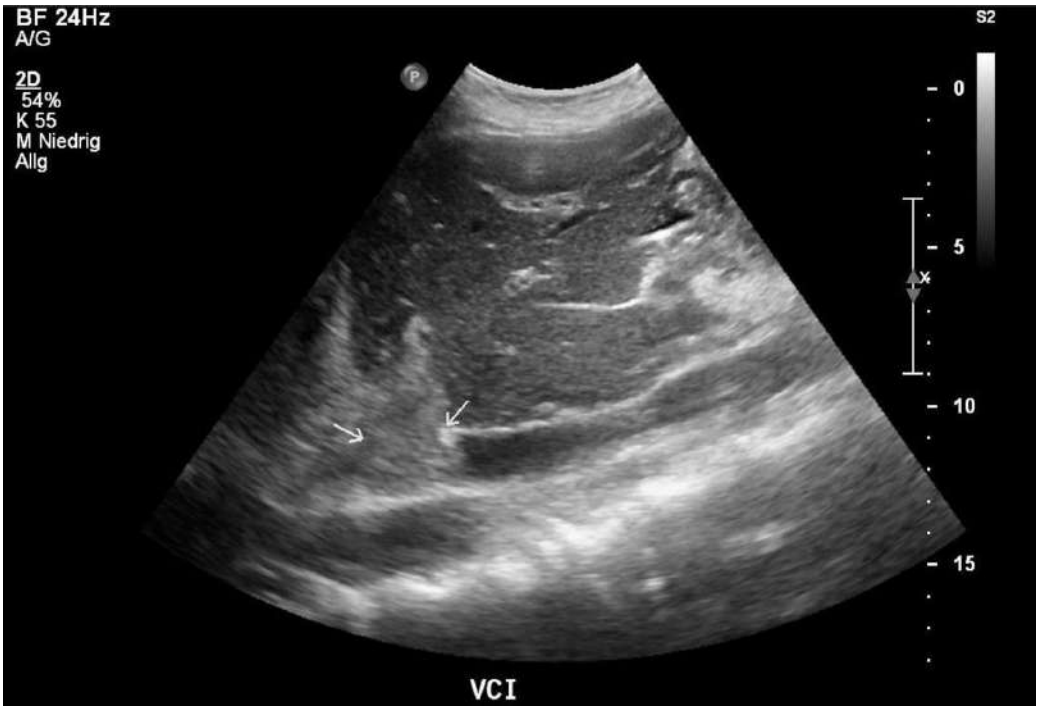
C - Hepatic venous congestion

Image



Explanation Why

Hepatic venous congestion is seen in Budd-Chiari syndrome, which could explain this patient's portal hypertension. However, the absence of ascites and ultrasonographic features of Budd-Chiari syndrome (e.g., hepatomegaly or a hypertrophic caudate lobe, reversed flow in the hepatic veins) in this patient suggests a different cause for the patient's symptoms.

D - Increased serum bilirubin levels

Explanation Why

Increased serum bilirubin levels are seen in cirrhosis, which is a possible explanation for this patient's portal hypertension. However, additional findings of cirrhotic portal hypertension (e.g., ascites) and features of cirrhosis on hepatic ultrasound (e.g., increased surface nodularity, coarse or

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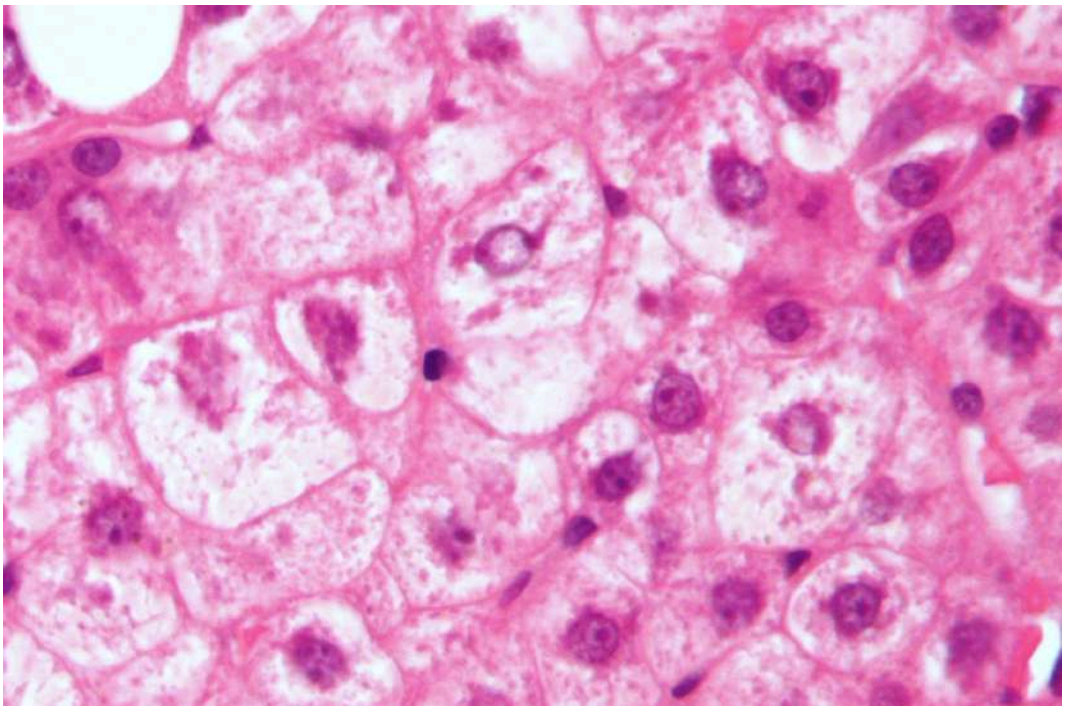
heterogeneous echotexture) are absent here.

E - Councilman bodies

Image



Explanation Why

Councilman bodies are apoptotic hepatocytes caused by acute viral hepatic infections. Fulminant hepatic failure can result in abdominal pain and, rarely, features of portal hypertension. However, in patients with portal hypertension due to liver disease, ascites would also be present. In addition, hepatic ultrasound would show changes such as hepatomegaly and decreased hepatic echotexture. Moreover, jaundice and fever, which are characteristic of acute viral hepatitis, are not present here. Also, fulminant viral hepatitis has a rapidly progressive course, unlike this patient who has had symptoms for the past 3 months.

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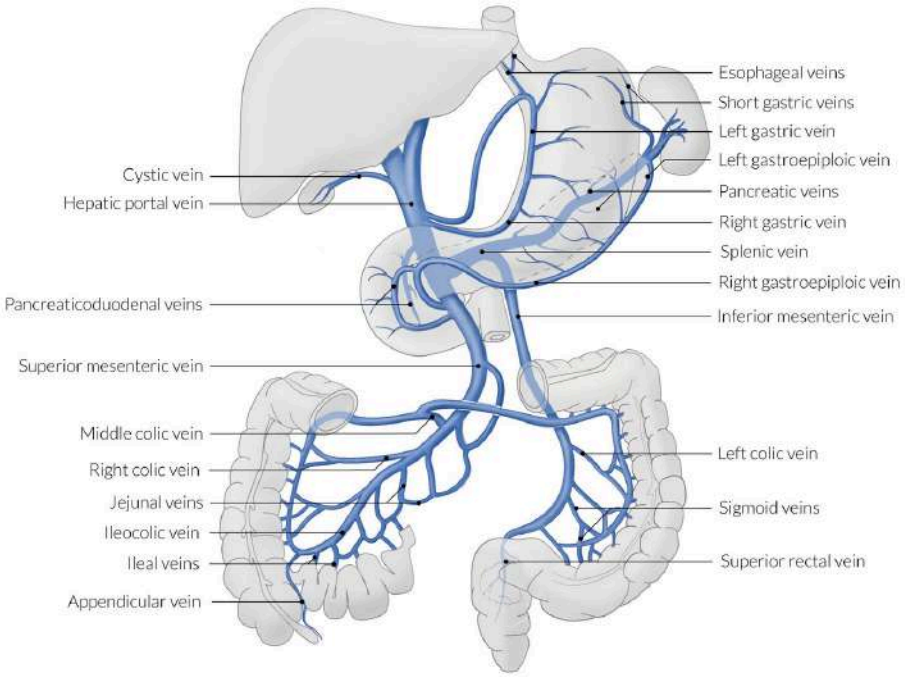
F - Thrombocytopenia

Image



Explanation Why

Thrombocytopenia is a common presentation in patients with an enlarged spleen because enlargement can increase splenic activity (hypersplenism), leading to the rapid clearance of platelets from the blood stream. Splenic enlargement and esophageal varices (collateral circulation) are seen in all forms of portal hypertension. However, unlike post-hepatic and hepatic causes of portal hypertension (e.g., Budd-Chiari syndrome, cirrhosis), pre-hepatic causes of portal hypertension such as splenic or portal vein thrombosis are usually not associated with ascites. Repeated spontaneous miscarriages in patients with thrombophilia, as suggested here by the diagnosis of portal vein thrombosis, is suspicious of antiphospholipid syndrome (APS).

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Question # 8

A previously healthy 52-year-old woman is brought to the emergency department after sustaining burns over 45% of her body in a house fire. On arrival, she is in acute distress but is fully oriented. Aggressive intravenous fluid resuscitation is begun and the patient is transferred to the intensive care unit of a burn center. 20 hours later, she has several large, tarry black stools and develops hypotension and tachycardia. Despite appropriate lifesaving measures, she dies. Which of the following is the most likely underlying cause of the patient's tarry black stools?

	Answer	Image
A	Decreased prostaglandin synthesis	
B	Erosion of tortuous submucosal arteriole	
C	Bacterial colonization of the gastric antrum	
D	Decreased gastric blood flow	
E	Increased stomach acid production	

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Hint

This patient's tarry stools, hypotension, and tachycardia prior to her death suggest an acute upper GI bleed that was precipitated by her extensive burn injury.

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Correct Answer

A - Decreased prostaglandin synthesis

Explanation Why

Decreased prostaglandin synthesis, which occurs with NSAID use, compromises the protective mucosal barrier of the stomach and predisposes to gastric ulcer formation and subsequent upper GI bleeding. Although this patient did have symptoms of upper GI bleeding, she did not have a history of prolonged NSAID use, making this etiology unlikely.

B - Erosion of tortuous submucosal arteriole

Explanation Why

Damage to a tortuous submucosal arteriole describes the pathophysiology of a Dieulafoy lesion, which can also cause sudden, severe GI bleeding. However, Dieulafoy lesion is a very rare cause of gastrointestinal bleeding and is not associated with extensive burns.

C - Bacterial colonization of the gastric antrum

Explanation Why

Infection with *H. pylori* is estimated to affect two-thirds of the world's population and is a risk factor for peptic ulcer disease, gastritis, and gastrointestinal malignancies. Although the mechanism underlying this association is not entirely understood, chronic infection with *H. pylori* disrupts the physiology of the stomach mucosa, leading to increased stomach acid secretion and decreased expression of protective factors such as mucin. Although it is very possible that this patient's stomach was colonized by *H. pylori*, sudden GI bleeding occurring after extensive burns suggests a different cause.

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D - Decreased gastric blood flow

Explanation Why

Curling ulcers are a subtype of stress gastritis seen in patients with extensive burns and occur due to hypovolemia and subsequent hypoperfusion of the stomach. The resultant ischemic tissue injury to the stomach epithelium results in an interruption in the normal mucosal barrier of the stomach, and ulcer formation. PPI should be administered in patients with extensive burns to prevent the formation of Curling ulcers.

E - Increased stomach acid production

Explanation Why

Increased stomach acid release from parietal cells is stimulated in part by acetylcholine and occurs in response to increased vagal stimulation. This can occur in the setting of severe brain injury and is the mechanism underlying Cushing ulcers. This patient was fully oriented and did not have a history of severe brain injury, making this etiology unlikely.

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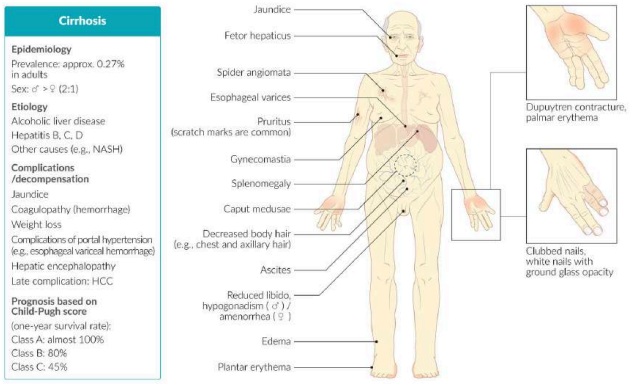
Question # 9

A 56-year-old man is brought to the emergency department by his wife because of increasing confusion and lethargy for the past 12 hours. He is oriented only to person. His temperature is 37.3°C (99.1°F), pulse is 109/min, respirations are 18/min, and blood pressure is 108/67 mm Hg. Examination shows abdominal distention and several erythematous, lacy lesions on the chest that blanch with pressure. His hands make a flapping motion when they are dorsiflexed. Which of the following is the most likely precipitating factor for this patient's symptoms?

	Answer	Image
A	Elevated systemic vascular resistance	
B	Destruction of gut anaerobes	
C	Thiamine pyrophosphate deficiency	
D	Accumulation of hemoglobin in the intestine	
E	Low protein consumption	

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Hint

The acute mental status changes, signs of liver cirrhosis (e.g., ascites, spider telangiectasias), and asterixis in this patient indicate hepatic encephalopathy.

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Correct Answer

A - Elevated systemic vascular resistance

Explanation Why

Severely elevated systemic vascular resistance can lead to hypertensive encephalopathy from cerebral edema. Hypertensive encephalopathy may present with confusion and lethargy, as seen in this patient, but would also manifest with high blood pressure rather than the low blood pressure seen here. This patient's tachycardia and symptoms of impaired liver function furthermore make another cause more likely.

B - Destruction of gut anaerobes

Explanation Why

Destruction of gut anaerobes, which represent most of the flora of the intestine, can cause symptoms including diarrhea and gut distention from malabsorption but is not a known trigger of hepatic encephalopathy in patients with cirrhosis. Antibiotics that target NH_3-producing gut bacteria (e.g., rifaximin, neomycin) are actually used for the prevention and treatment of hepatic encephalopathy (by decreasing the amount of systemically-absorbed ammonia).

C - Thiamine pyrophosphate deficiency

Explanation Why

Thiamine pyrophosphate is the active form of thiamine and an important cofactor in glucose metabolism. Clinically, thiamine deficiency can manifest with Wernicke-Korsakoff syndrome and/or beriberi. Neurologic symptoms of thiamine deficiency include confusion and lethargy, but, classically, ophthalmoplegia and ataxia would also be present. Meanwhile, the asterixis, low blood pressure, and symptoms of reduced liver function seen in this patient make another cause for his presentation more likely.

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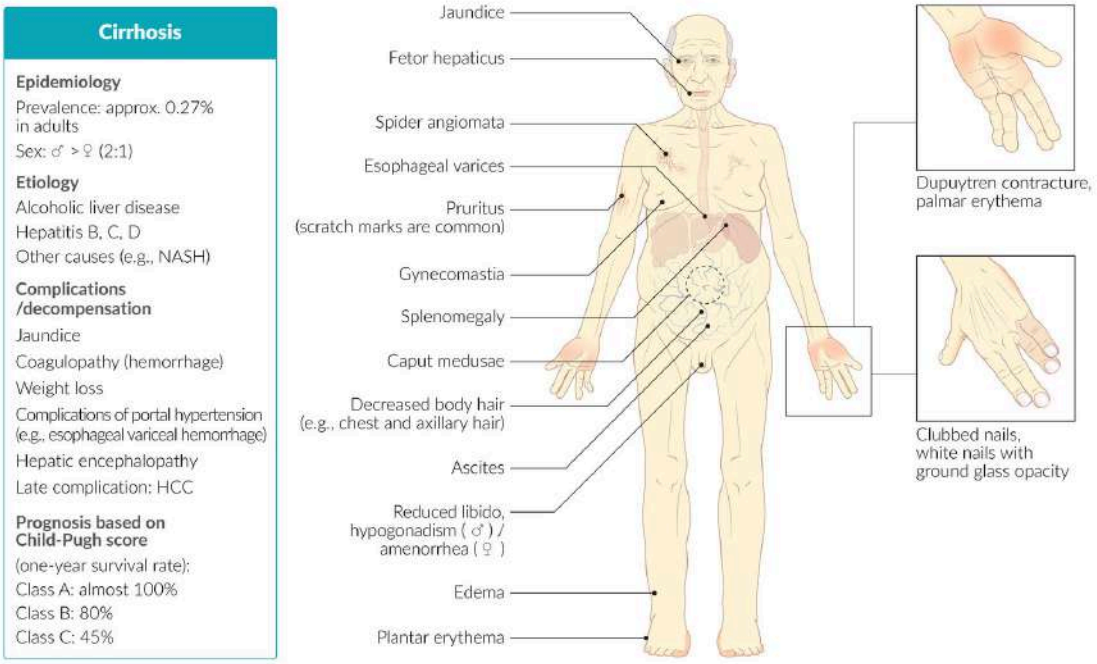
D - Accumulation of hemoglobin in the intestine

Image



Explanation Why

Hemoglobin in the intestine (e.g., from a gastrointestinal bleed) can precipitate hepatic encephalopathy (HE), which this patient has. Ammonia is neurotoxic and one of the metabolic end-products of the enzymatic breakdown of hemoglobin and is absorbed in the gut during a GI bleed. A cirrhotic liver cannot rapidly metabolize large quantities of ammonia, which leads to systemic hyperammonemia and manifests with the findings of altered mental status and asterixis seen here. Other common triggers of hepatic encephalopathy include infection, recent transjugular intrahepatic portosystemic shunt placement, sedatives, and metabolic alkalosis.

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E - Low protein consumption

Explanation Why

Low protein consumption (e.g., due to protein-losing enteropathy or kwashiorkor) could present with lethargy and ascites, but would also typically show muscle wasting, anemia, and depigmentation of hair and skin. It would not cause the asterixis or liver disease stigmata seen in this patient. High protein, not low protein, would increase ammonia production and is a common trigger of hepatic encephalopathy.

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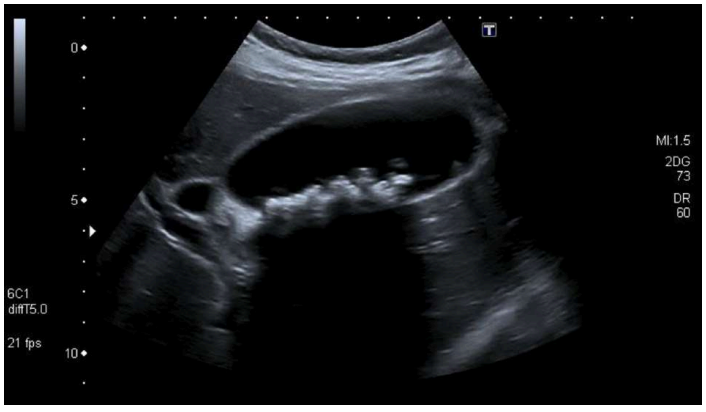
Question # 10

A 34-year-old woman with Crohn disease comes to the physician because of a 4-week history of nausea, bloating, and epigastric pain that occurs after meals and radiates to the right shoulder. Four months ago, she underwent ileocecal resection for an acute intestinal obstruction. An ultrasound of the abdomen shows multiple echogenic foci with acoustic shadows in the gallbladder. Which of the following mechanisms most likely contributed to this patient's current presentation?

	Answer	Image
A	Increased bilirubin production	
B	Increased hepatic cholesterol secretion	
C	Increased activity of β-glucuronidase	
D	Decreased fat absorption	
E	Decreased motility of the gallbladder	
F	Decreased biliary concentration of bile acids	

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Hint

In this patient who had ileocecal resection for complicated Crohn disease, the clinical features (nausea, bloating, and epigastric pain) and ultrasonographic findings (gallbladder echogenic foci with an acoustic shadow) indicate a diagnosis of cholelithiasis. Enterohepatic circulation is impaired in patients with Crohn disease and ileocecal resection.

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Correct Answer

A - Increased bilirubin production

Explanation Why

Increased bilirubin production can be caused by hemolysis. The resulting unconjugated hyperbilirubinemia predisposes to the development of black pigment gallstones. However, this patient lacks clinical features of hemolysis (e.g., jaundice, fatigue, weakness).

B - Increased hepatic cholesterol secretion

Explanation Why

Increased hepatic cholesterol secretion can result in cholesterol supersaturation in the bile and precipitation of cholesterol gallstones. Increased hepatic cholesterol secretion can result from increased circulating estrogen levels (e.g., during pregnancy). Formation of cholesterol gallstones in patients with a history of Crohn disease and ileocecal resection is caused by a different mechanism.

C - Increased activity of β-glucuronidase

Explanation Why

Increased β-glucuronidase activity can occur due to β-glucuronidase production by bacteria in the biliary tract. Endogenous β-glucuronidase deconjugates bilirubin in the gut for reabsorption. Increased β-glucuronidase activity, therefore, results in excess bilirubin absorption and presence in the biliary tract as well as eventual precipitation with calcium to form brown pigment gallstones. Formation of gallstones in patients with a history of Crohn disease and ileocecal resection is caused by a different mechanism.

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D - Decreased fat absorption

Explanation Why

This patient likely has decreased fat absorption in the gut due to Crohn disease and ileal resection. Malabsorption of fatty acids leads to increased concentrations of fatty acids in the gut that then bind to calcium. Thus, calcium is not available to bind and aid in oxalate excretion, which leads to increased absorption of oxalate that results in hyperoxaluria. This predisposes to the formation of calcium oxalate kidney stones, not gallstones.

E - Decreased motility of the gallbladder

Explanation Why

Decreased motility of the gallbladder can result in biliary stasis, which predisposes to gallstone development, as seen here. This patient's symptoms are likely caused by contraction of the gallbladder against an impacted stone (e.g., in the neck of the gallbladder), rather than by decreased motility of the gallbladder.

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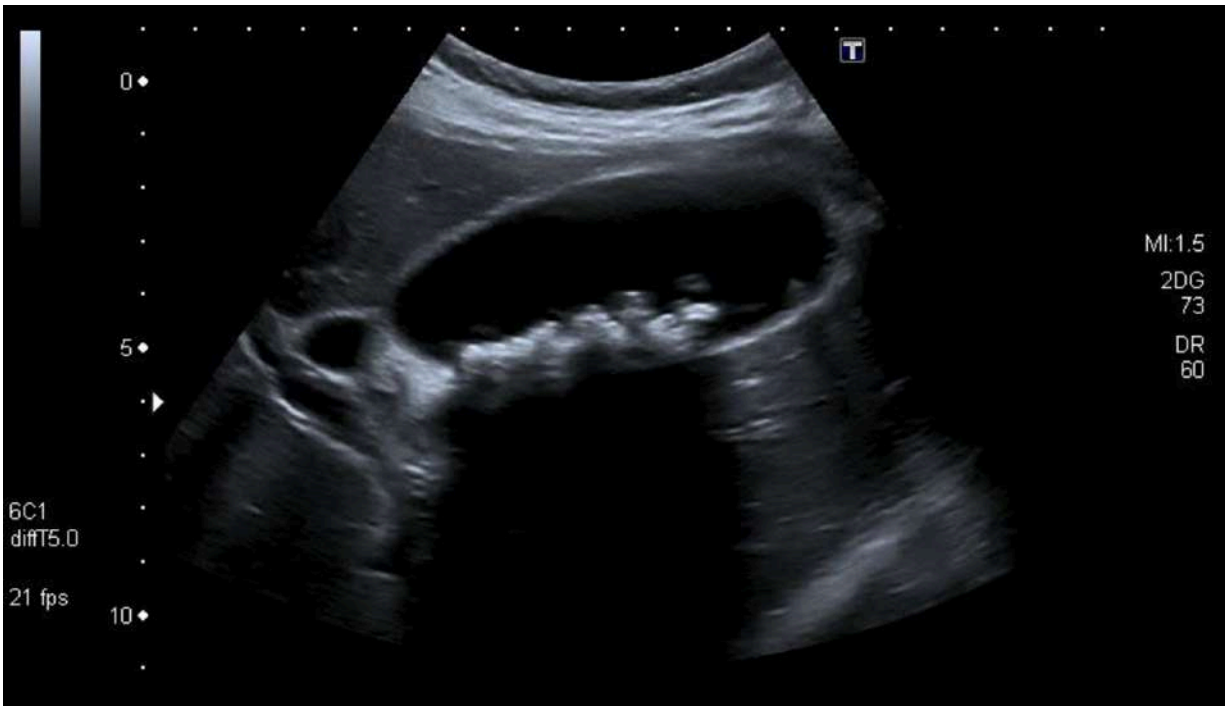
F - Decreased biliary concentration of bile acids

Image



Explanation Why

A decreased concentration of bile acids in the bile can occur in patients with Crohn disease. Bile acids are normally reabsorbed in the terminal ileum and returned to the liver for reuse via the enterohepatic circulation. However, bile acid malabsorption occurs in patients with Crohn disease due to ileitis and/or terminal ileum resection as seen in this case. A decreased bile acid to cholesterol ratio causes cholesterol supersaturation and predisposes to cholesterol gallstone formation, which can lead to cholelithiasis and cholecystitis.

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Question # 11

A 33-year-old woman, gravida 2, para 1, at 24 weeks' gestation is brought to the emergency department by her husband for lethargy, nausea, and vomiting for 4 days. She returned from a trip to South Asia 2 weeks ago. Her immunizations are up-to-date and she has never received blood products. Her temperature is 38.9°C (102°F). She is not oriented to person, place, or time. Examination shows jaundice and mild asterixis. Her prothrombin time is 18 sec (INR=2.0), serum alanine aminotransferase is 3911 U/L, and serum aspartate aminotransferase is 3724 U/L. This patient's current condition is most likely associated with increased titers of which of the following serum studies?

	Answer	Image
A	Anti-HBc IgM	
B	HBsAg	
C	Anti-HEV IgM	
D	Anti-HCV IgG	
E	Anti-HAV IgM	
F	HCV RNA	
G	Anti-HAV IgG	

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Hint

Fever, nausea, vomiting, lethargy, and jaundice with extremely high liver enzyme levels are diagnostic of acute viral hepatitis. Features of hepatic encephalopathy (confusion, asterixis) and increased prothrombin time indicate fulminant hepatic failure. A particular hepatotropic virus is associated with an increased risk of fulminant hepatitis during pregnancy.

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Correct Answer

A - Anti-HBc IgM

Explanation Why

Anti-HBc antibody titers (both IgG and IgM) would be increased in hepatitis B infection. Hepatitis B infection manifests with features of acute viral hepatitis in 30% of cases and fulminant hepatic failure in 0.1–0.5% of cases. However, hepatitis B is a bloodborne pathogen spread by direct contact with bodily fluids or sexual activity. There is no history of drug use, blood transfusion, hemodialysis, risky sexual behavior to suggest HBV infection.

B - HBsAg

Explanation Why

HBsAg would be present in hepatitis B infection. Hepatitis B infection manifests with features of acute viral hepatitis in 30% of cases and fulminant hepatic failure in 0.1–0.5% of cases. However, hepatitis B is a bloodborne pathogen spread by direct contact with bodily fluids or sexual activity. There is no history of drug use, blood transfusion, hemodialysis, risky sexual behavior to suggest HBV infection.

C - Anti-HEV IgM

Explanation But

Anti-HEV antibodies begin to rise (IgM first and IgG after a few days) 2 weeks after hepatitis E infection. IgG antibodies can persist for life. Therefore, IgM antibodies, which would return to baseline within 4–6 months, are used to differentiate between acute HEV infection and a past infection.

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Explanation Why

Hepatitis E virus infection during pregnancy is associated with a high mortality rate (as high as 10–25% during the third trimester) due to fulminant hepatic failure. The exact mechanism behind this phenomenon is not known. The history of recent travel to an HEV-endemic area (e.g., South Asia) is a risk factor for hepatitis E infection, which is transmitted feco-orally.

D - Anti-HCV IgG

Explanation Why

Anti-HCV antibody titers (both IgG and IgM) would be increased in hepatitis C infection. Up to 30% of patients with hepatitis C infection present with features of acute viral hepatitis such as jaundice, nausea, vomiting, lethargy, and elevated liver transaminase enzymes. However, hepatitis C is a bloodborne pathogen spread by direct contact with bodily fluids or sexual activity. There is no history of drug use, blood transfusion, hemodialysis, risky sexual behavior to suggest HCV infection. Finally, fulminant hepatic failure is extremely rare in hepatitis C infection.

E - Anti-HAV IgM

Explanation Why

Anti-HAV IgM titers would be increased in hepatitis A infection. Hepatitis A infection, which can occur following travel to endemic regions such as South Asia, can lead to fulminant hepatitis. However, hepatitis A vaccination is indicated for all individuals travelling to an endemic region that have not received hepatitis A vaccination as a part of the routine immunization schedule. This patient's vaccinations are up-to-date; hepatitis A infection is therefore unlikely. Furthermore, fulminant hepatic failure is rare in hepatitis A infection.

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F - HCV RNA

Explanation Why

HCV RNA concentration would be increased in HCV infection. Up to 30% of patients with hepatitis C infection present with features of acute viral hepatitis such as jaundice, nausea, vomiting, lethargy, and elevated liver transaminases. However, fulminant hepatic failure is extremely rare in hepatitis C infection. Moreover, hepatitis C is a bloodborne virus that is transmitted sexually or via contact with bodily fluids. There is no history of drug use, blood transfusion, hemodialysis, risky sexual behavior to suggest HCV infection.

G - Anti-HAV IgG

Explanation Why

Anti-HAV IgG titers would be increased following hepatitis A vaccination, which is indicated for all individuals traveling to an endemic region who have not received hepatitis A vaccination as a part of the routine immunization schedule. However, the fact that she is fully-vaccinated makes hepatitis A infection unlikely. Furthermore, fulminant hepatic failure is rare in hepatitis A infection. Anti-HAV IgG titers are also seen following vaccinations and would therefore be increased in this patient. However, this would not account for this patient's current condition.

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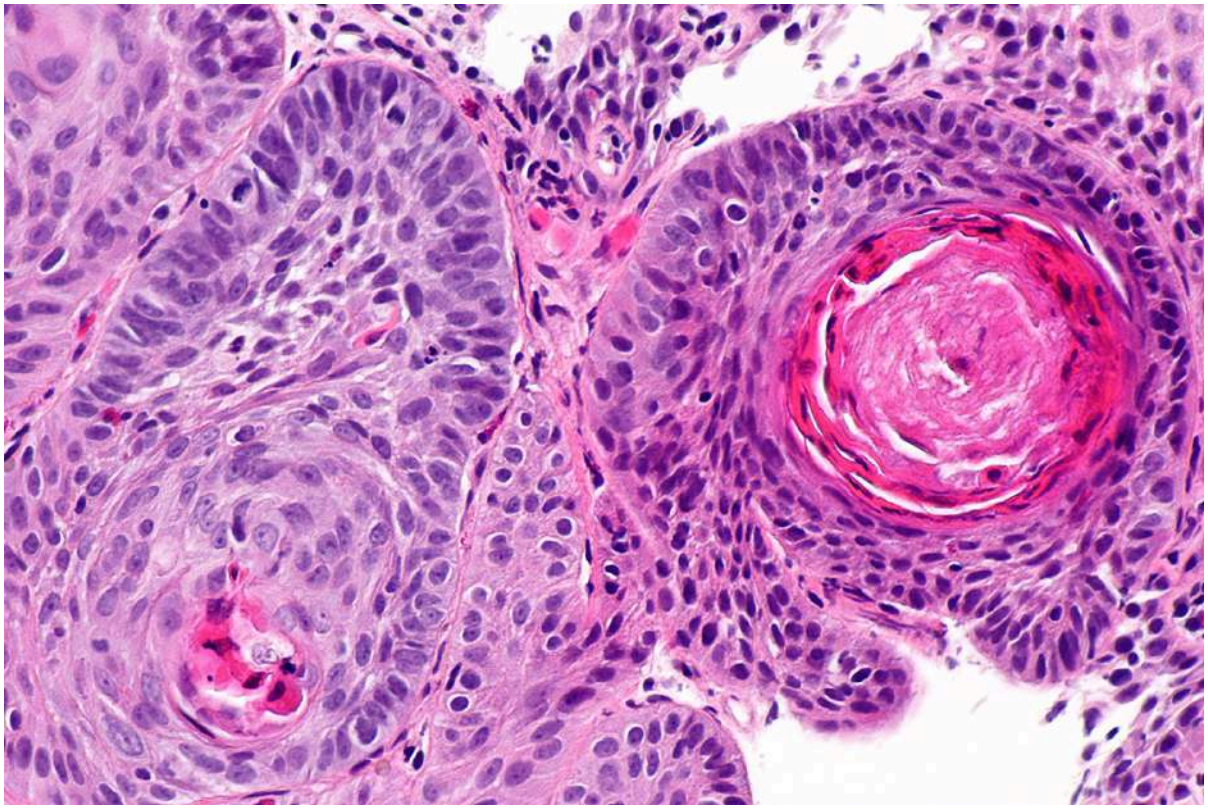
Question # 12

A 68-year-old man comes to the physician because of a 4-month history of bad breath and progressive difficulty swallowing solid food. Physical examination shows no abnormalities. An upper endoscopy is performed and a photomicrograph of a biopsy specimen obtained from the mid-esophagus is shown. Which of the following best explains the findings in this patient?



	Answer	Image
A	Well-differentiated neoplastic glandular proliferation	
B	Atrophy and fibrosis of the esophageal smooth muscle	

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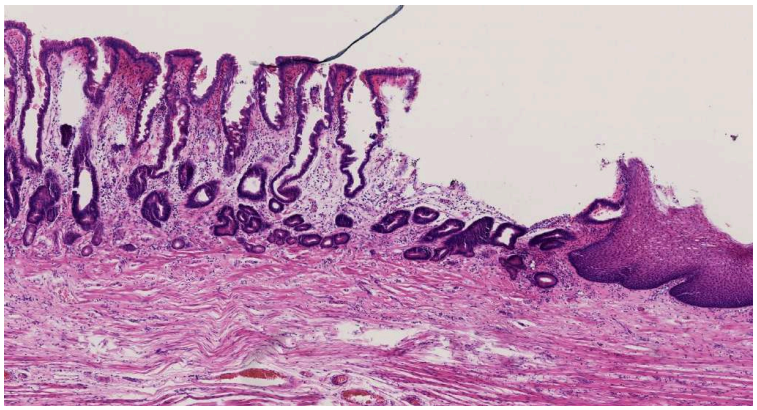
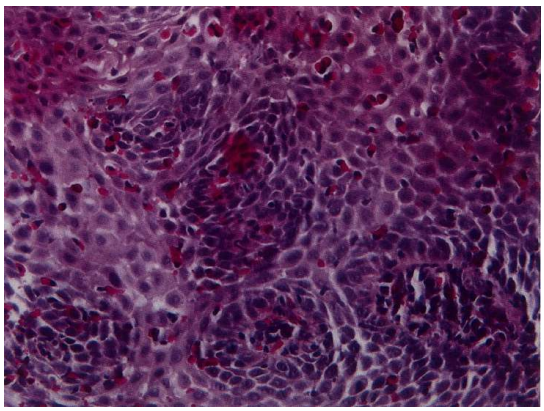
	Answer	Image
C	Metaplastic transformation of esophageal mucosa	
D	Neoplastic proliferation of squamous epithelium	
E	Eosinophilic infiltration of the esophageal walls	

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Hint

The concentric eosinophilic lesions seen in this image are known as keratin pearls.

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Correct Answer

A - Well-differentiated neoplastic glandular proliferation

Explanation Why

Well-differentiated neoplastic glandular proliferation is associated with adenocarcinoma of the esophagus, which can manifest with progressive dysphagia and halitosis. Biopsy would, however, not show clusters of keratin pearls but rather high-grade dysplasia of columnar epithelium with adjacent Barrett mucosa. In addition, adenocarcinoma typically involves the lower third rather than the middle of the esophagus.

B - Atrophy and fibrosis of the esophageal smooth muscle

Explanation Why

Atrophy and fibrosis of the esophageal smooth muscle can be seen in CREST syndrome or systemic sclerosis. These diagnoses may manifest with dysphagia and halitosis in the setting of severe esophageal dysmotility. However, biopsy findings would not show keratinization but rather fibroblast proliferation and smooth muscle atrophy. Moreover, patients with either condition typically present with other findings such as sclerodactyly and Raynaud phenomenon.

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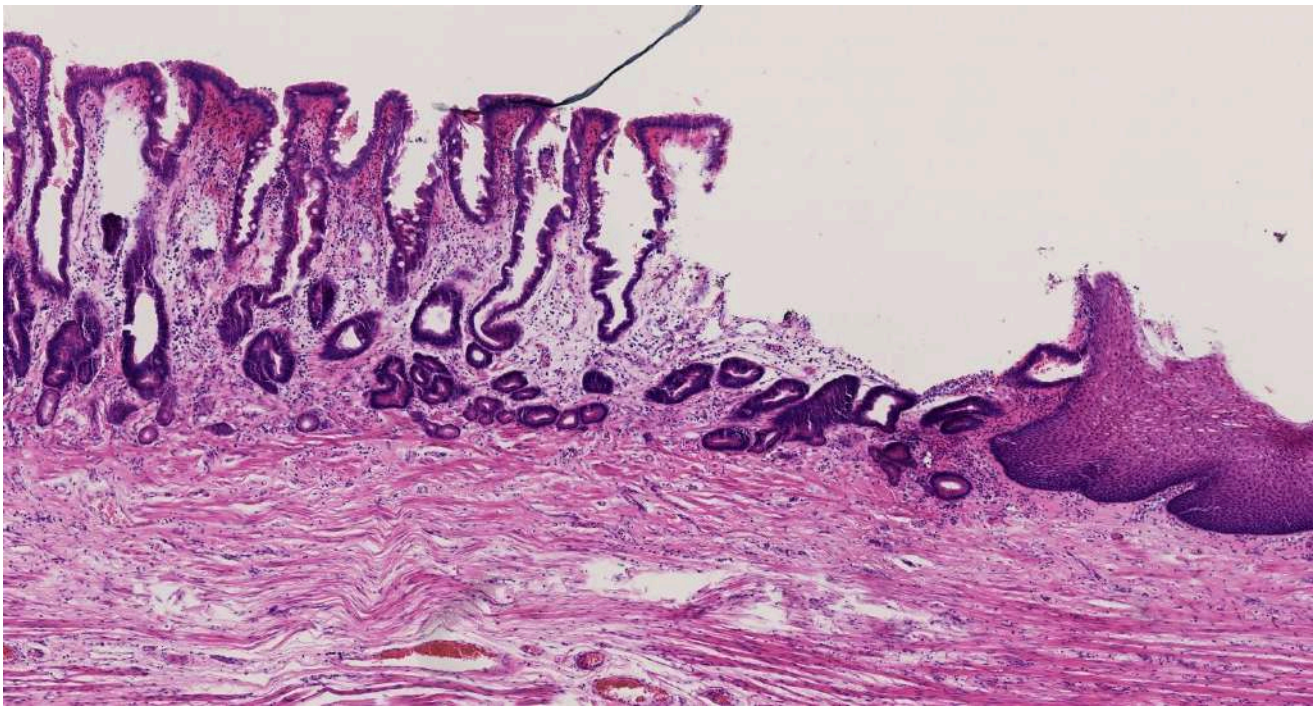
C - Metaplastic transformation of esophageal mucosa

Image



Explanation Why

Metaplastic transformation of esophageal mucosa is seen in Barrett esophagus, which can manifest with halitosis, as seen in this patient. However, biopsy would not show the keratin pearls seen here. Instead, it would typically show an extension of the physiologic transformation zone as esophageal squamous epithelium is replaced with intestinal-type columnar epithelium with goblet cells.

D - Neoplastic proliferation of squamous epithelium

Explanation Why

Neoplastic proliferation of squamous epithelium is the hallmark of squamous cell carcinoma (SCC) of the esophagus, which can manifest with progressive dysphagia and halitosis due to food particles retained in the esophagus. The histopathology involves clusters of keratin pearls destroying normal

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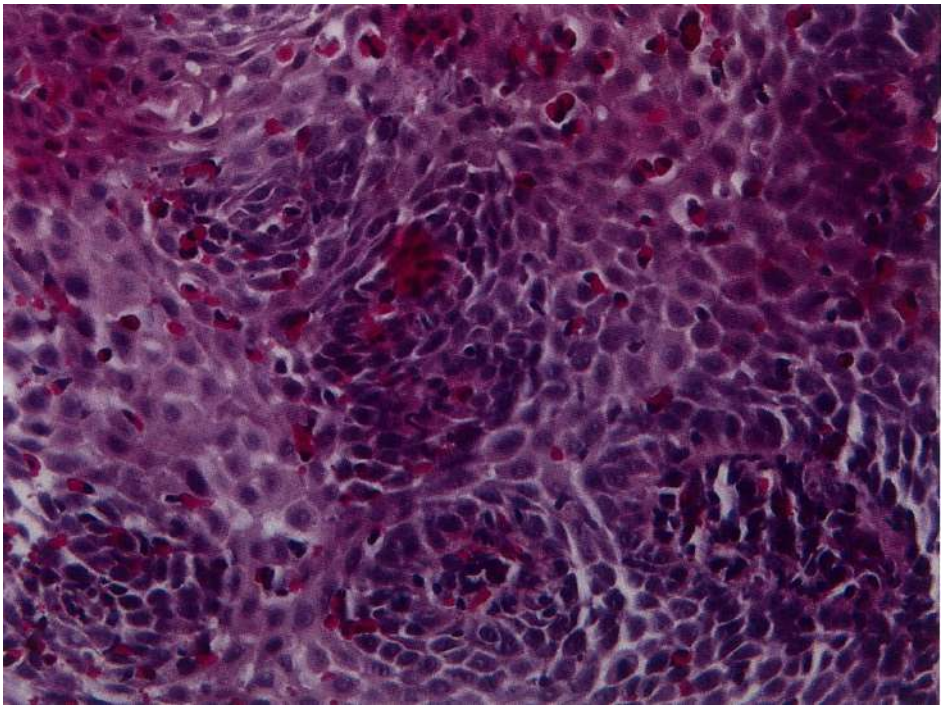
tissue structure in the upper two-thirds of the esophagus. It typically affects patients with risk factors such as long-term alcohol use, tobacco exposure, achalasia, and diets low in fruits and vegetables.

E - Eosinophilic infiltration of the esophageal walls

Image



Explanation Why

Eosinophilic infiltration of the esophageal walls is associated with eosinophilic esophagitis, which can manifest with dysphagia and, in some cases, halitosis due to food impaction. However, biopsy would not show the keratin pearls seen in this patient. Instead, it would show circumferential mucosal lesions and, possibly, eosinophilic infiltration. Moreover, patients with eosinophilic esophagitis typically present with a history of allergic disease as well as acute symptoms associated with exposure to a particular food.

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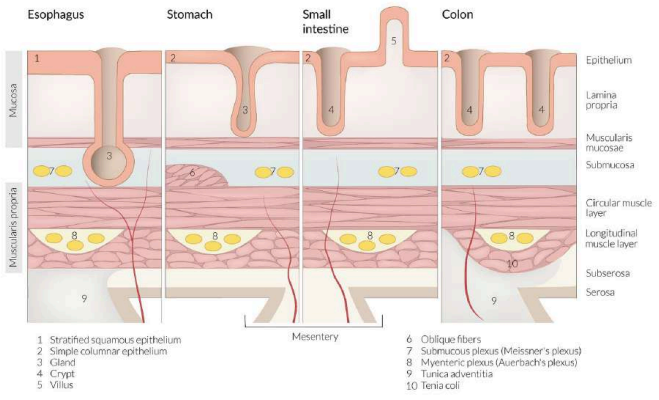
Question # 13

A 30-year-old man is brought to the emergency department because of severe shortness of breath, fever, and cough for 5 days. He says he has smoked one pack of cigarettes daily for 12 years and occasionally uses cocaine on weekends. After intubation in the emergency department for worsening tachypnea and hypoxia, he is admitted to the intensive care unit for management of pneumococcal sepsis. One week later, the patient develops hematemesis. Abdominal examination shows epigastric tenderness; there is no guarding or rebound tenderness. Urgent endoscopy shows multiple shallow hemorrhagic lesions, predominantly in the gastric fundus and greater curvature. Biopsies show patchy epithelial defects that do not extend beyond the muscularis mucosa. Which of the following is the most likely diagnosis?

	Answer	Image
A	Type B gastritis	
B	Dieulafoy lesion	
C	Cushing ulcer	
D	Penetrating ulcer	
E	Curling ulcer	
F	Erosive gastropathy	

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Hint

The lesions do not extend into the submucosa, which indicates that they are very superficial.

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Correct Answer

A - Type B gastritis

Explanation Why

Type B gastritis (EMAG) is a subtype of atrophic gastritis involving the gastric antrum and associated with *H. pylori* infection. It may manifest with epigastric pain and hematemesis. However, endoscopy and biopsy would not show multiple erosions limited by the muscularis mucosa, as seen here, but rather chronic mucosal inflammation with atrophy, gland loss, and metaplastic changes.

B - Dieulafoy lesion

Explanation Why

A Dieulafoy lesion is an erosion of the proximal stomach related to an aberrant submucosal artery. Dieulafoy lesion can manifest with hematemesis and epigastric pain, and biopsy findings would show an intact submucosa, all of which is seen here. However, a Dieulafoy lesion is typically singular and located along the lesser curvature, near the esophagogastric junction (not along the greater curvature). Endoscopy would show a dilated submucosal vessel.

C - Cushing ulcer

Explanation Why

A Cushing ulcer may result from stress gastritis and manifests with epigastric pain and hematemesis. Cushing ulcers, however, occur in patients with brain injuries, whereas this patient presents with pneumococcal sepsis. Moreover, Cushing ulcers are more likely to be solitary and have a tendency to perforate, which would manifest with severe pain and peritoneal signs. More importantly, gastric ulcers extend beyond the muscularis mucosa layer, which is inconsistent with this patient's biopsy findings.

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D - Penetrating ulcer

Explanation Why

A penetrating ulcer is a stress ulcer that extends through all layers of gastric mucosa into serosa or adventitia and, therefore, penetrates the stomach. It may cause hematemesis and epigastric pain, as seen here, but peritoneal signs would also be expected as a result of gastric acid leaking into the peritoneal cavity. Thus, patients are likely to present with intense, persistent pain and an acute abdomen.

E - Curling ulcer

Explanation Why

A Curling ulcer is a stress ulcer that occurs in patients with recent severe burn injuries. It may manifest with hematemesis and epigastric pain, as seen here. However, Curling ulcers have a tendency to perforate, which would manifest with severe pain and peritonitis due to perforation. More importantly, biopsy findings for Curling ulcers show damage extending through the muscularis mucosa, which is inconsistent with this patient's biopsy findings.

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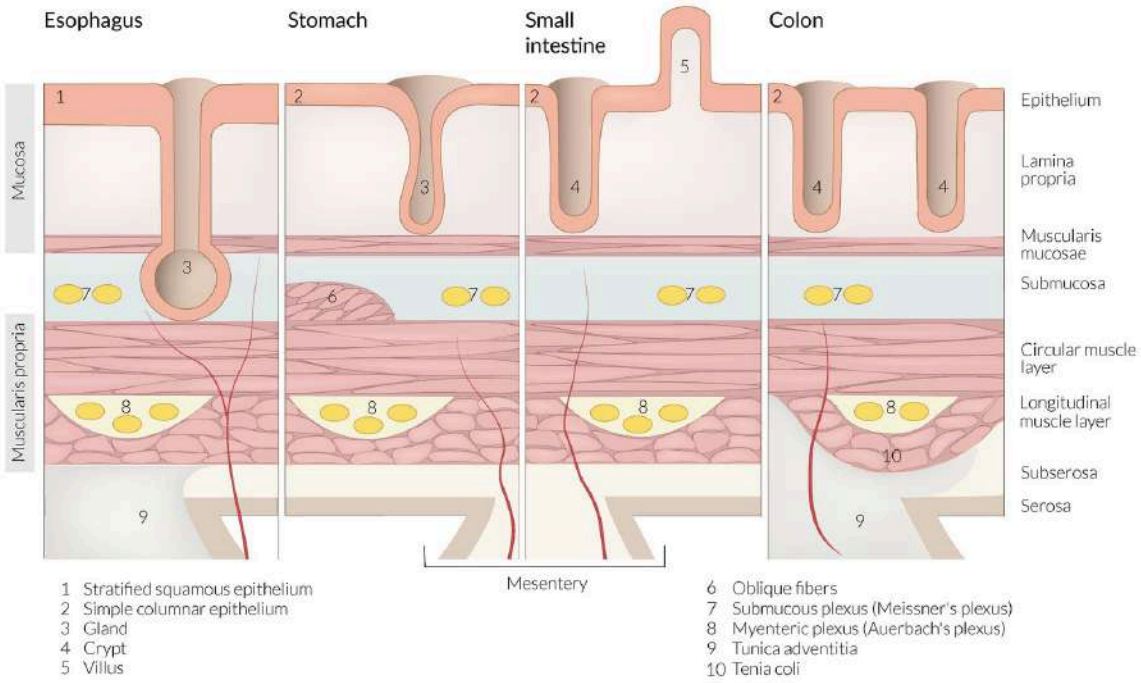
F - Erosive gastropathy

Image



Explanation Why

This patient's history of epigastric pain and hematemesis after pneumococcal sepsis is suggestive of acute erosive gastropathy. Erosions are more superficial than ulcers, which involve damage to the gastric mucosa extending beyond the muscularis mucosa layer into the submucosa. Acute erosive gastropathy is characterized by ischemia of the mucosa due to hypovolemia (e.g., sepsis) and exposure to injurious substances (e.g., smoking, cocaine use). In acute erosive gastropathy, hemorrhage and loss of the superficial epithelium occur, further compromising the normal protective barrier of the stomach and allowing acid to penetrate through the mucosa, which directly damages the vasculature. This damage exacerbates the mucosal ischemia, causing the release of inflammatory mediators and leading to the erosions seen here.

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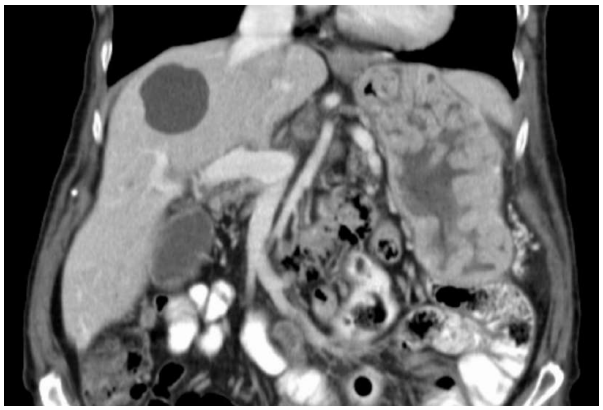
Question # 14

An otherwise healthy 50-year-old man comes to the physician because of a 6-month history of increasingly frequent episodes of upper abdominal pain, nausea, vomiting, and diarrhea. He has had a 3.2-kg (7-lb) weight loss during this time. Physical examination shows bilateral pitting pedal edema. An endoscopy shows prominent rugae in the gastric fundus. Biopsy shows parietal cell atrophy. Which of the following is the most likely underlying cause?

	Answer	Image
A	Serotonin-secreting gastric tumor	
B	Proliferation of gastric mucus-producing cells	
C	Neoplasia of submucosal lymphoid tissue	
D	Chronic Helicobacter pylori infection	
E	Excessive somatostatin secretion	
F	Ectopic secretion of gastrin	

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Hint

This patient presents with dyspeptic symptoms (i.e., abdominal pain, nausea, vomiting, and diarrhea), weight loss, and possible hypoproteinemia (as evidenced by bilateral pedal edema). In combination with prominent gastric rugae on endoscopy and atrophic parietal cells on histology, these features are diagnostic of Ménétrier disease.

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Correct Answer

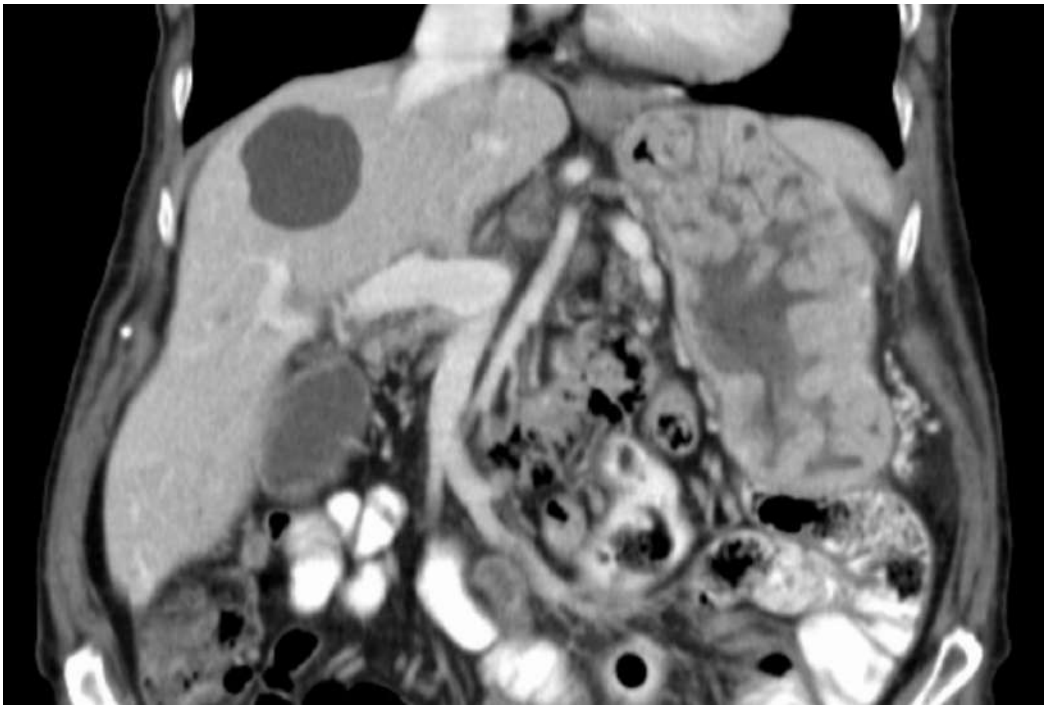
A - Serotonin-secreting gastric tumor

Explanation Why

A serotonin-secreting gastric tumor, or gastric carcinoid tumor, may be asymptomatic or manifest with symptoms of carcinoid syndrome, which most commonly occurs if the tumor spreads to the liver. Episodic flushing, bronchospasm, and diarrhea are typical manifestations of carcinoid syndrome. However, endoscopy would reveal a submucosal mass, not the prominent gastric rugae seen in this patient. Biopsy would show prominent rosettes.

B - Proliferation of gastric mucus-producing cells

Image



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Explanation Why

The patient's findings are consistent with Ménétrier disease (protein-losing hypertrophic gastropathy), which is a result of the proliferation of gastric mucus-producing cells. The pathogenesis involves increased signaling of EGFR, which results in proliferation of epithelial cells of the mucous cell compartment.

C - Neoplasia of submucosal lymphoid tissue

Explanation Why

Neoplasia of the submucosal lymphoid tissue, or gastric lymphoma, can also present with abdominal pain and weight loss, although edema would be unlikely. Endoscopic findings may also include thickened rugae. However, histopathologic examination would show abnormal lymphoid tissue rather than the parietal cell atrophy seen in this patient.

D - Chronic Helicobacter pylori infection

Explanation Why

Chronic *H. pylori* infection may cause similar symptoms of dyspepsia, including abdominal pain, nausea, and vomiting, as in this patient. However, it would not cause edema. On endoscopy, the fundus is typically spared, with predominantly antral lesions showing gastritis or peptic ulcer disease.

E - Excessive somatostatin secretion

Explanation Why

Excessive somatostatin secretion can be caused by a somatostatinoma. Patients present with abdominal pain and weight loss, in addition to the triad of glucose intolerance, gallstones, and diarrhea/steatorrhea. Edema is not a common feature. If localized to the stomach, the tumor can be seen as a submucosal mass on endoscopy, which is not the case in this patient. In addition,

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histopathologic examination would show densely granular cells in a rosette pattern, a common finding of neuroendocrine tumors.

F - Ectopic secretion of gastrin

Explanation Why

Ectopic secretion of gastrin is responsible for Zollinger-Ellison syndrome (ZES). Patients with ZES commonly present with therapy-resistant peptic ulcer disease and diarrhea, as in this patient. Abdominal pain and weight loss can also occur. Although over 90% of patients with ZES have prominent gastric folds on endoscopy, a biopsy would show parietal cell hyperplasia rather than atrophy. In addition, peptic ulcers are also a common manifestation, particularly in the duodenum.

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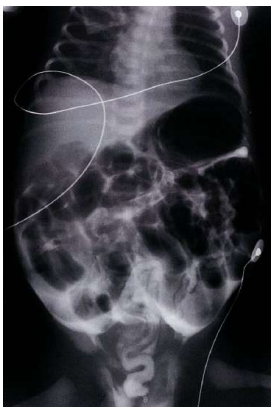
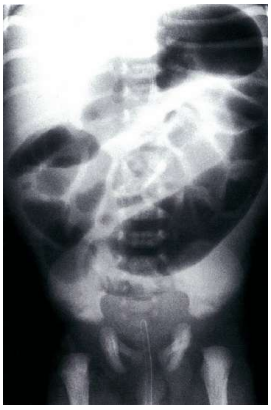
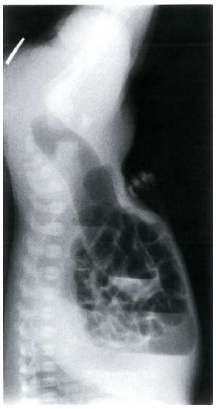
Question # 15

A 3175-g (7-lb) female newborn is delivered at term. Initial examination shows a distended abdomen and a flat perineal region without an opening. A dark green discharge is coming out of the vulva. Which of the following is the most likely diagnosis?

	Answer	Image
A	Meconium ileus	
B	Hirschsprung disease	
C	Imperforate anus	

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	Answer	Image
D	Colonic atresia	
E	Meconium plug syndrome	

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Hint

This newborn's findings indicate a diagnosis that is commonly part of a constellation of congenital birth defects known as the VACTERL association.

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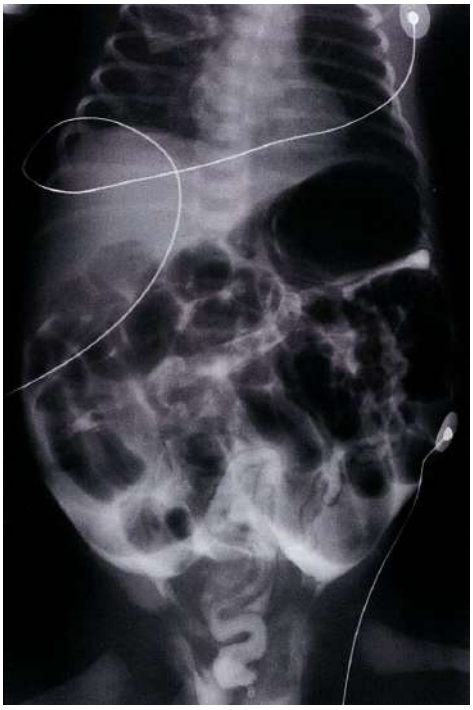
Correct Answer

A - Meconium ileus

Image



Explanation Why

Meconium ileus classically presents as abdominal distention and failure to pass meconium within the first 24–48 hours after birth and is commonly observed in patients with cystic fibrosis. However, the absence of an anal opening is inconsistent with meconium ileus. Also, an association of fistula formation with meconium ileus has not been described.

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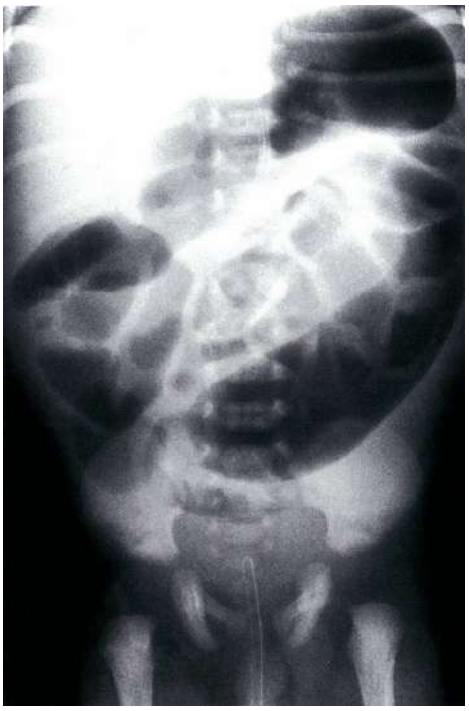
B - Hirschsprung disease

Image



Explanation Why

Hirschsprung disease is due to an aganglionic segment leading to uncoordinated peristalsis and spastic contraction of the rectum. It causes functional intestinal obstruction, which results in abdominal distention and failure to pass meconium as seen in this patient. However, examination of affected individuals reveals merely an extremely tight sphincter, not the total absence of an anal opening. Also, rectovaginal fistula formation is not a feature of Hirschsprung disease.

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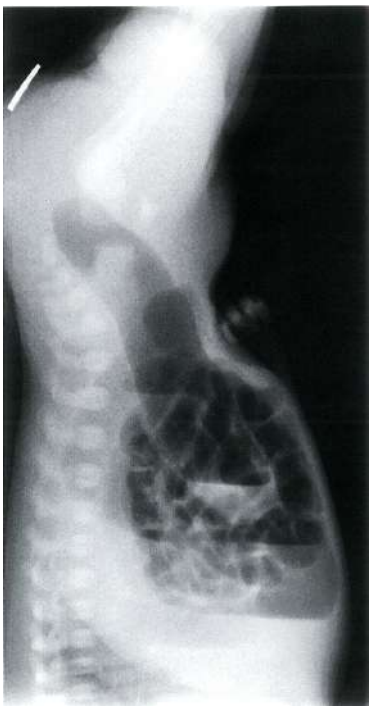
C - Imperforate anus

Image



Explanation Why

Imperforate anus generally presents with a poorly developed midline groove between the buttocks and absence of an anal opening. It is commonly associated with fistula formation, which may lead to meconium excretion through a rectovaginal fistula, all of which is observed in this patient. This patient should be closely examined for other possible features of VACTERL association.

D - Colonic atresia

Explanation Why

Colonic atresia is a rare congenital malformation that results in colonic obstruction with ensuing abdominal distention. Some patients may also present with delayed passage of meconium after birth as seen in this patient. However, affected individuals have a normal anal opening without fistula

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formation.

E - Meconium plug syndrome

Explanation Why

Meconium plug syndrome is a temporary form of intestinal obstruction associated with polycythemia, Hirschsprung disease, and small left bowel syndrome. Affected individuals generally present with delayed passage of meconium (> 24–48 hours) in combination with abdominal distention, both of which this patient exhibits. However, the absence of an anal opening and fistula formation is incompatible with meconium plug syndrome.

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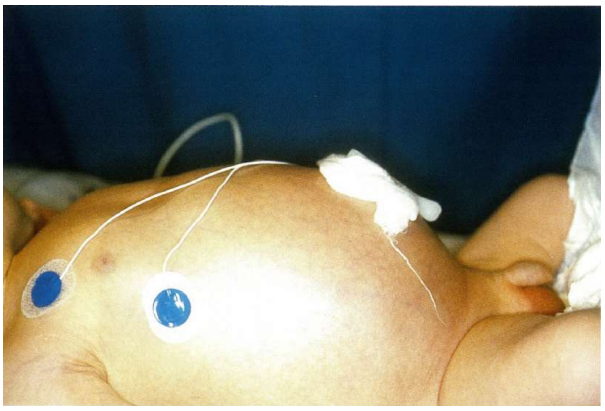
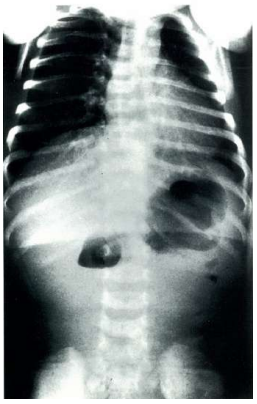
Question # 16

A 2-week-old infant is brought to the emergency room because of 4 episodes of bilious vomiting and inconsolable crying for the past 3 hours. Abdominal examination shows no abnormalities. An upper GI contrast series shows the duodenojejunal junction to the right of the vertebral midline; an air-filled cecum is noted in the right upper quadrant. Which of the following is the most likely cause of this patient's condition?

	Answer	Image
A	Defective neural crest migration	
B	Failure of duodenal recanalization	
C	Nonrotation of the intestines	

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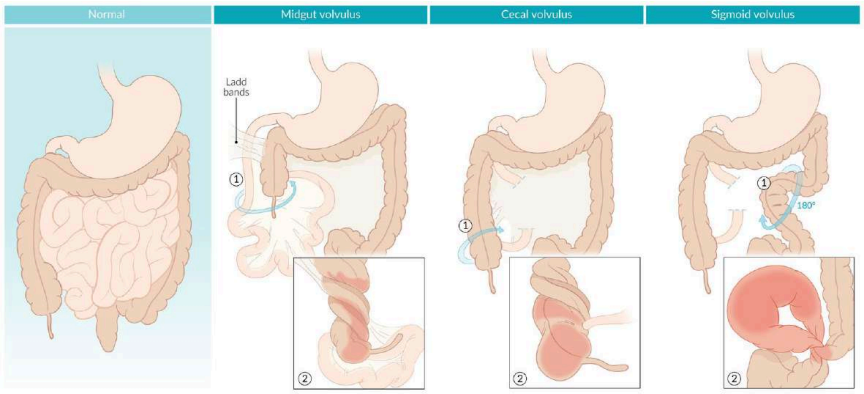
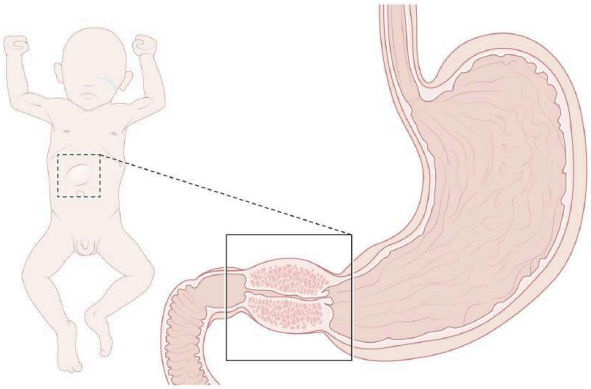
	Answer	Image
D	Incomplete intestinal rotation	
E	Arrested rotation of ventral pancreatic bud	
F	Hypertrophy and hyperplasia of the pyloric sphincter	
G	Resorption of a small bowel segment	

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Hint

The duodenojejunal junction normally lies to the left of the midline, adjacent to the vertebral bodies.

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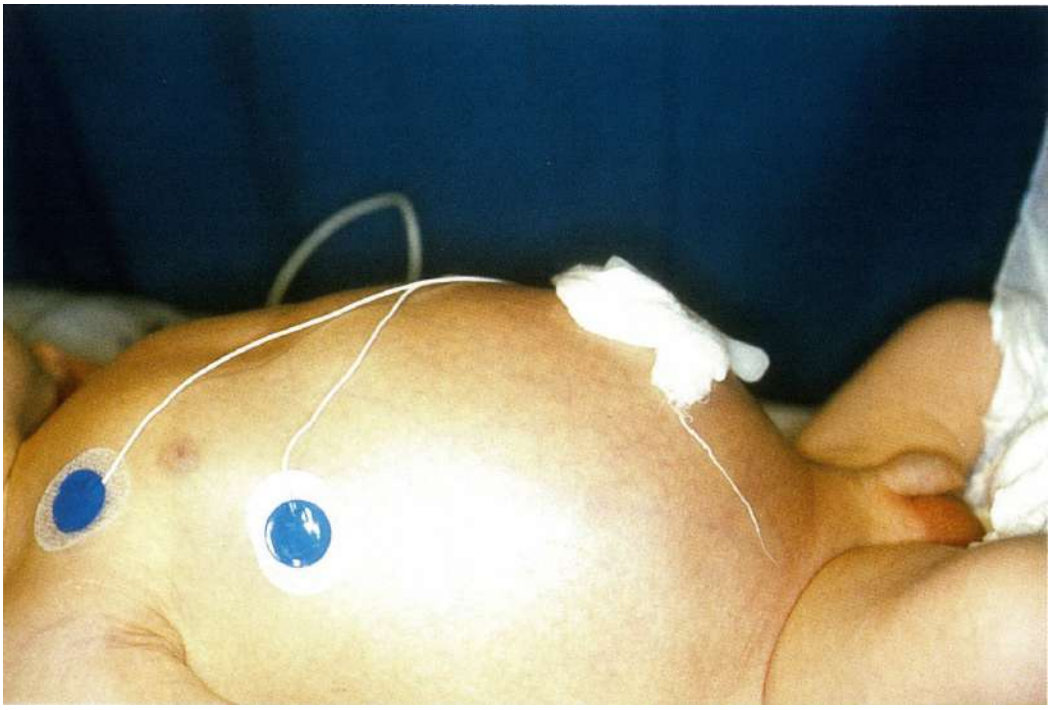
Correct Answer

A - Defective neural crest migration

Image



Explanation Why

Defective neural crest migration to the distal colon results in Hirschsprung disease. The aganglionic segment of the colon fails to relax, which causes functional intestinal obstruction. Although Hirschsprung disease would manifest with bilious vomiting, it also causes significant abdominal distension. Moreover, it typically manifests right after birth with failure to pass meconium within 48 hours or later in childhood with constipation and abdominal distention.

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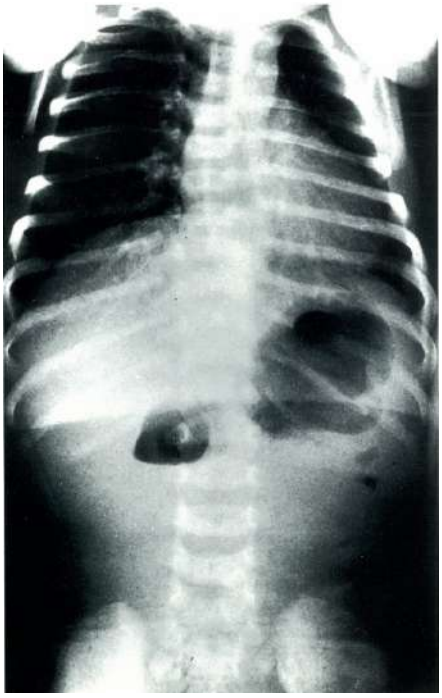
B - Failure of duodenal recanalization

Image



Explanation Why

Failure of duodenal recanalization results in duodenal atresia, which would manifest with complete intestinal obstruction at birth. Hallmark imaging findings are the double bubble sign as well as a completely gasless distal small bowel, neither of which are seen in this patient. Moreover, duodenal atresia is associated with maternal polyhydramnios.

C - Nonrotation of the intestines

Explanation Why

With complete nonrotation of the intestine, the cecum usually remains in the left lower quadrant. However, this patient's GI series shows a cecum located in the right upper quadrant. Patients with nonrotation may be asymptomatic or present with varying degrees of small bowel obstruction.

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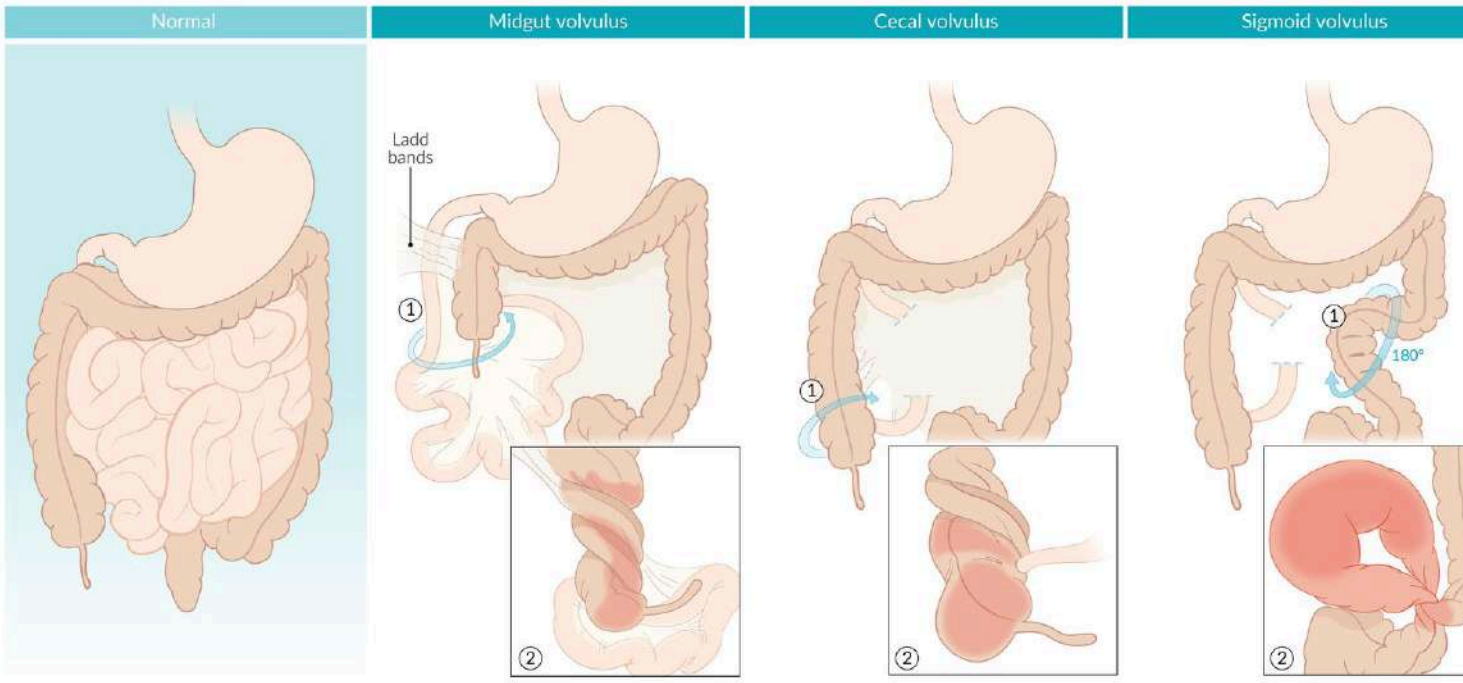
Radiologically, the small bowel is seen to occupy the right side of the abdomen, with the colon predominantly on the left.

D - Incomplete intestinal rotation

Image



Explanation Why

Incomplete intestinal rotation, indicated by a malpositioned duodenojejunal junction (usually located to the left of the midline) and cecum (normally located in the right lower quadrant), can manifest as duodenal obstruction, causing bilious vomiting without abdominal distension, as seen in this infant. Obstruction is due to an extrinsic duodenal compression by peritoneal bands (Ladd bands) that cross over the duodenum to fix the abnormal cecum to the liver or peritoneum.

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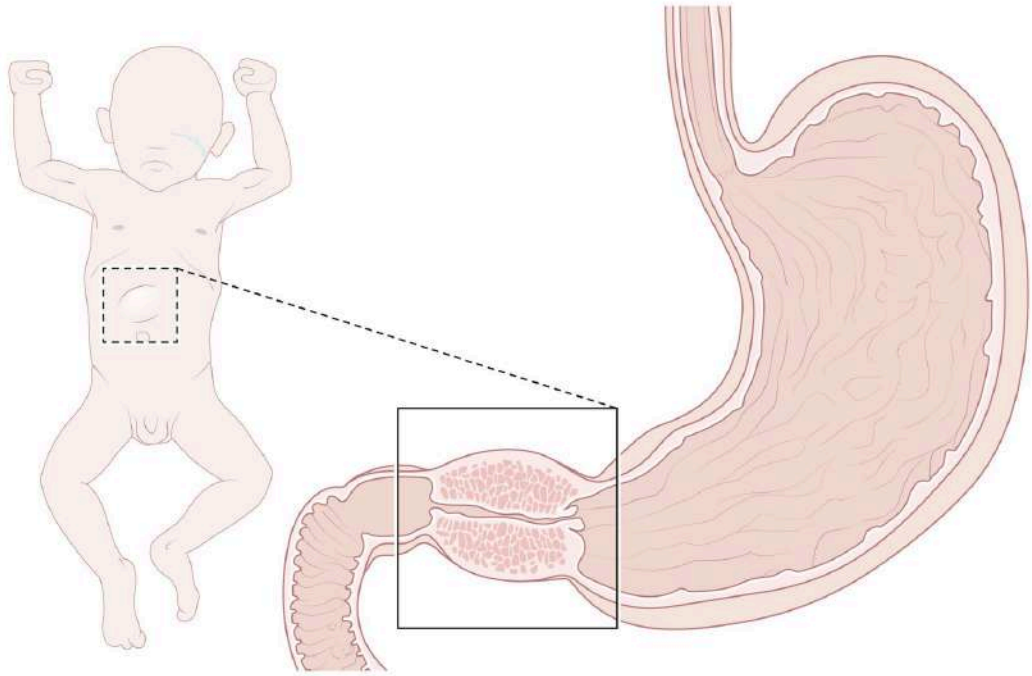
E - Arrested rotation of ventral pancreatic bud

Explanation Why

An arrested ventral pancreatic bud rotation causes annular pancreas, which can result in extrinsic compression of the duodenum, usually proximal to the major duodenal papilla. Unlike this patient, neonates with annular pancreas typically present with nonbilious vomiting and abdominal distension. Findings on an upper GI series include eccentric or concentric narrowing of the second portion of the duodenum, double bubble sign, and symmetrical dilatation of the proximal duodenum. Moreover, annular pancreas is associated with maternal polyhydramnios.

F - Hypertrophy and hyperplasia of the pyloric sphincter

Image



Explanation Why

Hypertrophy and hyperplasia of the pyloric sphincter lead to pyloric stenosis, which can cause

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gastric outlet obstruction. Unlike this patient, infants with pyloric stenosis typically present at 3–6 weeks of age with nonbilious vomiting. Other symptoms include early satiety, progressive gastric dilation, weight loss, a succussion splash, and/or hypokalemic, hypochloremic metabolic alkalosis.

G - Resorption of a small bowel segment

Explanation Why

Jejunal atresia and ileal atresia occur as a result of resorption of a small bowel segment thought to be caused by an in-utero vascular disruption that leads to ischemic necrosis of the fetal intestine. The necrotic tissue is resorbed, leaving blind proximal and distal ends, often with a gap in the mesentery. Although neonates may present with bilious vomiting as in this case, jejunal/ileal atresia would also cause a distension of the upper abdomen, delayed meconium passage, and a triple bubble sign on x-ray. Moreover, jejunal/ileal atresia has been associated with maternal polyhydramnios.

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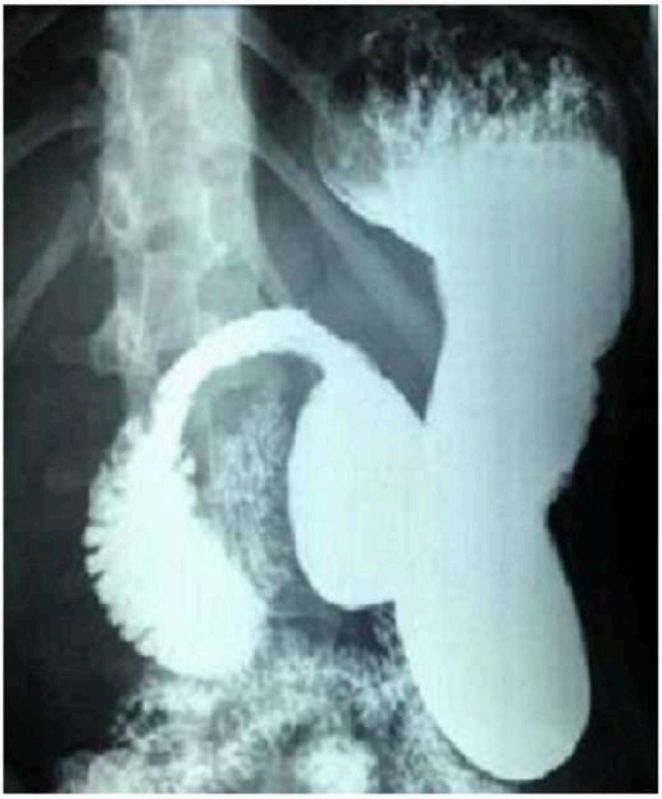
Question # 17

A 10-day-old male newborn is brought to the physician by his mother because of difficulty feeding and frequent nonbilious vomiting. His stool is soft and yellow-colored. The pregnancy was complicated by polyhydramnios and results from chorionic villus sampling showed a 47, XY, +21 karyotype. Physical examination shows mild abdominal distention and normal bowel sounds. An x-ray of the abdomen with oral contrast is shown. The most likely cause of his condition is due to a defect in which of the following embryologic processes?



	Answer	Image
A	Rotation of the ventral pancreatic bud	
B	Foregut septation	
C	Ganglion cell migration	

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	Answer	Image
D	Duodenal recanalization	
E	Umbilical ring closure	

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Hint

The karyotype of this patient has an additional chromosome 21 with a total of 47 chromosomes, indicating Down syndrome. Abdominal x-ray shows the double bubble sign with contrast in the stomach and the proximal duodenum.

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Correct Answer

A - Rotation of the ventral pancreatic bud

Explanation Why

During embryologic development of the pancreas, the endoderm forms two buds: a ventral and a dorsal one. In the process of foregut rotation, the ventral pancreatic bud normally fuses with the dorsal pancreatic bud. A defect in this process can lead to the fusion of abnormally rotated buds, resulting in a ring of pancreatic tissue surrounding the duodenum (annular pancreas) and duodenal stenosis. In the antenatal period, this manifests as polyhydramnios and in the neonatal period, it manifests as feeding intolerance, vomiting (typically non-bilious, but can be bilious depending on whether the obstruction is proximal or distal to the major duodenal papilla), and abdominal distension. Annular pancreas is associated with Down syndrome.

B - Foregut septation

Explanation Why

A defect in the lateral septation of the foregut into the esophagus and trachea is the mechanism behind esophageal atresia. Esophageal atresia can lead to polyhydramnios due to the fetus's inability to swallow and would also present with feeding difficulties and nonbilious vomiting after birth. However, other symptoms such as excessive drooling, choking, and respiratory distress would also be expected. Furthermore, x-ray would show an airless abdomen, not a double bubble sign.

C - Ganglion cell migration

Explanation Why

Failure of migration of neural crest cells (precursors of enteric ganglion cells) to the distal colon during embryonic development causes Hirschsprung disease. Hirschsprung disease is also associated with Down syndrome and classically presents with abdominal distention and vomiting. However, bilious vomiting would be expected rather than nonbilious vomiting, as would failure to pass meconium within the first 48 hours after birth. A double bubble sign would not be present on x-ray.

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D - Duodenal recanalization

Explanation Why

Incomplete duodenal recanalization during weeks eight to ten of embryonic development leads to duodenal atresia. Duodenal atresia is associated with Down syndrome and would also present with feeding difficulties, distension of the abdomen, and the double bubble sign on x-ray. However, bilious vomiting would be expected, rather than the nonbilious vomiting seen here. Furthermore, delayed meconium passage would also be seen, which is not the case in this patient.

E - Umbilical ring closure

Explanation Why

Incomplete umbilical ring closure after physiologic herniation of the intestines leads to an umbilical hernia, which is also associated with Down syndrome. Whereas small defects are often asymptomatic and close spontaneously, larger hernias that contain bowel can lead to feeding difficulties. However, bilious vomiting rather than nonbilious vomiting would be expected. Additionally, physical examination would show an abdominal wall defect, particularly when there is increased intraabdominal pressure from crying. A double bubble sign in x-ray would not be expected in umbilical hernia.

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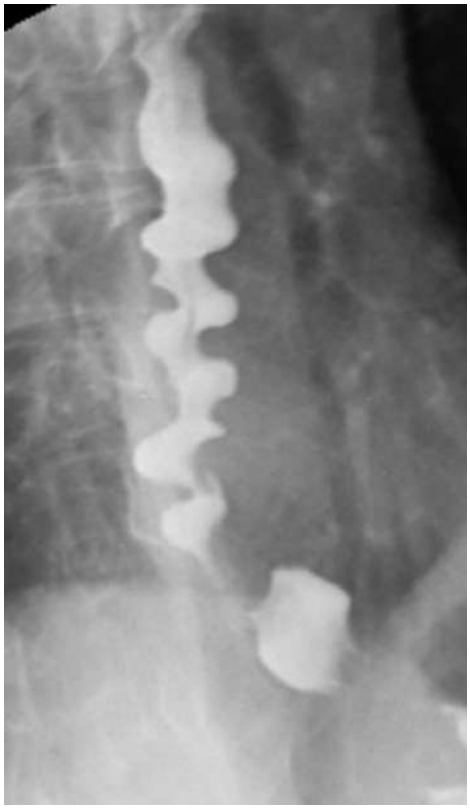
Question # 18

A previously healthy 49-year-old woman comes to the emergency department because of chest pain that radiates to her back. The pain started 45 minutes ago while she was having lunch. Over the past 3 months, she has frequently had the feeling of food, both liquid and solid, getting “stuck” in her chest while she is eating. The patient's vital signs are within normal limits. An ECG shows a normal sinus rhythm with no ST-segment abnormalities. An esophagogram is shown. Further evaluation is most likely to show which of the following?



	Answer	Image
A	Simultaneous multi-peak contractions on manometry	
B	Multiple mucosal erosions on endoscopy	

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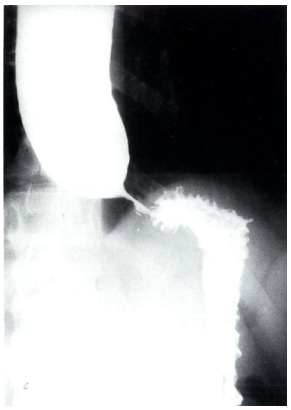
	Answer	Image
C	Elevated lower esophageal sphincter pressure on manometry	
D	Gastroesophageal junction mass on endoscopy	
E	Hypertensive contractions on manometry	

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Hint

The esophagogram in this patient with chest pain and dysphagia to solids and liquids shows a corkscrew or rosary bead appearance, which is typical of diffuse esophageal spasm (DES).

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Correct Answer

A - Simultaneous multi-peak contractions on manometry

Explanation But

Symptoms and relieving factors (nitrates) of DES can closely resemble those of cardiac pathologies. Therefore, acute coronary syndrome should always be ruled out before considering a gastrointestinal disorder, especially if there are risk factors such as age > 45 years and hypertension.

Explanation Why

Simultaneous multi-peak contractions on esophageal manometry are the characteristic finding of DES. Repetitive nonperistaltic, nonprogressive contractions impede the progression of solid and liquid foods down the esophagus, which classically leads to dysphagia and/or a squeezing retrosternal chest pain, as seen in this patient. Medical treatment consists of calcium channel blockers, anticholinergics, or nitrates.

B - Multiple mucosal erosions on endoscopy

Explanation Why

Multiple mucosal erosions on endoscopy are consistent with reflux esophagitis caused by gastroesophageal reflux disease (GERD). This condition can cause acute retrosternal pain that radiates to the back and, in some cases, dysphagia. However, an esophagogram is usually normal in patients with GERD.

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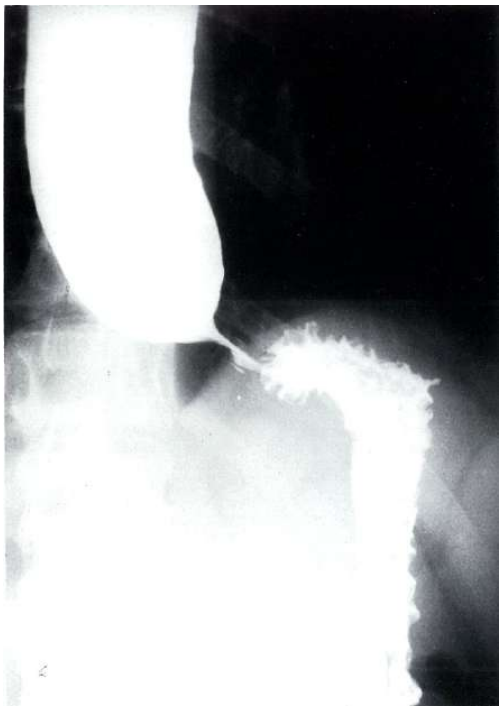
C - Elevated lower esophageal sphincter pressure on manometry

Image



Explanation Why

High pressure in the lower esophageal sphincter is diagnostic of achalasia, which can manifest with dysphagia to both solids and liquids as well as retrosternal chest pain. However, an esophagogram would show dilation of the pre-stenotic esophageal segment and a “bird-beak” appearance at the stenotic segment.

D - Gastroesophageal junction mass on endoscopy

Explanation But

A less common cause for a mass in the distal esophagus is an esophageal leiomyoma (benign tumor).

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Explanation Why

A mass at the gastroesophageal junction on imaging is consistent with esophageal adenocarcinoma, which can cause dysphagia. However, dysphagia associated with esophageal carcinoma worsens progressively (for solids at first and liquids later) and an esophagogram would usually show irregular, asymmetrical narrowing of the lumen at the distal esophagus ("apple-core" appearance). Moreover, other features suggestive of esophageal carcinoma (e.g., weight loss, fatigue, smoking history, alcohol consumption, history of chronic GERD) are not present in this patient.

E - Hypertensive contractions on manometry

Explanation Why

Hypertensive contractions on esophageal manometry are consistent with hypertension peristalsis (nutcracker esophagus), which can cause dysphagia and chest pain while eating. However, an esophagogram is usually normal in patients with a nutcracker esophagus.

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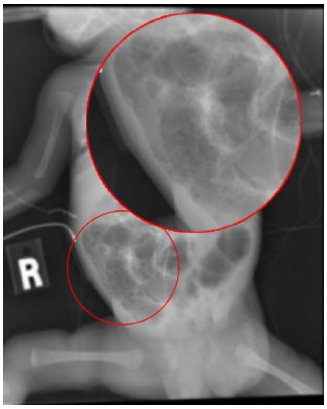
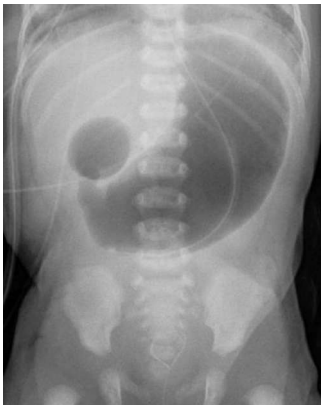
Question # 19

Six hours after delivery, a 3100-g (6-lb 13-oz) male newborn has an episode of bilious projectile vomiting. He was born at term to a 21-year-old woman. The pregnancy was complicated by polyhydramnios. The mother smoked a pack of cigarettes daily during the pregnancy. Physical examination shows a distended upper abdomen. An x-ray of the abdomen shows 3 distinct, localized gas collections in the upper abdomen and a gasless distal abdomen. Which of the following is the most likely diagnosis?

	Answer	Image
A	Necrotizing enterocolitis	
B	Duodenal atresia	

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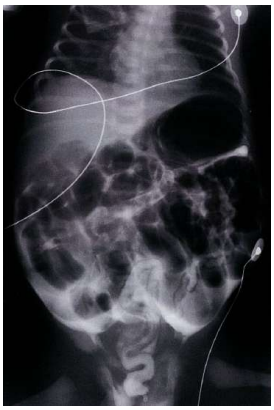
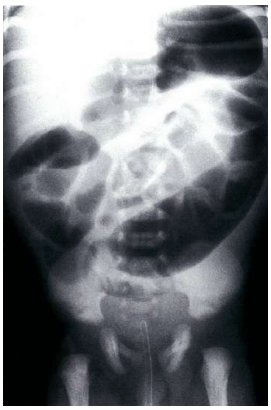
	Answer	Image
C	Meconium ileus	
D	Malrotation with volvulus	
E	Hypertrophic pyloric stenosis	
F	Jejunal atresia	
G	Hirschsprung disease	

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Hint

The 3 localized gas collections (“triple bubble sign”) are in 3 separate portions of the GI tract proximal to an obstruction.

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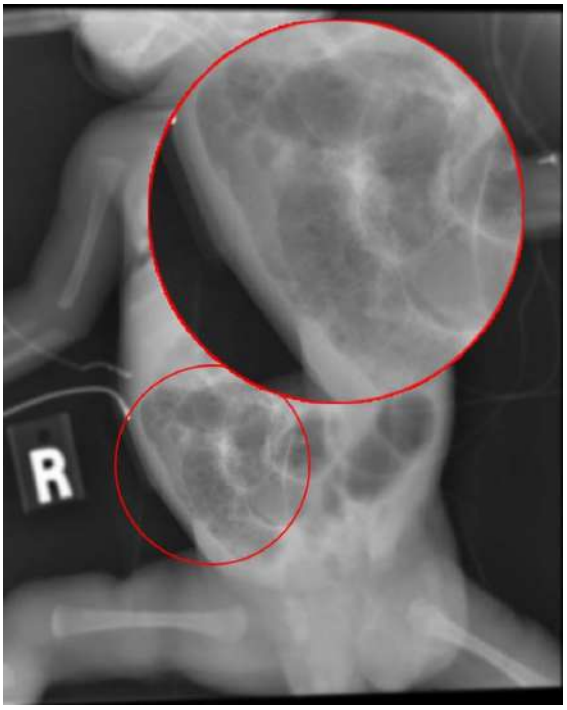
Correct Answer

A - Necrotizing enterocolitis

Image



Explanation Why

Necrotizing enterocolitis (NEC) can manifest with abdominal distention and emesis. However, patients in the early stages of NEC also have diarrhea, rectal bleeding, and abdominal tenderness. Furthermore, this newborn lacks pneumatosis intestinalis on abdominal x-ray, which would confirm NEC. Lastly, NEC is most common in premature infants and usually occurs 2–4 weeks after birth, once oral feeding has been started. It would be rare for NEC to present within the first few hours of life.

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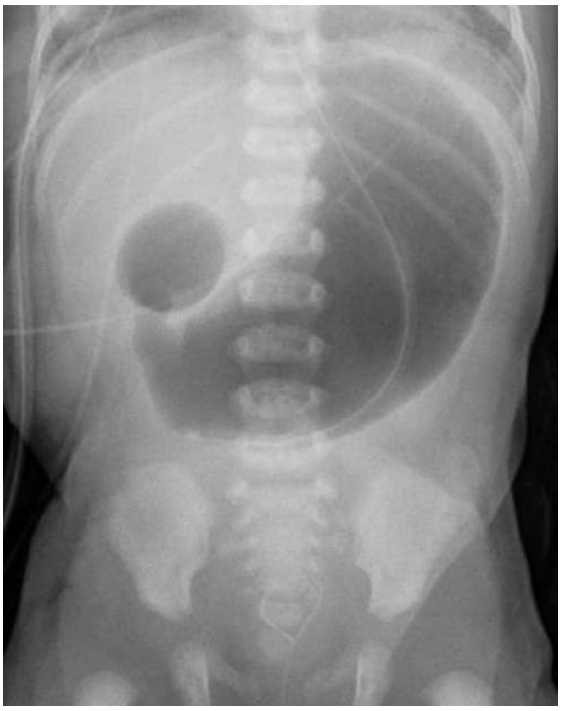
B - Duodenal atresia

Image



Explanation Why

Duodenal atresia can manifest with abdominal distention, bilious emesis, and a prenatal history of polyhydramnios. However, abdominal x-ray would show a double bubble sign rather than the triple bubble sign seen here. In about a third of cases, duodenal atresia is associated with chromosomal abnormalities, especially Down syndrome, of which there are no signs (i.e., dysmorphic features) in this patient. Finally, maternal use of a vasoconstrictive drug (tobacco) during pregnancy makes another diagnosis more likely.

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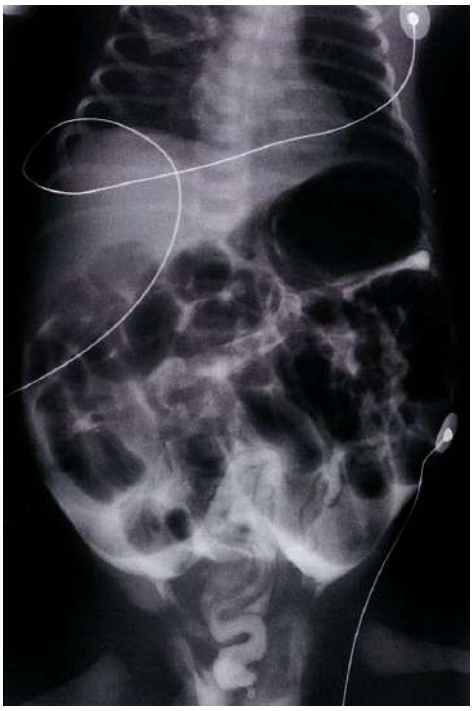
C - Meconium ileus

Image



Explanation Why

Meconium ileus can manifest with abdominal distention and bilious emesis due to ileal obstruction from the impacted stool. This diagnosis should be suspected if meconium fails to pass within the first 48 hours of life, whereas this newborn is only 6 hours old. Abdominal x-ray would show dilated loops of the small bowel above the terminal ileum, and rectal enema would reveal a microcolon. This infant's abdominal x-ray shows an obstruction more proximal to the ileum.

D - Malrotation with volvulus

Explanation But

Because malrotation and midgut volvulus often disrupt the intestinal blood supply, they can predispose to this patient's condition.

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Explanation Why

Malrotation with volvulus can manifest with abdominal distention and bilious emesis due to intestinal obstruction from twisting of the bowel. Infants with midgut volvulus are usually acutely ill and present with hemodynamic instability and, in the case of perforation, signs of peritonitis (e.g., abdominal rigidity). Plain abdominal x-ray may be completely normal, reveal a double bubble sign (indicating duodenal obstruction), or demonstrate pneumoperitoneum (indicating perforation). This patient's history of polyhydramnios and triple bubble sign on x-ray suggest a different diagnosis.

E - Hypertrophic pyloric stenosis

Explanation Why

Hypertrophic pyloric stenosis (IHPS) can manifest with abdominal distention and emesis due to obstruction at the pylorus and maternal cigarette smoking during pregnancy and male sex are risk factors for the development of IHPS. However, the emesis is non-bilious and projectile and will not present until the pylorus has had time to hypertrophy several weeks after birth. A palpable, olive-shaped mass is also usually present, and abdominal x-ray will show distention of the stomach only. This infant's bilious emesis, age, and triple bubble sign suggest another diagnosis.

F - Jejunal atresia

Explanation But

Intestinal atresia of any origin is suggested by a prenatal history of polyhydramnios, since the fetus cannot drink the amniotic fluid due to the intestinal obstruction.

Explanation Why

A distended abdomen and bilious emesis suggest an intestinal obstruction distal to the pylorus. A triple bubble sign on abdominal x-ray confirms the diagnosis of jejunal atresia. This malformation occurs due to a vascular disruption of the mesenteric blood vessels in utero, resulting in necrosis and segmental reabsorption of the intestine. The residual small bowel distal to the atresia may wind around the stalk of the ileocolic artery in spirals, resembling an apple peel (apple peel atresia). Maternal use of vasoconstrictive drugs (e.g., cocaine, MDMA, or cigarettes) increases the risk for this malformation.

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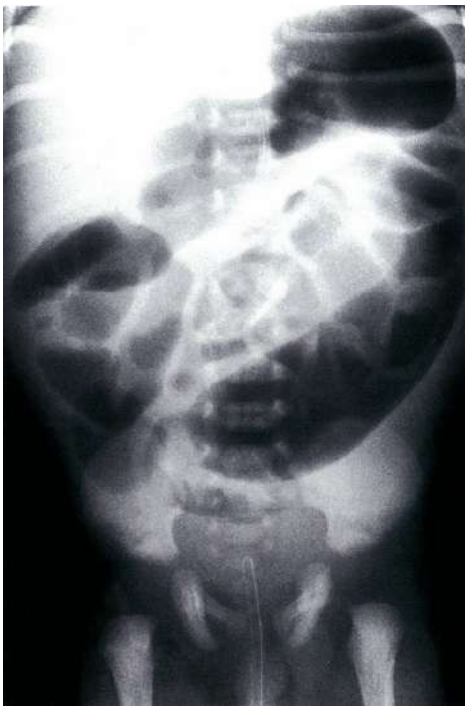
G - Hirschsprung disease

Image



Explanation Why

Hirschsprung disease can manifest with abdominal distention and bilious emesis secondary to obstruction from an aganglionic portion of the rectosigmoid colon. Failure to pass meconium for > 48 hours and a positive squirt sign would support this diagnosis. This patient is still within the expected time frame for meconium passage, however, and his gasless distal abdomen on x-ray suggests a bowel obstruction more proximal than the rectosigmoid colon. Dilated loops of the large bowel would be expected in Hirschsprung disease.

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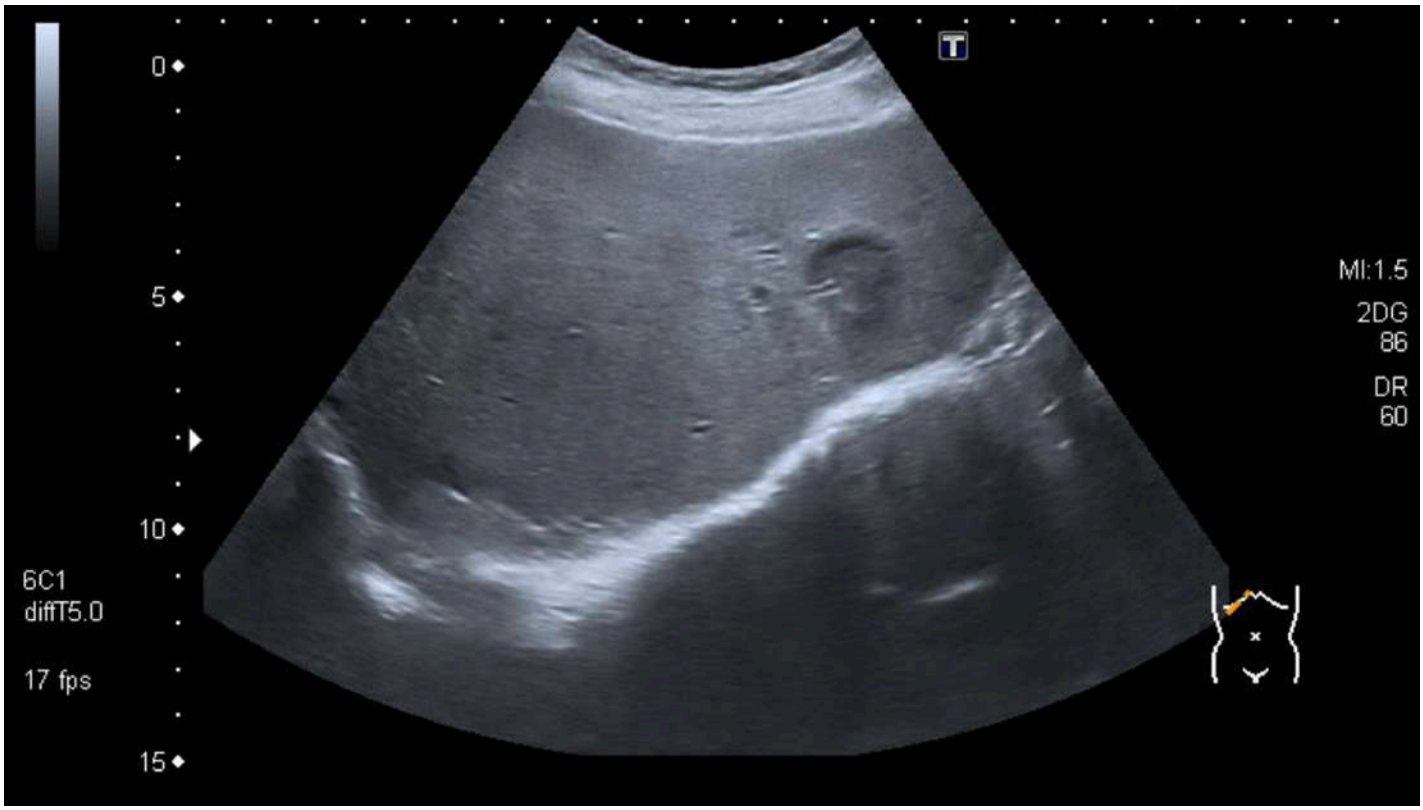
Question # 20

A 61-year-old man comes to the physician because of fatigue and a 5-kg (11-lb) weight loss over the past 6 months. He experimented with intravenous drugs during his 20s and has hepatitis C. His father died of colon cancer. He has smoked one pack of cigarettes daily for 35 years. Physical examination shows scleral icterus and several telangiectasias on the abdomen. The liver is firm and nodular. Laboratory studies show:

Hemoglobin	10.9 g/dL
Mean corpuscular volume	88 μm^3
Leukocyte count	10,400/mm^3
Platelet count	260,000/mm^3

Ultrasonography of the liver is shown. Which of the following additional findings is most likely?



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	Answer	Image
A	Bacteremia	
B	Bile duct strictures alternating with dilation	
C	Elevated antimitochondrial antibodies	
D	Elevated α-fetoprotein	
E	Lesion with eccentric calcification on chest CT	
F	Elevated carcinoembryonic antigen	
G	Annular colonic lesion on colonoscopy	

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Hint

This patient presents with signs of liver cirrhosis (scleral icterus, telangiectasias, nodular liver surface); ultrasonography shows a solitary, solid, isoechoic hepatic lesion. A history of hepatitis C is a risk factor for this patient's condition.

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Correct Answer

A - Bacteremia

Explanation Why

In a patient with a solitary liver lesion on ultrasonography, bacteremia, as indicated by positive blood cultures, is indicative of a pyogenic liver abscess. Pyogenic liver abscesses most commonly develop secondary to biliary tract obstructions but may also be caused by bacteremia (e.g., in IV drug users). However, since this patient no longer actively uses IV drugs, he is not at increased risk of bacteremia. While an abscess can be both the first manifestation or a complication of this patient's condition, in the absence of fever, malaise, RUQ pain, and leukocytosis, this diagnosis is less likely. Ultrasound findings would consist of a fluid-filled, hypoechoic lesion, unlike the solid, isoechoic lesion seen in this patient.

B - Bile duct strictures alternating with dilation

Explanation Why

Multifocal strictures alternating with dilation on cholangiography is seen in patients with primary sclerosing cholangitis (PSC). Although later disease stages can cause cirrhosis and hepatic tumors (e.g., HCC, cholangiocellular carcinoma [CCC]) that cannot be differentiated on ultrasound, ~ 90% of patients also have inflammatory bowel disease (IBD). Considering this patient's history of hepatitis C infection and the absence of symptoms of IBD, another diagnosis is more likely.

C - Elevated antimitochondrial antibodies

Explanation Why

In a patient with symptoms of liver cirrhosis, elevated antimitochondrial antibodies are indicative of primary biliary cholangitis (PBC). Although PBC is not directly associated with the formation of solitary liver lesions, it could be the cause of this patient's condition. However, PBC is much more common in women than in men. Additionally, the patient's history of hepatitis C makes another

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diagnosis more likely.

D - Elevated α-fetoprotein

Explanation Why

Both hepatitis infections and liver cirrhosis are risk factors for the development of hepatocellular carcinoma, which is usually asymptomatic except for features of the underlying disease. Diagnostic features include detection of a single hepatic lesion on ultrasound or CT and elevated levels of serum alpha-fetoprotein (AFP). Further symptoms may occur in advanced disease stages, including weight loss, cachexia, ascites, and jaundice.

E - Lesion with eccentric calcification on chest CT

Explanation Why

Detection of a lesion with eccentric calcification on chest CT is a finding highly suggestive of lung cancer. This patient is at increased risk for developing lung cancer because he has a history of smoking and is over 40 years old. However, since he has no symptoms of lung cancer (e.g., cough, hemoptysis, dyspnea), this diagnosis is less likely. Additionally, while lung cancer can metastasize to the liver, it would more likely manifest as multiple liver tumors rather than a solitary one. The patient's history of hepatitis C and signs of cirrhosis suggest another diagnosis.

F - Elevated carcinoembryonic antigen

Explanation Why

Elevated carcinoembryonic antigen (CEA) is a tumor marker that is primarily elevated in patients with colorectal and pancreatic cancer. Although both types of cancer can metastasize to the liver, symptomatic metastatic disease is unlikely without any prior symptoms of the underlying malignancy (e.g., melena, hematochezia, epigastric pain).

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G - Annular colonic lesion on colonoscopy

Explanation Why

An annular colonic lesion on colonoscopy is highly suggestive of colorectal cancer. The liver is the most common site of metastasis, which spreads via the portal vein. The patient has a family history of colorectal cancer and would require further workup to fully exclude this malignancy. However, he lacks typical symptoms of colorectal cancer (e.g., hematochezia, changes in bowel habits, iron deficiency anemia). Additionally, the presence of hepatitis C and cirrhosis suggests another diagnosis.

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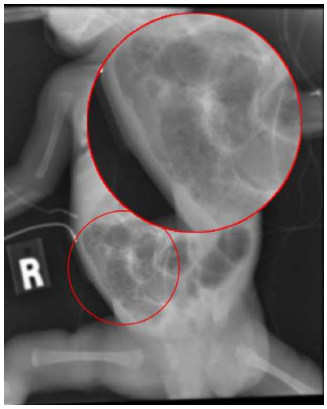
Question # 21

Two days after delivery, a 3470-g (7-lb 10-oz) newborn has an episode of bilious vomiting. He has not yet passed meconium. He was born at term to a 26-year-old woman; pregnancy and delivery were uncomplicated. His vital signs are within normal limits. Examination shows a distended abdomen. There is tympany to percussion. Digital rectal examination shows elevated sphincter tone; when the finger is removed, there is an explosive release of stool and air. An x-ray of the abdomen shows a massively dilated colon proximal to a narrowed segment of colon. Which of the following is the underlying cause of these findings?

	Answer	Image
A	Low serum T4 concentration	
B	Ischemic necrosis of the intestinal mucosa	
C	Jejunal vascular accident in utero	
D	Telescoping of intestinal segment into itself	
E	Incomplete coiling of the intestine	
F	Hypertrophy of the pyloric sphincter	

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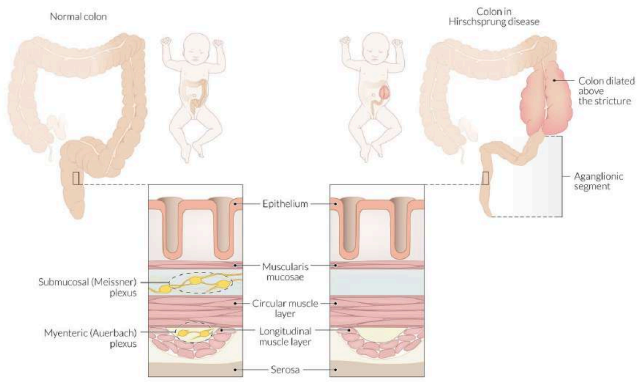
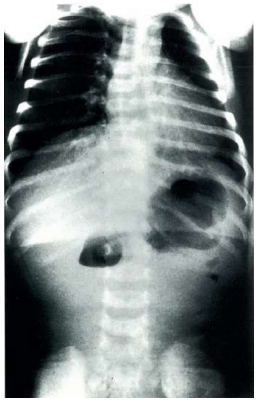
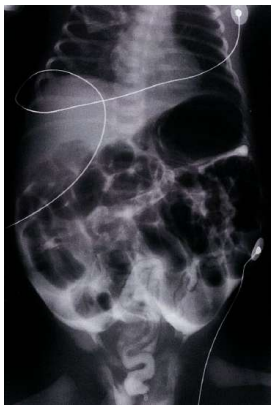
	Answer	Image
G	Impaired migration of neural crest cells	
H	Failure to restore patency to fetal duodenum	
I	Mutation in the CFTR gene	

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Hint

The patient presents with signs of distal intestinal obstruction (delayed passage of meconium, abdominal distention, bilious vomiting), and a DRE shows anal sphincter hypertonicity with an explosive release of stool and air, indicating elevated intraluminal pressure in the colon. X-ray of the abdomen shows megacolon with an area of distal narrowing. These findings are highly suggestive of Hirschsprung disease.

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Correct Answer

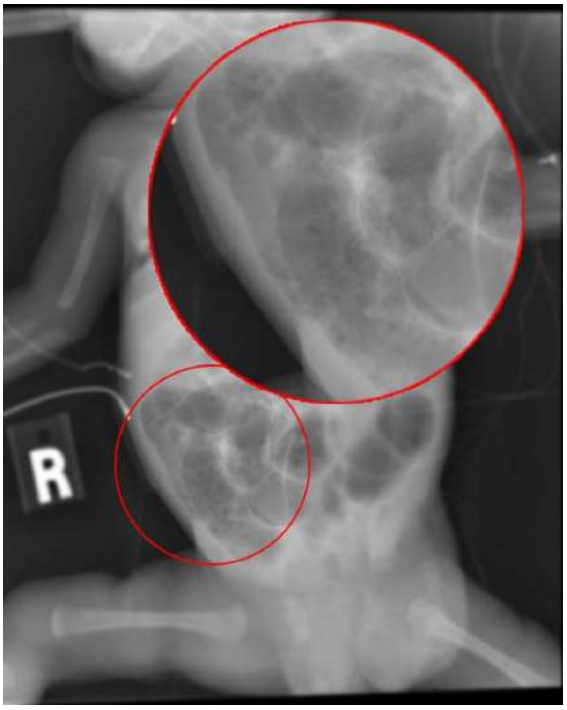
A - Low serum T4 concentration

Explanation Why

Low free T4 and high TSH concentrations indicate congenital hypothyroidism, which may in rare cases result in abdominal distention, a delay in passing meconium, bilious vomiting, and dilated bowel loops due to an adynamic ileus (pseudo-obstruction). However, both the small and large intestinal loops would be dilated. Features such as macroglossia, umbilical hernia, hypotonia, delayed reflexes, cool mottled skin, and/or prolonged neonatal jaundice would also be expected.

B - Ischemic necrosis of the intestinal mucosa

Image



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Explanation But

Prolonged intestinal obstruction in Hirschsprung disease can also result in enterocolitis and perforation of the bowel wall.

Explanation Why

Ischemic necrosis of the intestinal mucosa is seen in necrotizing enterocolitis, which can manifest with abdominal distention and bilious vomiting shortly after birth, However, an x-ray would typically show bowel wall edema, pneumatosis intestinalis, and/or free air within the abdomen (due to intestinal perforation). Also, patients typically have a history of bloody diarrhea (unlike this neonate, who has delayed passage of meconium), and the child would appear seriously ill with tachypnea and tachycardia. Moreover, this patient lacks the risk factors commonly associated with necrotizing enterocolitis, such as preterm birth and neonatal asphyxia.

C - Jejunal vascular accident in utero

Explanation Why

Disruption of blood flow to the fetal jejunum is responsible for jejunal atresia, which can also present with bilious vomiting, abdominal distention, and delayed passage of meconium. However, symptoms usually appear in feeding infants within 24 hours of birth, and x-ray of the abdomen would show a triple bubble sign.

D - Telescoping of intestinal segment into itself

Explanation Why

Intussusception, or telescoping of the proximal intestinal segment into the distal segment, is more common in males and may result in abdominal distention, bilious vomiting, and dilated bowel loops on x-ray due to intestinal obstruction. However, the small bowel would be distended (not the large bowel), since intussusception typically occurs at the ileocolic junction. Moreover, intussusception usually occurs between 5 months and 3 years of age; it is extremely rare in the neonatal period. Finally, blood in the rectum is often found on digital rectal examination, which was not the case here.

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E - Incomplete coiling of the intestine

Explanation Why

Intestinal malrotation can manifest within the first month of life with bilious vomiting and abdominal distention due to intestinal obstruction caused by Ladd bands or a midgut volvulus. However, x-ray would show a double bubble sign or multiple air-fluid levels proximal to the site of obstruction, in contrast to the distended descending colon seen in this patient

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F - Hypertrophy of the pyloric sphincter

Explanation Why

Hypertrophic pyloric stenosis, which is more common in males, may result in vomiting in the neonatal period. However, the vomiting is nonbilious, projectile, occurs following feeds, and usually begins 3–6 weeks after birth. An x-ray of the abdomen would show a distended stomach with minimal distention of the bowels. Other clinical features include decreased soiling of diapers (due to decreased urine output), as well as a hypertrophic “olive” in the epigastric region and/or a gastric peristaltic wave on examination.

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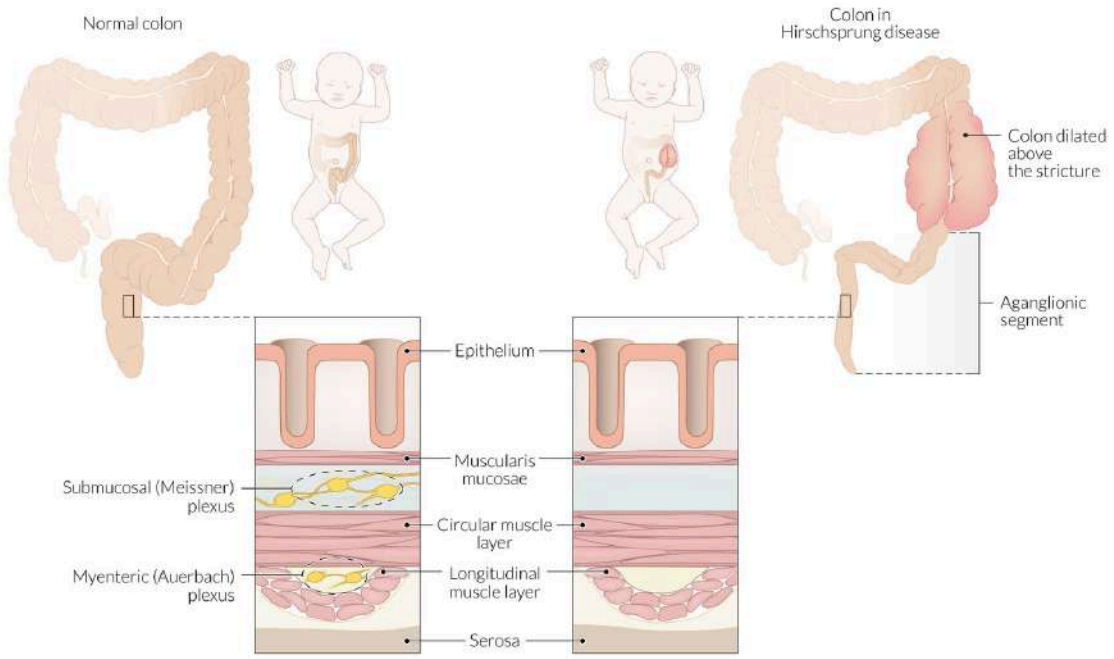
G - Impaired migration of neural crest cells

Image



Explanation Why

Impaired migration of neural crest cells is the underlying cause of Hirschsprung disease. Parasympathetic neural crest cells migrate in a rostral to caudal direction, from the foregut to the midgut to the hindgut. Failure of the neural crest cells to complete this migration typically results in an aganglionic distal sigmoid and rectum (i.e., without the myenteric and submucosal plexus). As a result, there is hypertonicity in the walls of the rectum and sigmoid, and the internal anal sphincter fails to relax in response to rectal distention. The net effect is intestinal obstruction and dilation of the colon (megacolon). The diagnosis is confirmed via rectal biopsy, which would show aganglionosis, increased acetylcholinesterase activity, and/or hyperplasia of parasympathetic fibers.

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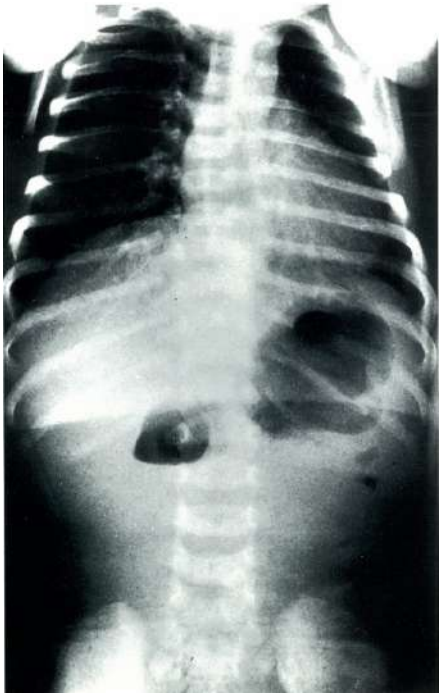
H - Failure to restore patency to fetal duodenum

Image



Explanation Why

Failure to restore patency to fetal duodenum results in duodenal atresia, which would also present with bilious vomiting and delayed passage of meconium. However, abdominal distention is typically not as prominent, and symptoms are usually evident on the first day after birth with the initiation of feeds. Additionally, the prenatal period is often complicated by polyhydramnios, and an x-ray of the abdomen would show a double bubble sign and absence of gas in the small and large intestine.

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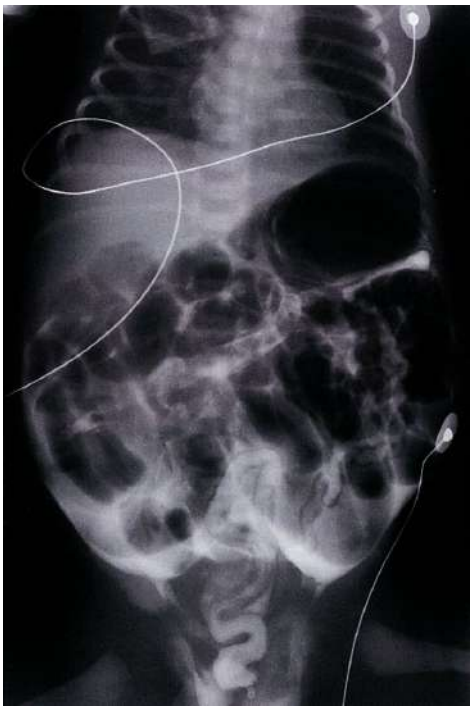
I - Mutation in the CFTR gene

Image



Explanation Why

A mutation in the CFTR gene is the underlying cause of cystic fibrosis, which may result in abdominal distention and bilious vomiting due to intestinal obstruction caused by thickened, inspissated meconium within the distal ileum (meconium ileus). However, x-ray in meconium ileus would typically show small bowel distention or a soap-bubble appearance (Neuhauser sign) rather than the distention of the descending colon seen here. A meconium plug in the rectum (meconium plug syndrome), which is seen with increased frequency in patients with cystic fibrosis, may manifest with distention of the descending colon and symptoms of functional intestinal obstruction. However, the sigmoid colon would usually be distended (unlike the narrow-caliber sigmoid colon seen here, and inspissated meconium would be palpable in the rectal cavity on digital examination.

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Question # 22

A 48-year-old woman comes to the emergency department because of a 1-day history of fever, vomiting, and abdominal pain. Two weeks ago, while visiting Guatemala, she had an emergency appendectomy under general inhalational anesthesia. During the surgery, she received a transfusion of 1 unit of packed red blood cells. Her temperature is 38.3°C (100.9°F) and blood pressure is 138/76 mm Hg. Examination shows jaundice and tender hepatomegaly. Serum studies show:

Alkaline phosphatase	132 U/L
Aspartate aminotransferase	760 U/L
Bilirubin	
Total	3.8 mg/dL
Direct	3.1 mg/dL
Anti-HAV IgG	positive
Anti-HAV IgM	negative
Anti-HBs	positive
HBsAg	negative
Anti-HCV antibodies	negative

Abdominal ultrasonography shows an enlarged liver. A biopsy of the liver shows massive centrilobular necrosis. Which of the following is the most likely underlying cause of this patient's condition?

	Answer	Image
A	Excessive lysis of red blood cells	
B	Acalculous inflammation of the gallbladder	

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	Answer	Image
C	Virus-mediated hepatocellular injury	
D	Trauma to the bile duct	
E	Adverse effect of anesthetic	
F	Gram-negative bacteria in the bloodstream	

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Hint

After undergoing surgery, this patient developed jaundice, fever, vomiting, and tender hepatomegaly, with highly elevated serum transaminases, which indicates acute postoperative hepatitis.

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Correct Answer

A - Excessive lysis of red blood cells

Explanation Why

Excessive lysis of red blood cells can occur postoperatively due to hemolytic transfusion reactions. This patient's transfusion of 1 unit of packed red blood cells during surgery may have caused a hemolytic transfusion reaction. However, clinical features (e.g., fever, chills, nausea, flank pain, allergic symptoms) would have appeared shortly after transfusion and laboratory findings would most likely show indirect hyperbilirubinemia. Furthermore, the findings on this patient's liver biopsy are not consistent with a hemolytic transfusion reaction.

B - Acalculous inflammation of the gallbladder

Explanation Why

While acalculous cholecystitis can manifest with postoperative jaundice and increased ALP levels, this diagnosis is unlikely in the absence of a positive Murphy sign and evidence of gallbladder inflammation on ultrasound (e.g., gallbladder wall thickening and pericholecystic fluid). Moreover, very high AST levels and the finding on this patient's liver biopsy are not consistent with acalculous cholecystitis.

C - Virus-mediated hepatocellular injury

Explanation Why

While viral hepatitis is an uncommon cause of postoperative hepatitis, it may result from a hospital outbreak or an exacerbation of chronic hepatitis. However, given this patient's hepatitis antibody panel, viral hepatitis is unlikely. This patient is positive for anti-HAV IgG but negative for anti-HAV IgM, indicating a previous hepatitis A infection that has resolved. She is also negative for hepatitis C antibodies. In addition, this patient is anti-HBs positive, but HBsAg-negative, indicating either a resolved prior infection or a vaccination. Moreover, viral hepatitis predominantly affects the periportal region unlike this patient with centrilobular necrosis.

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D - Trauma to the bile duct

Explanation Why

Trauma to the bile duct is a common complication of upper-abdominal surgery, especially cholecystectomy, and can manifest with acute hepatitis, which is seen in this patient. Subsequent scarring of the bile duct may lead to stricture formation, which in turn causes cholestasis. However, this complication is rare after appendectomy. Moreover, liver biopsy would show intraparenchymal cholestasis (not centrilobular necrosis), manifesting as bile pigment accumulation.

E - Adverse effect of anesthetic

Explanation But

Halothane is not commonly used as an anesthetic in the United States (and most other industrialized countries) because of its side effects. Instead, it has been replaced with other inhalational anesthetics, such as desflurane, sevoflurane, or isoflurane. However, halothane is still frequently used in developing countries because it is less expensive than other substances.

Explanation Why

This patient's acute postoperative hepatitis is highly suggestive of halothane hepatitis. Halothane hepatitis commonly leads to elevated serum aminotransferases, elevated bilirubin, eosinophilia, and slightly elevated alkaline phosphatase, as seen in this patient. This patient's symptoms began 13 days following surgery, which is consistent with the timeframe for postoperative onset of halothane hepatitis (2 days to 3 weeks). Liver biopsy is not necessary for diagnosis but typically shows massive centrilobular hepatic necrosis.

F - Gram-negative bacteria in the bloodstream

Explanation Why

Gram-negative sepsis is a complication of surgery that can manifest with acute hepatitis as a result of

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liver damage secondary to endotoxin release. However, in the case of sepsis, the patient would also likely present with hypotension and high spiking fevers.

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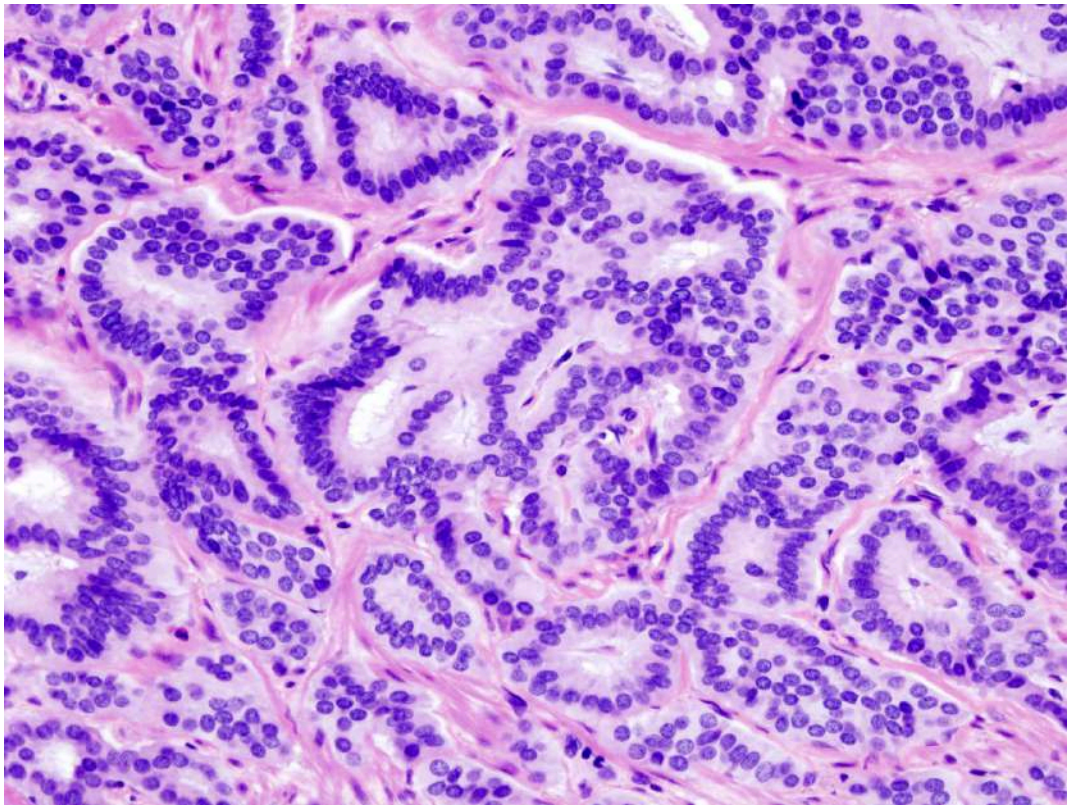
Question # 23

A previously healthy 67-year-old man comes to the physician because of a history of recurrent right lower abdominal pain for the past 2 years. A CT scan shows a 1.2-cm (0.47-in) mass located in the terminal ileum. He undergoes surgical removal of the mass. A photomicrograph of the resected specimen is shown. Cells from this tissue are most likely to stain positive for which of the following?



	Answer	Image
A	Desmin	
B	Chromogranin A	

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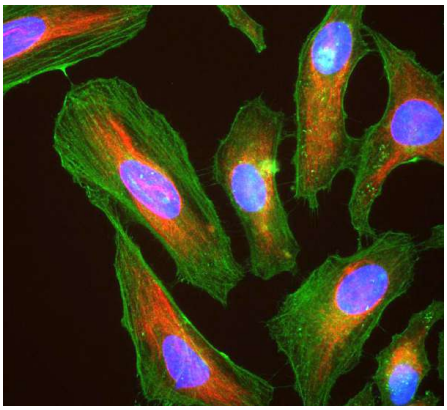
	Answer	Image
C	Vimentin	
D	P-glycoprotein	
E	Cytokeratin	
F	Glial fibrillary acid protein	

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Hint

The photomicrograph shows a tissue specimen of a neuroendocrine origin consistent with a carcinoid tumor.

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Correct Answer

A - Desmin

Explanation Why

Desmin is a protein that is found in all types of muscle (i..e, skeletal, smooth, and cardiac muscle). Therefore, immunostaining with desmin would be positive for a sarcoma arising from muscle (i.e., rhabdomyosarcoma). As sarcomas mimic the cell of origin on histology, muscular sarcomas will show skeletal/smooth/cardiac muscle cells in various stages of differentiation. This image shows monomorphic cells arranged in a rosette pattern characteristic of a carcinoid tumor. Since it does not originate from muscular cells, it would not stain with desmin.

B - Chromogranin A

Explanation Why

Chromogranin A is a protein that is found in neuroendocrine cells, which are mainly present in the pancreas (i.e., islet cells), gastrointestinal tract, lungs, and adrenal glands. The biopsy of this patient's ileal mass shows numerous small cells of similar shape and size (monomorphic cells) arranged in a rosette pattern that is typical of a carcinoid tumor. Chromogranin A, synaptophysin, and neuron-specific enolase can be used as an immunostain to confirm the neuroendocrine origin of this tumor.

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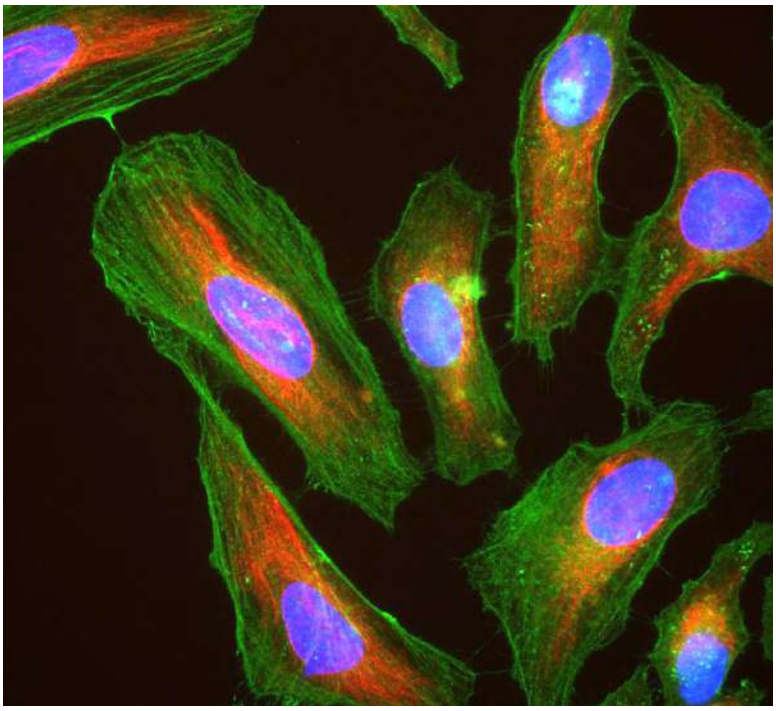
C - Vimentin

Image



Explanation Why

Vimentin is a cytoskeletal protein that is predominantly found in cells of mesenchymal origin, including cells of the musculoskeletal system (i.e., osteoblasts, chondroblasts, fibroblasts, adipocytes, endothelial cells) and cells of lymphatic and circulatory systems. Therefore, immunostaining with vimentin would be positive for mesenchymal tumors such as sarcomas. Sarcomas typically resemble the tissue of origin on histology (e.g., adipocytes in liposarcoma). This image shows monomorphic cells arranged in a rosette pattern characteristic of a carcinoid tumor. Since it is not of mesenchymal origin, it would not stain with vimentin.

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D - P-glycoprotein

Explanation Why

P-glycoprotein (Pgp) is a transporter protein found in most cells of the body and functions to remove certain metabolites, toxins, and drugs from within the cell (i.e., it is an efflux transporter). Pgp is overexpressed by several tumors (e.g., HCC, colonic cancer, adrenocortical tumor), but not carcinoid tumor, which this patient presents with.

E - Cytokeratin

Explanation Why

Cytokeratin is an intracytoplasmic protein found in cells of epithelial origin (i.e., lining cells of the gastrointestinal, respiratory, urinary, and reproductive tracts). Therefore, immunostaining with cytokeratin would be positive in epithelial tumors (e.g., squamous cell carcinoma (SCC), adenocarcinoma). On histology, well-differentiated SCC would show evidence of keratinization, while adenocarcinomas would show glandular architecture. This image shows monomorphic cells arranged in a rosette pattern characteristic of a carcinoid tumor. Since it does not originate from epithelial cells, it would not stain with cytokeratin.

F - Glial fibrillary acid protein

Explanation Why

Glial fibrillary acid protein (GFAP) is a cytoskeletal protein found exclusively in some cells of the CNS (i.e., astrocytes, Schwann cells, and oligodendrocytes), so immunostaining with GFAP would be positive in certain CNS tumors (e.g., astrocytoma, glioblastoma). As this patient has a tumor of neuroendocrine origin, cells from this mass would not stain with GFAP.

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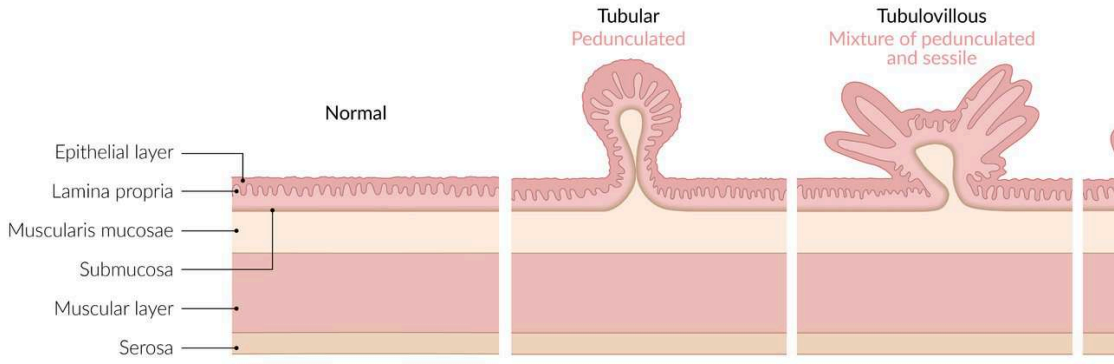
Question # 24

A 67-year-old woman comes to the physician because of a 9-month history of progressive fatigue. Examination shows pallor. Her hemoglobin concentration is 8.9 g/dL, mean corpuscular volume is 75 μm^3, and serum ferritin is 6 ng/mL. Test of the stool for occult blood is positive. Colonoscopy shows an irregular, bleeding 3-cm exophytic ulcer in the right colon. Which of the following lesions is the greatest risk factor for this patient's condition?

	Answer	Image
A	Submucosal lipomatous polyp	
B	Sessile hamartomatous polyp	
C	Serrated hyperplastic polyp	
D	Villous adenomatous polyp	

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	Answer	Image
E	Tubular adenomatous polyp	
F	Submucosal leiomyomatous polyp	
G	Pedunculated inflammatory polyp	

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Hint

This patient presents with symptomatic iron deficiency anemia and is found to have an irregular, ulcerative growth in the right colon. These findings are highly suggestive of colorectal cancer.

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Correct Answer

A - Submucosal lipomatous polyp

Explanation Why

A submucosal lipomatous polyp carries a very low risk of malignant transformation. Lipomas are most commonly found subcutaneously. When found in the colon, they can become large, fungating, and ulcerated, which can mimic the appearance of primary colorectal cancer. If ulcerated, they may also rarely lead to (occult) gastrointestinal bleeding. However, lipomas do not cause constitutional symptoms, which this patient has.

B - Sessile hamartomatous polyp

Explanation Why

Sessile hamartomatous polyps are generally a benign finding and unlikely to result in malignant transformation, although in the context of certain conditions (i.e., Peutz-Jeghers syndrome, Juvenile polyps, and Cowden syndrome), they have an increased risk of malignant transformation.

C - Serrated hyperplastic polyp

Explanation Why

Serrated polyps carry a moderate risk of malignant transformation. Of the three main types of serrated polyps (hyperplastic, sessile serrated, and traditional serrated), hyperplastic polyps carry the lowest risk of malignancy because there is no dysplasia present.

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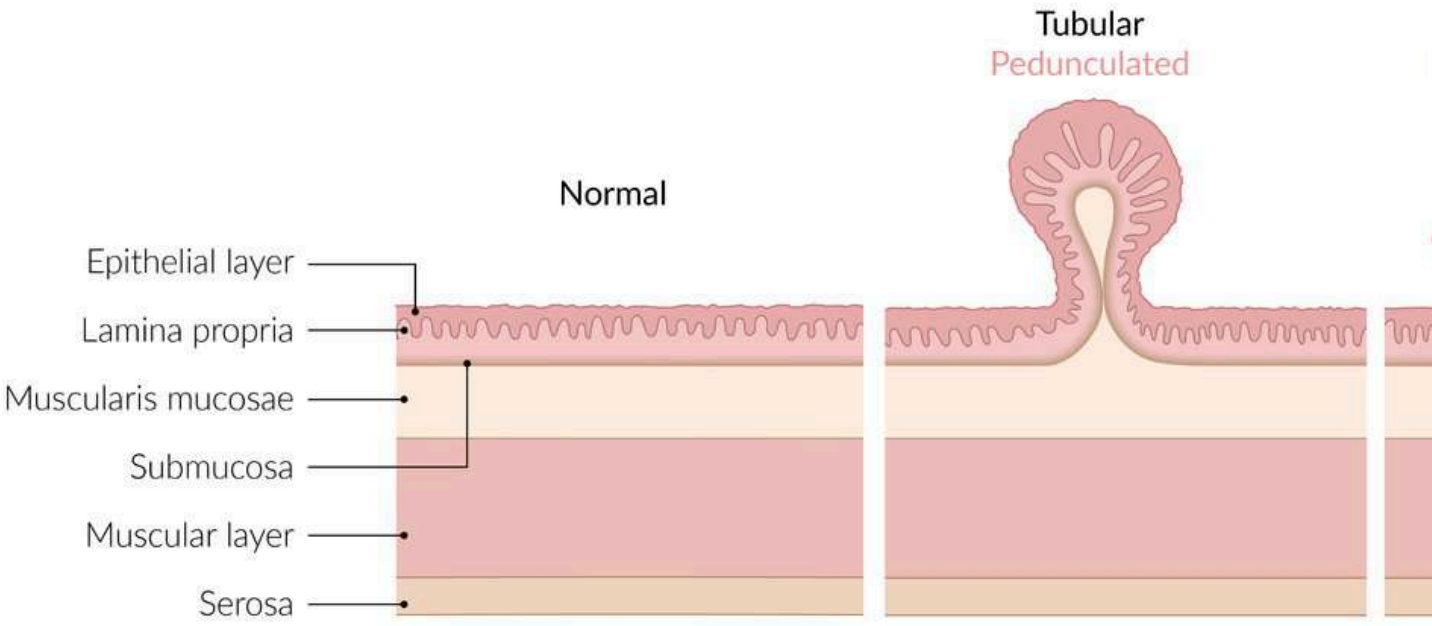
D - Villous adenomatous polyp

Image



Explanation Why

Adenomatous polyps (i.e., tubular adenoma, tubulovillous adenoma, or villous adenoma) carry the highest risk of malignant transformation of all types of colonic polyps. A villous adenomatous polyp has the highest risk (~ 50%) of malignant transformation of the three types of adenomatous polyps.

E - Tubular adenomatous polyp

Explanation Why

Tubular adenoma is the most common histological variety of colonic adenoma, comprising ~ 80% of all adenomatous polyps. These common polyps carry a relatively small risk of malignant transformation (~ 5%). Increasing size is associated with a higher risk of malignancy. However,

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another type of polyp is a greater predisposing factor for this patient's condition.

F - Submucosal leiomyomatous polyp

Explanation Why

A leiomyomatous polyp is most often a benign lesion of the muscularis propria or muscularis mucosa (smooth muscle of the gastrointestinal tract) with a very low potential for malignancy. Although they can present with pain, constipation, weight loss, and blood in stool, bleeding, as seen in this patient, it is unlikely to have been a predisposing factor as this type of polyp chiefly affects young women and girls.

G - Pedunculated inflammatory polyp

Explanation Why

A pedunculated inflammatory polyp, which is seen only in advanced IBD, does not carry any risk of neoplastic transformation. The tissue surrounding a pedunculated inflammatory polyp, as opposed to the inflammatory polyp itself, is prone to dysplasia and therefore at higher risk of neoplastic transformation.

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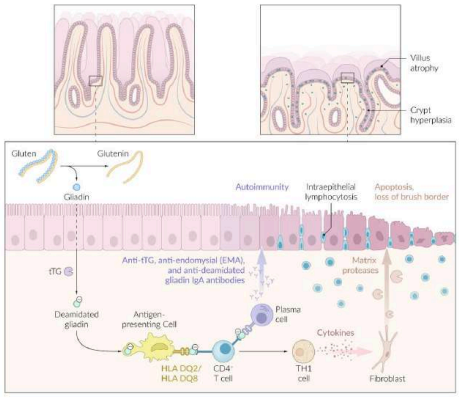
Question # 25

A 15-year-old girl is brought to the physician because of a 8-month history of fatigue, intermittent postprandial abdominal bloating and discomfort, foul-smelling, watery diarrhea, and a 7-kg (15-lb) weight loss. She developed a pruritic rash on her knees 3 days ago. Physical examination shows several tense, excoriated vesicles on the knees bilaterally. The abdomen is soft and nontender. Her hemoglobin concentration is 8.2 g/dL and mean corpuscular volume is 76 μm^3. Further evaluation of this patient is most likely to show which of the following findings?

	Answer	Image
A	IgA tissue transglutaminase antibodies	
B	Intraluminal esophageal membrane	
C	Oocysts on acid-fast stain	
D	Granulomatous inflammation of the terminal ileum	
E	Periodic acid-Schiff-positive macrophages	
F	Elevated serum amylase concentration	

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	Answer	Image
G	Trophozoites in stool	
H	Positive hydrogen breath test	

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Hint

Postprandial abdominal discomfort and bloating, chronic diarrhea, and severe microcytic anemia (likely secondary to iron deficiency) point to a malabsorptive syndrome. The additional presence of dermatitis herpetiformis (several tense, grouped subepidermal blisters) is strongly suggestive of celiac disease.

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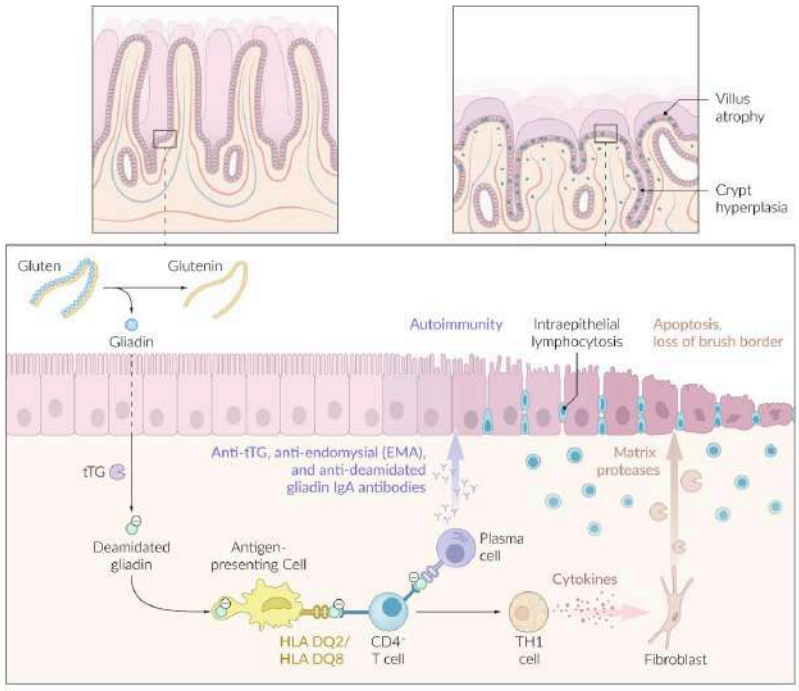
Correct Answer

A - IgA tissue transglutaminase antibodies

Image



Explanation Why

Testing for IgA tissue transglutaminase antibodies is the gold standard for diagnosing celiac disease and is also useful in monitoring a patient's response to treatment, as antibody levels start to decline and usually normalize 3–12 months following the introduction of a gluten-free diet. Although celiac disease can occur at any age, it most commonly manifests either in early childhood or between 20–40 years of age.

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B - Intraluminal esophageal membrane

Explanation Why

Esophageal webs are thin membranes of normal esophageal tissue protruding into the esophagus. They occur in Plummer-Vinson syndrome, which is associated with iron deficiency anemia. However, patients with Plummer-Vinson syndrome usually present with dysphagia and a burning sensation of the tongue; they can have an atrophic, smooth tongue on exam. Plummer-Vinson syndrome is not associated with abdominal pain, diarrhea, or dermatitis herpetiformis.

C - Oocysts on acid-fast stain

Explanation Why

Oocysts on acid-fast stain are seen in infection with *Cryptosporidium*, which can cause watery diarrhea. However, the infection is usually self-limited in immunocompetent hosts and resolves within 1–2 weeks. It is not associated with malabsorption or dermatitis herpetiformis.

D - Granulomatous inflammation of the terminal ileum

Explanation Why

Granulomatous intestinal inflammation, especially in the terminal ileum, is characteristic of Crohn disease, which can present with abdominal pain, symptoms of malabsorption such as iron deficiency anemia, and dermatologic diseases (e.g., erythema nodosum, acrodermatitis enteropathica). However, it is not associated with dermatitis herpetiformis.

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E - Periodic acid-Schiff-positive macrophages

Explanation Why

The finding of Periodic acid-Schiff-positive (PAS-positive) macrophages within the mucosa of the small intestine is the diagnostic hallmark of Whipple disease. Although patients with Whipple disease may also experience abdominal pain and malabsorption, this condition is primarily found in middle-aged men following infection with *Tropheryma whipplei*, and it is not associated with dermatitis herpetiformis.

F - Elevated serum amylase concentration

Explanation Why

Elevated serum amylase concentration is a nonspecific sign of acute pancreatitis, which can present with abdominal pain. The classic presentation is severe epigastric pain that radiates toward the back, worsening after meals; colicky episodes are present in gallstone pancreatitis. However, diarrhea is not usually seen in acute pancreatitis. Ileus (due to inflammation), fever, and a distended or elastic abdomen on palpation are common features of acute pancreatitis not seen in this patient. Finally, this patient has no risk factors for acute pancreatitis such as a history of gallstones, alcohol abuse, medication use, viral infections, or congenital disease.

G - Trophozoites in stool

Explanation Why

Multinucleated trophozoites in stool are characteristic of infection with *Giardia*, which can also cause abdominal pain, diarrhea, and malabsorption. However, the infection tends to self-resolve within a few weeks, and this patient has no history that indicates exposure to the waterborne parasite (e.g., drinking river water while camping). Infection with *Giardia* is not associated with dermatitis herpetiformis.

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H - Positive hydrogen breath test

Explanation Why

The hydrogen breath test is positive in patients with lactose intolerance, which can cause postprandial abdominal pain and diarrhea. However, lactose intolerance does not typically cause malabsorption, nor it is associated with dermatitis herpetiformis.

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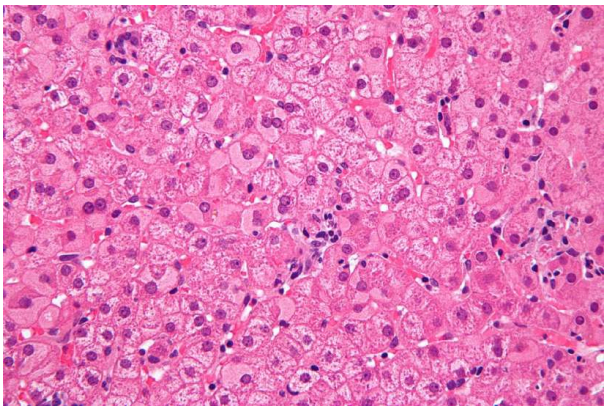
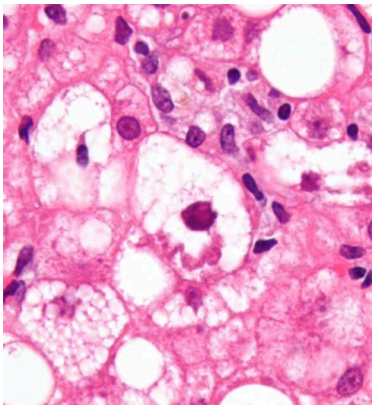
Question # 26

Two weeks after returning from vacation in Mexico, a 21-year-old man comes to the emergency department because of malaise, nausea, vomiting, fever, and abdominal pain. He has no history of serious illness and takes no medications. Physical examination shows scleral icterus and right upper quadrant tenderness. The liver is palpated 1.5 cm below the right costal margin. A biopsy specimen of this patient's liver would most likely show which of the following findings?

	Answer	Image
A	Concentric periductal fibrosis	
B	Ground glass hepatocytes and periportal inflammation	
C	Hepatocyte swelling and bridging necrosis	
D	Necrosis with neutrophilic infiltrate and Mallory bodies	

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	Answer	Image
E	Lymphocytic infiltration and progressive ductopenia	
F	Piecemeal necrosis and fatty changes	

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Hint

Acute onset of nausea, vomiting, fever, scleral icterus, right upper quadrant abdominal pain, and hepatomegaly following recent travel to Mexico are suggestive of acute hepatitis A infection.

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Correct Answer

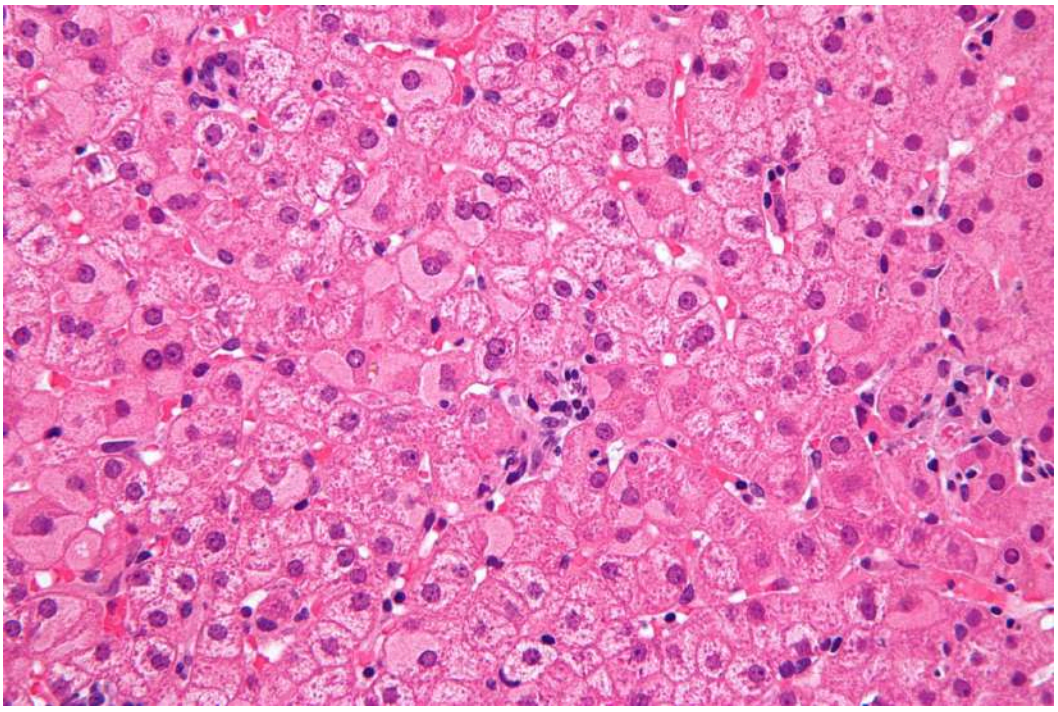
A - Concentric periductal fibrosis

Explanation Why

The onion-skin appearance of concentric periductal fibrosis of small bile ducts is a histopathological finding specific to primary sclerosing cholangitis (PSC). PSC manifests with jaundice, hepatomegaly, and right upper quadrant pain, similar to what is seen in this patient; however, PSC is a chronic, progressive disorder whereas this patient's symptoms developed over two weeks.

B - Ground glass hepatocytes and periportal inflammation

Image



Explanation Why

Ground glass hepatocytes are pathognomonic for chronic hepatitis B infection, while periportal

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inflammation with a lymphocytic infiltrate is a nonspecific histopathological finding consistent with chronic hepatitides. Acute hepatitis B infection can manifest with flu-like symptoms, scleral icterus, and right upper quadrant pain, all of which are seen here. However, hepatitis B is transmitted sexually and parenterally, and this patient does not have any risk factors for acquiring such an infection, e.g., IV drug use or high-risk sexual behavior.

C - Hepatocyte swelling and bridging necrosis

Explanation Why

Ballooning degeneration (swelling of hepatocytes due to depletion of ATP) and bridging necrosis (confluent necrosis spanning adjacent lobules) are histopathological findings seen in acute viral hepatitis. Other typical findings include Councilman bodies (reflecting shrunken hepatocytes that underwent apoptosis) and periportal infiltration with helper T cells, B cells, and plasma cells. While the virus has a minimally cytotoxic effect upon cells, the immunological response is the primary method of hepatocyte injury. Hepatitis A infection can manifest with acute symptoms or be asymptomatic, but it does not become chronic, unlike hepatitis B and hepatitis C infections.

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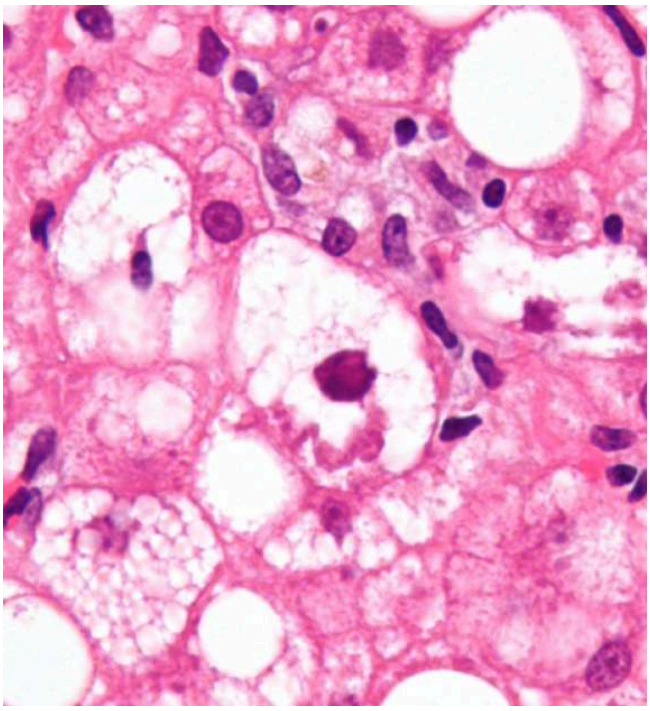
D - Necrosis with neutrophilic infiltrate and Mallory bodies

Image



Explanation Why

Necrosis with neutrophilic infiltrate and Mallory bodies is a histopathological finding that indicates alcoholic hepatitis. Patients with alcoholic hepatitis may present with nausea, icterus, fatigue, and hepatomegaly, all of which are seen here. However, alcoholic hepatitis typically manifests between 40–50 years of age in individuals with a history of daily, heavy alcohol use for more than 20 years, which is inconsistent with this patient's history.

E - Lymphocytic infiltration and progressive ductopenia

Explanation Why

Lymphocytic infiltration and progressive ductopenia are characteristic of primary biliary cholangitis (PBC). Patients present with malaise, jaundice, hepatomegaly, and right upper quadrant pain, as seen

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here. However, PBC is a chronic, progressive disorder whereas this patient's symptoms developed over two weeks. Moreover, additional symptoms such as pruritus, maldigestion, and xanthomas would be expected.

F - Piecemeal necrosis and fatty changes

Explanation Why

Piecemeal necrosis is characteristic of the degeneration of hepatocytes that occurs in chronic hepatitides such as hepatitis B and hepatitis C. Patients present with malaise, jaundice, hepatomegaly, and right upper quadrant pain, similar to what is seen here. However, this patient's symptoms developed over two weeks, and additional symptoms of chronic liver disease (e.g., spider angiomata, gynecomastia, easy bruising) would be expected. Moreover, this patient does not have any risk factors for acquiring these types of hepatitis infection, e.g., IV drug use or high-risk sexual behavior.

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Question # 27

A 57-year-old man comes to the physician because of generalized malaise, yellowish discoloration of the eyes, and pruritus on the back of his hands that worsens when exposed to sunlight for the past several months. He has not seen a physician in 15 years. Physical examination shows scleral icterus and mild jaundice. There is a purpuric rash with several small vesicles and hyperpigmented lesions on the dorsum of both hands. The causal pathogen of this patient's underlying condition was most likely acquired in which of the following ways?

	Answer	Image
A	Bathing in freshwater	
B	Ingestion of raw shellfish	
C	Needlestick injury	
D	Inhalation of spores	
E	Sexual contact	

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Hint

This patient's scleral icterus and jaundice should raise suspicion for liver disease. His pruritic rash that worsens upon exposure to sunlight is suggestive of porphyria cutanea tarda, a condition that is associated with hepatitis C virus infection.

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Correct Answer

A - Bathing in freshwater

Explanation Why

Bathing in freshwater is a risk factor for schistosomiasis, a helminthic infection that can manifest with various different clinical manifestations depending on the exact species involved. Hepatosplenic schistosomiasis could also cause signs of liver damage but it is not associated with porphyria cutanea tarda, as seen in this patient.

B - Ingestion of raw shellfish

Explanation Why

Ingestion of raw shellfish is one of the major transmission modes for hepatitis A, especially in regions with poor sanitation. Hepatitis C, which this patient most likely has, is not transmitted via food.

C - Needlestick injury

Explanation Why

Needlestick injury is a likely cause of this patient's hepatitis C infection as it is mainly transmitted parenterally. Therefore, certain populations such as health care workers and intravenous drug users are at increased risk of contracting the virus. Patients who received blood transfusions before 1992 are also at increased risk for hepatitis C, as donor blood was not screened for the virus before 1992. Other routes of transmission include vertical (from mother to fetus) and, rarely, sexual.

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D - Inhalation of spores

Explanation Why

The inhalation of spores is the mode of transmission for several different infections, including mucormycosis, Q fever, and pulmonary anthrax. Spore inhalation is not the mechanism of transmission for hepatitis C, which this patient has.

E - Sexual contact

Explanation Why

Sexual contact is the route of transmission for many infectious diseases, including syphilis, hepatitis B, and HIV. Hepatitis C may be transmitted sexually (especially in cases of HIV coinfection), however, this is very rare and another route of transmission is more likely.

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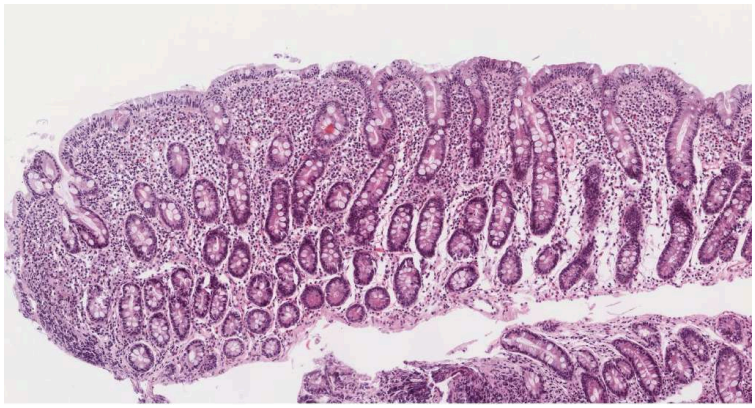
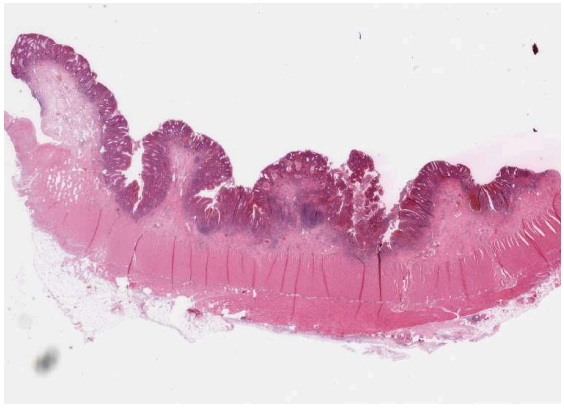
Question # 28

A 19-year-old woman comes to the physician because of a 1-year history of severe abdominal pain, bloating, and episodic diarrhea. She has also had a 10-kg (22-lb) weight loss over the past 10 months. Physical examination shows a mildly distended abdomen, diffuse abdominal tenderness, and multiple erythematous, tender nodules on the anterior aspect of both legs. There is a small draining lesion in the perianal region. Further evaluation of this patient's gastrointestinal tract is most likely to show which of the following findings?

	Answer	Image
A	Villous atrophy	
B	Crypt abscesses	
C	No structural abnormalities	

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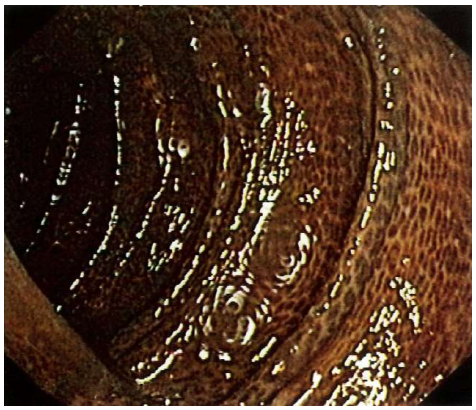
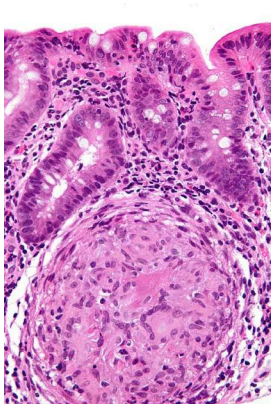
	Answer	Image
D	Melanosis coli	
E	Neuroendocrine tumor cells	
F	Transmural inflammation	

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Hint

Recurrent episodes of severe abdominal pain, diarrhea, and a perianal fistula with drainage in combination with erythema nodosum (multiple erythematous, tender nodules on the legs) are suggestive of a diagnosis of Crohn disease.

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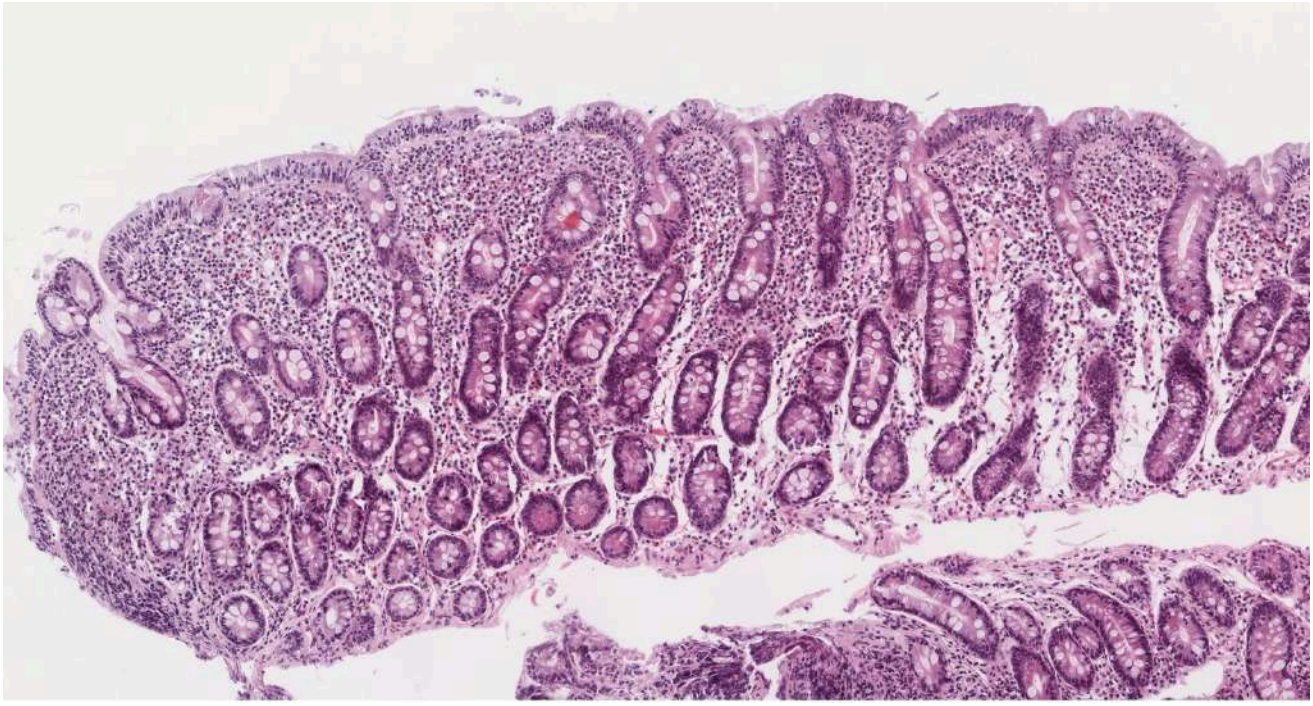
Correct Answer

A - Villous atrophy

Image



Explanation Why

Villous atrophy is a typical histopathologic finding in celiac disease. This condition can manifest with abdominal pain, bloating, diarrhea, and weight loss in some patients. However, extraintestinal symptoms are more common (e.g., vitamin deficiencies, dermatitis herpetiformis, depression, osteoporosis). This patient's erythema nodosum and fistulas are not associated with celiac disease.

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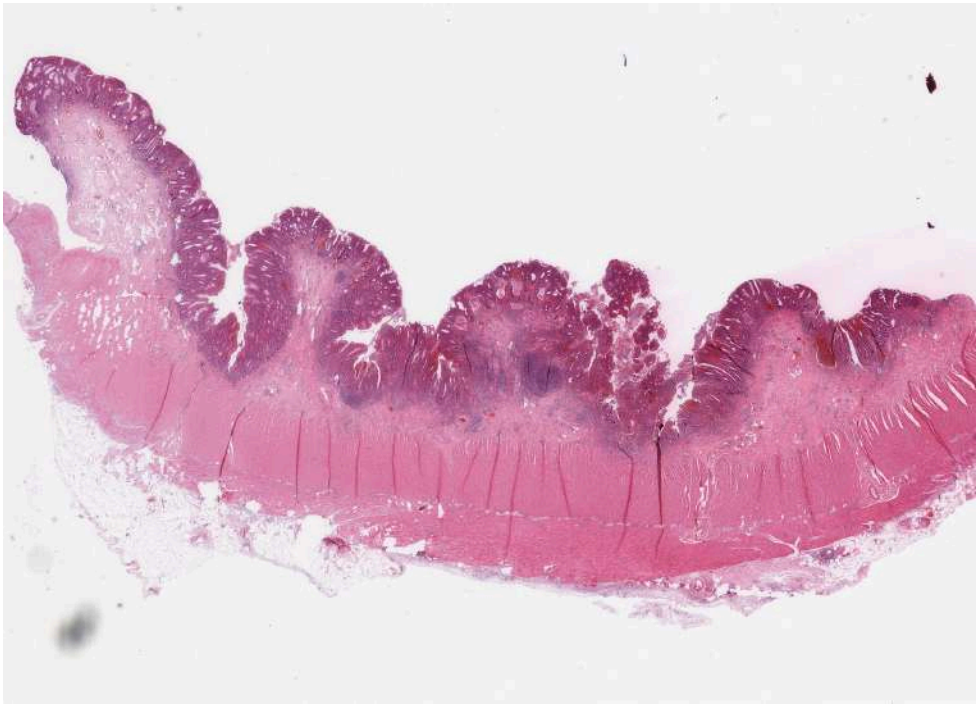
B - Crypt abscesses

Image



Explanation Why

Crypt abscesses are a typical histopathologic finding in ulcerative colitis (UC). UC can manifest with erythema nodosum, severe abdominal pain, bloating, and episodic diarrhea, which are seen in this patient. However, it is quite rare to see fistula formation in UC because inflammation is localized in the mucosal and submucosal layers.

C - No structural abnormalities

Explanation Why

No structural abnormalities of the gastrointestinal tract in a patient with abdominal pain, bloating, and episodic diarrhea would be concerning for irritable bowel syndrome (IBS). Though IBS could cause some of this patient's symptoms, it is not associated with findings like erythema nodosum or

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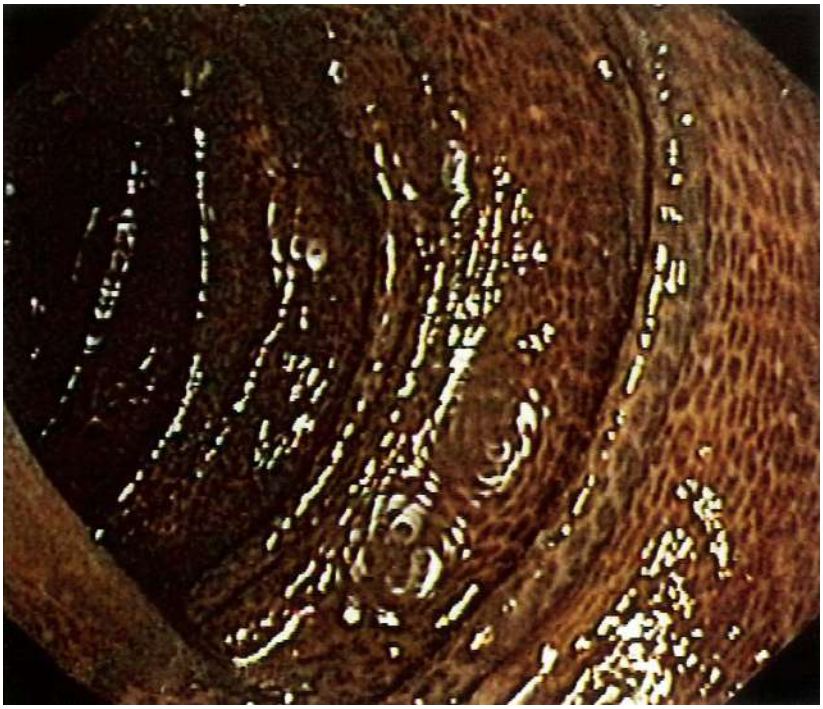
fistulas. In addition, patients with IBS generally appear healthy and do not typically manifest with weight loss.

D - Melanosis coli

Image



Explanation Why

Melanosis coli is a benign hyperpigmentation of the colonic epithelium seen in patients who abuse laxatives. Laxative abuse would cause abdominal pain, diarrhea, and weight loss, which are seen in this patient; however, it would not explain the presence of erythema nodosum or fistulas.

E - Neuroendocrine tumor cells

Explanation Why

Neuroendocrine tumor cells are found in carcinoid tumors. Diarrhea and abdominal cramps may

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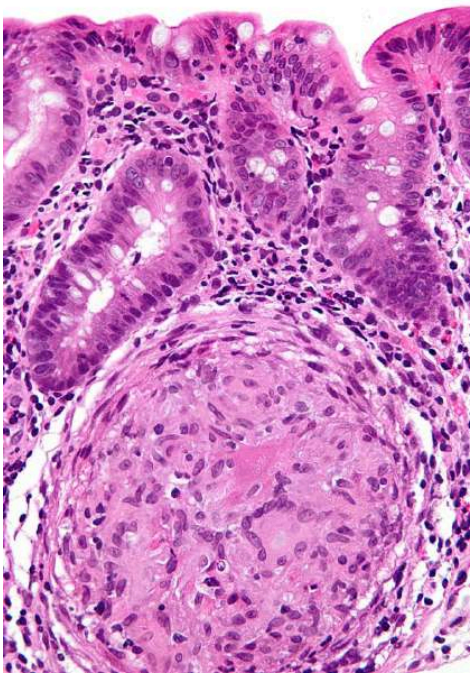
occur as part of carcinoid syndrome, but they are usually accompanied by other findings such as cutaneous flushing and bronchospasm (e.g., wheezing, dyspnea). Moreover, carcinoid tumors are not associated with erythema nodosum or fistulas.

F - Transmural inflammation

Image



Explanation Why

Transmural intestinal inflammation is a characteristic finding of Crohn disease. It commonly results in abscess and fistula formation, as seen in this patient. Endoscopy confirms the diagnosis, showing a discontinuous pattern of involvement with linear ulcers ("snail trails") and a cobblestone appearance of the affected GI areas (typically terminal ileum and colon). Biopsy reveals inflammation of all intestinal layers and noncaseating granulomas.

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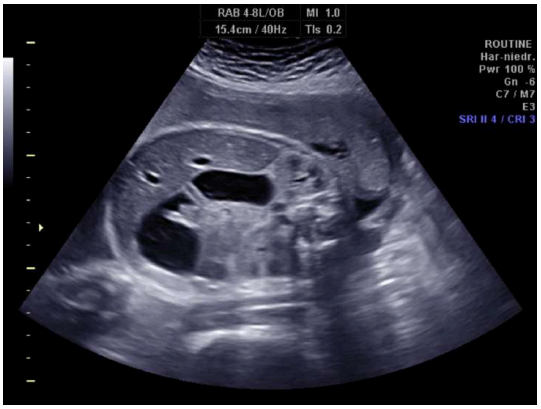
Question # 29

A 24-day-old infant girl is brought to the emergency department because of a 2-hour history of fever, vomiting, and diarrhea. She has fed less and has had decreased urine output for 1 day. She was born at 33 weeks' gestation and weighed 1400-g (3-lb 1-oz). Her diet consists of breast milk and cow milk protein-based formula. Examination shows abdominal rigidity, distention, and absent bowel sounds. Test of the stool for occult blood is positive. An x-ray of the abdomen shows gas within the intestinal wall and the peritoneal cavity. Which of the following is the most likely diagnosis?

	Answer	Image
A	Duodenal atresia	
B	Meckel diverticulum	
C	Meconium ileus	
D	Cow milk protein allergy	
E	Hirschsprung disease	

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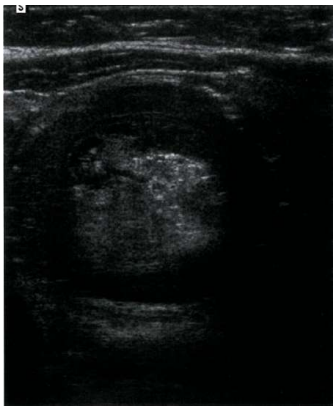
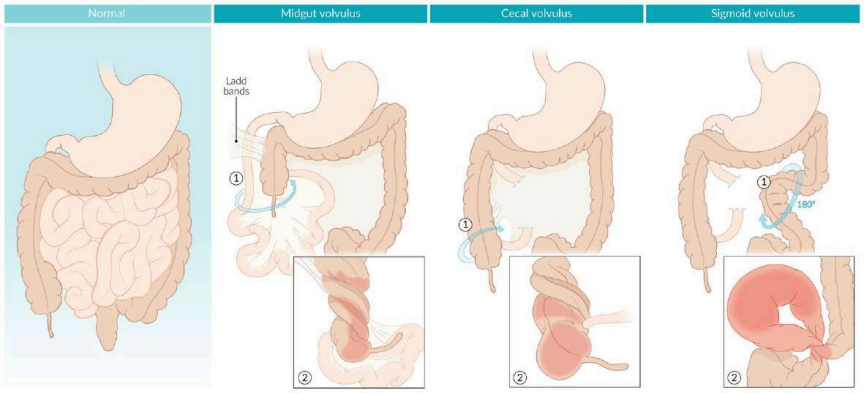
	Answer	Image
F	Intussusception	
G	Hypertrophic pyloric stenosis	
H	Necrotizing enterocolitis	
I	Malrotation with volvulus	

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Hint

Air in the intestinal wall, or pneumatosis intestinalis, is indicative of severe inflammation; air in the peritoneal cavity, or pneumoperitoneum, is suggestive of bowel rupture.

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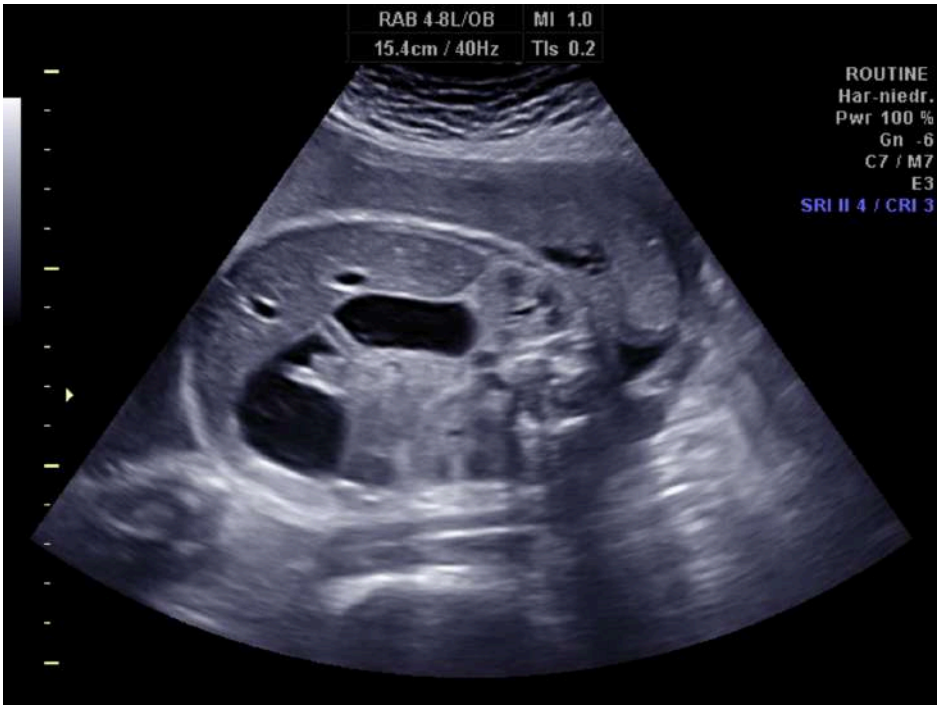
Correct Answer

A - Duodenal atresia

Image



Explanation Why

Duodenal atresia presents with abdominal distention, bilious emesis, and a prenatal history of polyhydramnios (since the fetus cannot drink the amniotic fluid due to the intestinal obstruction) but does not cause bloody diarrhea or peritonitis (i.e., abdominal rigidity and guarding). Abdominal x-ray would also show a double bubble sign rather than pneumatosis intestinalis. In addition, duodenal atresia is typically associated with chromosomal abnormalities, especially Down syndrome. This patient lacks any dysmorphic features to suggest a chromosomal abnormality.

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B - Meckel diverticulum

Explanation But

Remember the rule of 2's: Meckel's diverticulum occurs in 2% of the population, usually manifests in the first 2 years of life, has a length of 2 inches, is located 2 feet from the ileocecal valve, and often consists of 2 types of tissue (mostly gastric and pancreatic tissue).

Explanation Why

Meckel diverticulum is the most likely cause of painless hematochezia in children < 2 years old. Patients are often asymptomatic but may present with abdominal pain and hematochezia in case of infection, secondary volvulus, or bowel obstruction due to secondary intussusception. Meckel diverticulum requires a technetium-99m pertechnetate scan for visualization; it cannot be seen on a plain abdominal x-ray. Furthermore, it is not associated with pneumatosis intestinalis.

C - Meconium ileus

Explanation Why

Meconium ileus can present with abdominal distention and bilious emesis due to ileal obstruction from impacted stool. This diagnosis is suspected when meconium fails to pass within the first 48 hours of life; it is strongly associated with cystic fibrosis (~ 90% of cases). Abdominal x-ray of meconium ileus shows dilated loops of small bowel above the terminal ileum. Although this patient presents with absent bowel sounds and vomiting, a diagnosis of meconium ileus is inconsistent with his diarrhea, the x-ray findings, and the onset of symptoms > 2 weeks after delivery.

D - Cow milk protein allergy

Explanation But

Symptoms of cow milk protein allergy (CMA) typically resolve following withdrawal of the offending agent.

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Explanation Why

Cow milk protein allergy (CMA) is the most common food allergy in children and either presents with syndromes occurring immediately after ingestion of cow milk protein (IgE-mediated) such as anaphylaxis, urticaria, and angioedema, or in syndromes with a delayed onset (non-IgE-mediated) such as protein-induced proctocolitis and/or enterocolitis. Infants with protein-induced proctocolitis may present with rectal bleeding but otherwise appear well. Patients with food protein-induced enterocolitis present with diarrhea, severe vomiting 1–3 hours following antigen ingestion, dehydration, and lethargy, but symptoms that suggest peritonitis, such as abdominal rigidity, are uncommon. An abdominal x-ray in protein-induced colitis would show air-fluid levels rather than pneumatosis intestinalis.

E - Hirschsprung disease

Explanation Why

Hirschsprung disease can present with abdominal distention, bilious emesis, and an inability to pass stool secondary to obstruction from an aganglionic portion of the rectosigmoid colon. Failure to pass meconium for > 48 hours and a positive squirt sign would further support this diagnosis. If the disease is complicated by enterocolitis, explosive bloody diarrhea is common. However, in Hirschsprung disease, abdominal x-ray would show an absence of gas in the distal colon with a dilated bowel proximally rather than the pneumatosis intestinalis seen here.

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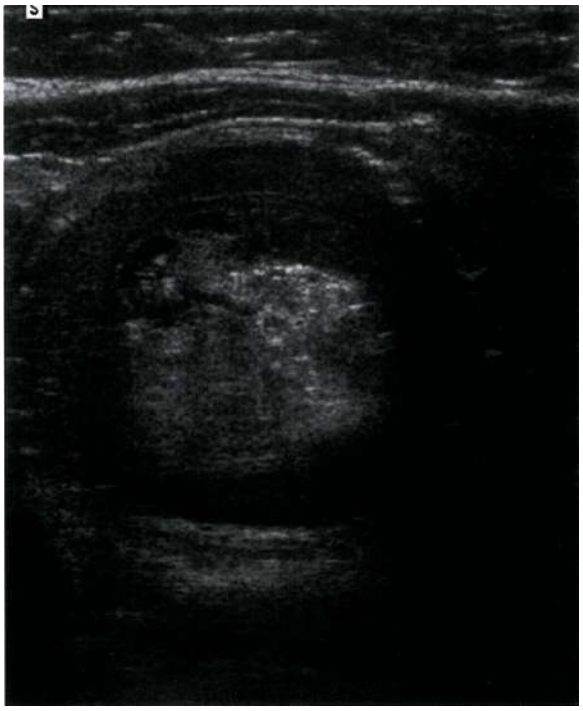
F - Intussusception

Image



Explanation But

Ultrasound is the imaging test of choice for the diagnosis of intussusception. Typical findings are the target sign and the pseudokidney sign.

Explanation Why

Patients with intussusception typically present with the classic triad of episodic abdominal pain, vomiting, and currant-jelly stool (composed of blood and mucus). While this patient presents with abdominal tenderness, vomiting, and lower gastrointestinal bleeding (albeit occult, not gross), she is younger than would be expected for this diagnosis (i.e., children 3 months to 6 years of age) and also does not have a characteristic sausage-shaped abdominal mass. In intussusception, an abdominal x-ray would not show pneumatosis intestinalis; instead, it may reveal a soft tissue mass (typically in the upper right quadrant in children) with proximal bowel obstruction (e.g., air-fluid levels and bowel dilation)

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G - Hypertrophic pyloric stenosis

Explanation But

Ultrasound is the diagnostic test of choice in hypertrophic pyloric stenosis and typically reveals an elongated and thickened pylorus.

Explanation Why

Hypertrophic pyloric stenosis (HPS) can present with abdominal distention, severe postprandial, nonbilious, projectile vomiting, and failure to thrive starting 3–6 weeks after birth, but it is not typically associated with diarrhea or hematochezia. Also, a palpable, olive-shaped mass is often present on examination of the epigastrium (hypertrophic pylorus). Abdominal x-ray in HPS may show stomach distention; it would not show pneumatosis intestinalis.

H - Necrotizing enterocolitis

Explanation But

If uncomplicated NEC (i.e., without perforation/peritonitis) is diagnosed, IV broad-spectrum antimicrobial regimen with supportive care (i.e., bowel rest, total parenteral nutrition, fluid replacement, and cardiovascular/respiratory support) are the management of choice. Serial abdominal x-rays should be conducted every 6 hours to exclude perforation.

Explanation Why

Necrotizing enterocolitis (NEC) is the most common cause of an acute abdomen in premature infants with low birth weight. It typically occurs 2–4 weeks after birth, once oral feeding has begun. Infants present with poor feeding, lethargy, vomiting, diarrhea, hematochezia, and/or a distended abdomen with decreased bowel sounds, all of which are present in this infant. X-ray of the abdomen showing pneumatosis intestinalis confirms the diagnosis of NEC. Other typical x-ray findings include dilated bowel loops, portal venous gas, and abdominal free air in the case of bowel perforation (seen in this case). Bowel perforation requires emergent laparotomy and likely resection of the affected bowel to prevent progression of bowel necrosis, DIC, and shock.

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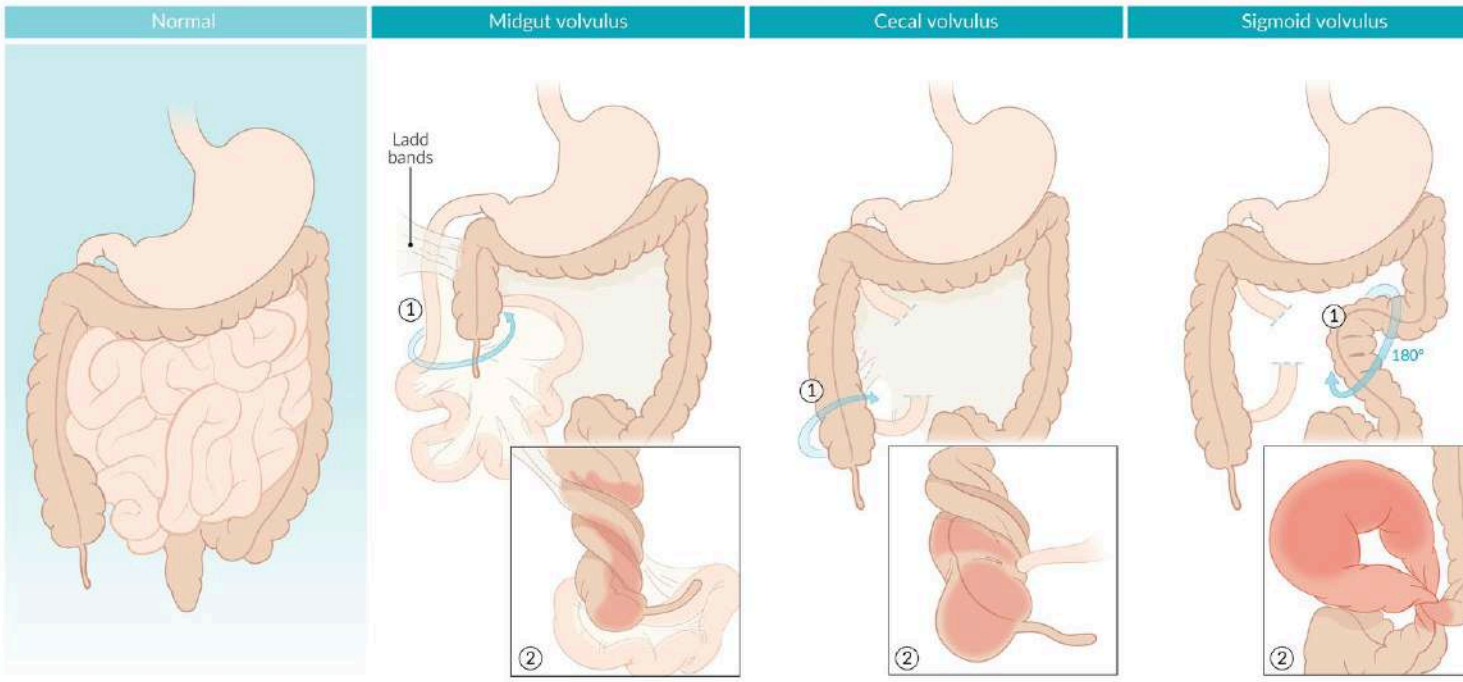
I - Malrotation with volvulus

Image



Explanation Why

Malrotation with volvulus can present with abdominal distention and bilious emesis due to intestinal obstruction from twisting (i.e., volvulus) of the bowel. Bright red blood per rectum may also be present due to intestinal necrosis. Abdominal x-ray may show a coffee bean sign in sigmoid volvulus and a kidney bean sign in cecal volvulus; it would not show pneumatosis intestinalis.

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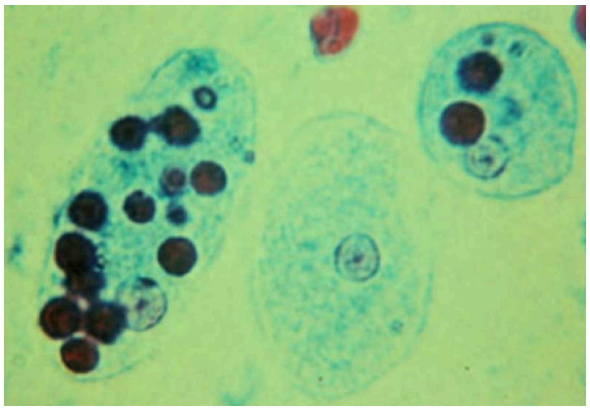
Question # 30

A 21-year-old woman comes to the physician because of a 2-month history of fatigue, intermittent abdominal pain, and bulky, foul-smelling diarrhea. She has had a 4-kg (8-lb 12-oz) weight loss during this period despite no changes in appetite. Examination of the abdomen shows no abnormalities. Staining of the stool with Sudan III stain shows a large number of red droplets. Which of the following is the most likely underlying cause of this patient's symptoms?

	Answer	Image
A	Ulcerative colitis	
B	Carcinoid syndrome	
C	Amebiasis	
D	Irritable bowel syndrome	
E	Lactose intolerance	
F	Celiac disease	

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Hint

Sudan III staining is used to identify lipids in a sample. Foul-smelling diarrhea with fat in the stool (steatorrhea) indicates fat malabsorption.

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Correct Answer

A - Ulcerative colitis

Explanation But

Fat malabsorption and steatorrhea are more common with Crohn disease, which often affects the small intestine. Rarely, ileal involvement can occur in UC due to "backwash ileitis".

Explanation Why

Ulcerative colitis (UC) can manifest with recurring episodes of diarrhea, intermittent abdominal pain, fatigue (due to anemia), and weight loss (due to recurrent inflammation and anorexia). However, patients with UC would also have symptoms such as tenesmus and mucoid or bloody stools (hematochezia), which are not reported in this patient. Fat malabsorption and steatorrhea are unusual in UC because the small intestine, which is the site of fat absorption, is usually spared.

B - Carcinoid syndrome

Explanation Why

Carcinoid syndrome can cause diarrhea, abdominal pain, and weight loss. However, carcinoid syndrome would not cause fat malabsorption and steatorrhea, and affected individuals commonly present with additional symptoms, such as cutaneous flushing, wheezing, and dyspnea, none of which are present here.

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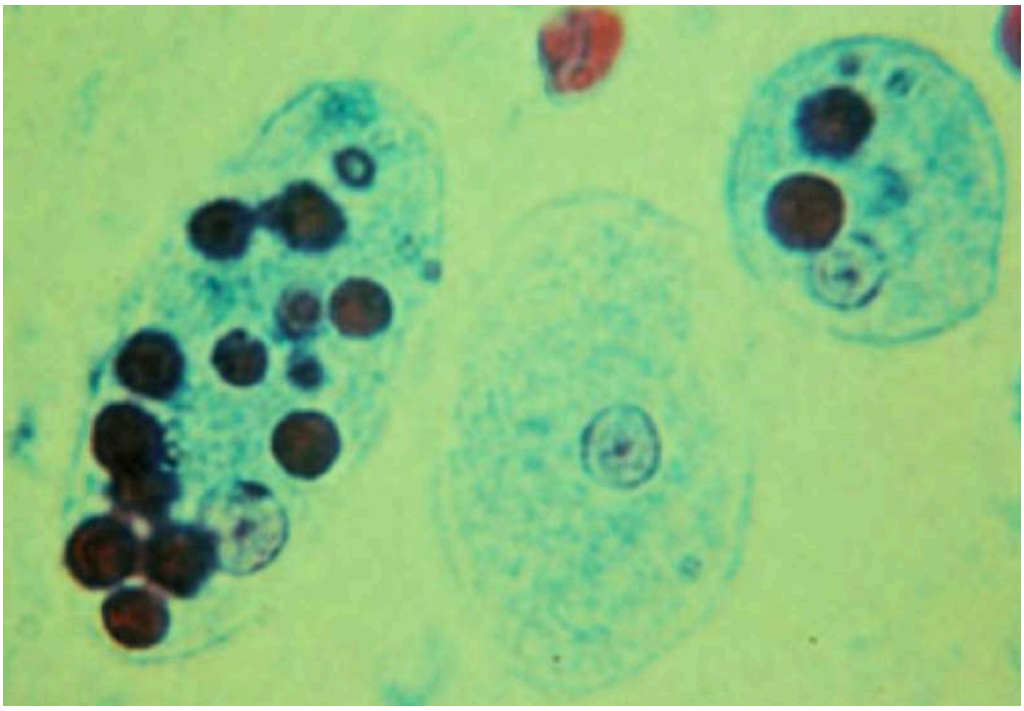
C - Amebiasis

Image



Explanation Why

Symptomatic intestinal amebiasis would result in abdominal pain but fever and bloody diarrhea rather than steatorrhea would be expected, and stool examination would show trophozoites with engulfed erythrocytes or cysts with 1–4 nuclei. Moreover, the organism that causes amebiasis, *E. histolytica*, is most commonly found in tropical and subtropical regions, and this patient does not report any recent travel history.

D - Irritable bowel syndrome

Explanation Why

Irritable bowel syndrome (IBS) can manifest with altered bowel movements (diarrhea or constipation) and abdominal cramping but weight loss, steatorrhea, and fatigue would not occur with

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irritable bowel syndrome.

E - Lactose intolerance

Explanation Why

Lactose intolerance can manifest with intermittent abdominal pain and diarrhea. However, individuals with lactose intolerance usually describe a direct connection between consumption of dairy products and onset of symptoms and complain of significant flatulence. Moreover, lactose intolerance alone would not cause fat malabsorption and steatorrhea.

F - Celiac disease

Explanation But

Other important causes of fat malabsorption and steatorrhea are pancreatic insufficiency (e.g., cystic fibrosis), Crohn disease, biliary cirrhosis, Whipple disease, abetalipoproteinemia, somatostatinoma and certain drugs (e.g., octreotide, ezetimibe, bile acid resins)

Explanation Why

Celiac disease (CD) is an inflammatory autoimmune condition caused by hypersensitivity to gliadin. It predominantly affects the duodenum and jejunum and is characterized by villous atrophy, crypt hyperplasia, and intraepithelial lymphocytosis. Patients are often asymptomatic but can present at any age with gastrointestinal symptoms such as crampy abdominal pain, fat malabsorption, and steatorrhea as well as extraintestinal manifestations (e.g., symptoms of fat-soluble vitamin deficiency, anemia, depression, dermatitis herpetiformis). Patients with celiac disease are often positive for IgA anti-tissue transglutaminase, anti-endomysial, and anti-deamidated gliadin peptide antibodies. Celiac disease is most common among individuals of northern European descent and is associated with HLA-DQ2 and HLA-DQ8 haplotypes.

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Question # 31

A 27-year-old woman who recently emigrated from Brazil comes to the physician because of fever, fatigue, decreased appetite, and mild abdominal discomfort. She has not seen a physician in several years and her immunization status is unknown. She drinks 2 alcoholic beverages on the weekends and does not use illicit drugs. She is sexually active with several male partners and uses condoms inconsistently. Her temperature is 38°C (99.8°F). Physical examination shows right upper quadrant tenderness and scleral icterus. Serology confirms acute infection with a virus that has partially double-stranded, circular DNA. Which of the following is most likely involved in the replication cycle of this virus?

	Answer	Image
A	Bacterial translation of viral DNA	
B	Cleavage of gp160 to form envelope glycoprotein	
C	Transcription of viral DNA to RNA in the cytoplasm	
D	Reverse transcription of viral RNA to DNA	
E	Adhesion of virus to host ICAM-1 receptor	

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Hint

This patient has been infected with hepatitis B virus (HBV), an enveloped hepadnavirus with only partially double-stranded DNA.

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Correct Answer

A - Bacterial translation of viral DNA

Explanation Why

Bacterial translation of viral DNA is found in the replication cycle of bacteriophages, a type of virus that infects and replicates within bacteria. HBV, however, targets hepatocytes, not bacteria.

B - Cleavage of gp160 to form envelope glycoprotein

Explanation Why

Cleavage of gp160 into gp120 and gp41 subunits occurs in the replication cycle of HIV. Gp120 and gp41 subunits are essential for the invasion of the HIV virus into CD4+ T cells. However, HBV is a DNA virus that targets hepatocytes, not CD4+ T cells.

C - Transcription of viral DNA to RNA in the cytoplasm

Explanation Why

Most viruses with double-stranded DNA require the host-cell RNA polymerase for transcription. Since this enzyme is located in the host cell nucleus, this part of viral replication cycle also typically takes place there. Poxviruses are the only type of DNA virus that code for their own RNA polymerase and can, therefore, execute transcription in the cytoplasm. HBV, which this patient has, is not capable of this.

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D - Reverse transcription of viral RNA to DNA

Explanation Why

After HBV enters the host hepatocyte, its partially double-stranded relaxed circular DNA (rcDNA) is transported into the cell nucleus, where the viral polymerase completes the partial strand of the viral DNA in the host nucleus. The rcDNA is converted to covalently closed circular DNA (cccDNA) primarily by host enzymes in a process that is not entirely understood. The viral cccDNA is then transcribed to mRNA by host RNA polymerase II, after which it enters the cytoplasm and after forming a capsid, is reverse transcribed into new rsDNA genomes. These genomes are either enveloped and packaged as new virions to be released from the cell, or used for further DNA amplification of the virus. HBV differs from retroviruses (e.g., HIV), in that the reverse transcription is a capsid-mediated process.

E - Adhesion of virus to host ICAM-1 receptor

Explanation Why

ICAM-1 receptors are adhesion molecules expressed on the cell surface of epithelial cells and white blood cells. They are the site of attachment for several organisms, including rhinovirus and *Haemophilus influenzae*, on respiratory epithelial cells. HBV, which this patient has, targets hepatocytes rather than epithelial cells and does not rely on ICAM-1 receptor adhesion.

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Question # 32

A 42-year-old man comes to the physician because of a 6-week history of intermittent fever, abdominal pain, bloody diarrhea, and sensation of incomplete rectal emptying. He also has had a 4.5-kg (10-lb) weight loss over the past 3 months. Abdominal examination shows diffuse tenderness. Colonoscopy shows circumferential erythematous lesions that extend without interruption from the anal verge to the cecum. A biopsy specimen taken from the rectum shows mucosal and submucosal inflammation with crypt abscesses. This patient is most likely at risk of developing colon cancer with which of the following characteristics?

	Answer	Image
A	Unifocal lesion	
B	Late p53 mutation	
C	Non-polypoid dysplasia	
D	Low-grade lesion	
E	Early APC mutation	

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Hint

The patient's symptoms and colonoscopy findings suggest ulcerative colitis (UC).

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Correct Answer

A - Unifocal lesion

Explanation Why

Sporadic colorectal carcinomas are commonly unifocal. Ulcerative colitis, however, is more likely to be associated with multifocal lesions, due to the underlying diffuse pattern of chronic mucosal and submucosal inflammation. These multifocal lesions are likely to induce a widespread field change effect within the colon that increases the chance of neoplasia in more than one focus.

B - Late p53 mutation

Explanation Why

Loss of heterozygosity of the p53 tumor suppressor is associated with the development of several different types of neoplastic lesions, including sporadic colorectal carcinomas (CRC). In sporadic CRC, p53 mutation occurs late in the course of the disease, leading to the adenoma to carcinoma sequence. However, in patients with inflammatory bowel disease, the development of colorectal carcinoma is characterized by early p53 mutation.

C - Non-polypoid dysplasia

Explanation Why

Recurrent cycles of inflammation, which are a common feature of UC, result in the release of inflammatory markers that initially promote cellular hyperplasia and, ultimately, non-polypoid dysplasia. Although reversible, dysplasia can progress to neoplasia and is the most likely cause of development of colorectal carcinoma in patients with chronic inflammatory bowel diseases.

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D - Low-grade lesion

Explanation Why

Low-grade lesions of the colon are typically well circumscribed and have an intact capsule; examples include hamartomatous, mucosal, and submucosal colonic polyps. Cancer that arises secondary to ulcerative colitis is more likely to result from chronic and extensive inflammation and is more typically characterized by a high-grade rather than low-grade lesion.

E - Early APC mutation

Explanation Why

Early APC tumor suppressor gene mutation is thought to be the inciting event in the pathogenesis of familial adenomatous polyposis (FAP) and sporadic colorectal carcinomas. However, in patients with IBD, this mutation is uncommon and when present, usually occurs late in the course of the disease process.

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Question # 33

A 26-year-old woman comes to the emergency department with fever, abdominal pain, and nausea for the past 7 hours. The pain started in the right lower abdomen but has now progressed to diffuse abdominal pain. Her temperature is 39.5°C (103.1°F). Physical examination shows generalized abdominal tenderness with rebound, guarding, and decreased bowel sounds. She is taken for an emergency exploratory laparoscopy, which shows a perforated appendix with an adjacent abscess and peritoneal inflammation. Cultures from the abscess fluid grow catalase-producing, anaerobic, gram-negative rods that have the ability to grow in bile. Which of the following is the most appropriate pharmacotherapy for this patient?

	Answer	Image
A	Vancomycin and azithromycin	
B	Gentamicin	
C	Piperacillin	
D	Cefazolin and doxycycline	
E	Ampicillin and sulbactam	
F	Aztreonam	

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Hint

The bacterial cultures suggest *Bacteroides fragilis* infection. *Bacteroides fragilis* is a normal part of the intestinal flora but can cause peritonitis and abscess formation.

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Correct Answer

A - Vancomycin and azithromycin

Explanation Why

Vancomycin and azithromycin would provide broad-spectrum coverage for atypical and gram-positive bacteria. However, this combination would not provide adequate anaerobic or gram-negative coverage for the treatment of *B. fragilis* infection.

B - Gentamicin

Explanation Why

Gentamicin is generally effective for the treatment of serious aerobic, gram-negative infections. While this patient is infected with a gram-negative bacillus, *B. fragilis* is also an anaerobic organism. Like all aminoglycosides, gentamicin is ineffective against anaerobic species.

C - Piperacillin

Explanation Why

Piperacillin provides broad-spectrum coverage for many gram-negative, gram-positive, and anaerobic species. However, it is susceptible to degradation by bacterial beta-lactamases. Administration of this agent alone would be inadequate in this patient because most strains of *B. fragilis* produce beta-lactamase.

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D - Cefazolin and doxycycline

Explanation Why

Combination treatment with cefazolin and doxycycline provides good coverage for gram-positive cocci and atypical bacterial species such as *Borrelia*, *Mycoplasma*, and *Rickettsia*. It would not be an appropriate regimen for a gram-negative bacillus such as *B. fragilis*, which frequently produces beta-lactamase and is often resistant to tetracyclines. Cefazolin is commonly used as prophylaxis against surgical site infection; doxycycline is often prescribed for acne vulgaris.

E - Ampicillin and sulbactam

Explanation But

Other treatment options in patients with *Bacteroides* infection include metronidazole, clindamycin, or another extended-spectrum penicillin with a penicillinase inhibitor, e.g., piperacillin/tazobactam or ticarcillin/clavulanate.

Explanation Why

A patient with perforated appendicitis and abscess formation requires antibiotics with anaerobic and gram-negative coverage. Because more than 90% of *B. fragilis* strains produce beta-lactamase, ampicillin should be combined with the beta-lactamase inhibitor sulbactam. Other indications for ampicillin/sulbactam therapy include skin/soft tissue infections caused by gram-positive organisms, including *Staphylococcus aureus* (but not MRSA) and complicated pelvic/gynecological infections.

F - Aztreonam

Explanation Why

Aztreonam provides broad-spectrum coverage for gram-negative organisms and its chemical structure also confers it some resistance to bacterial beta-lactamases. It is therefore especially useful in patients with severe penicillin or cephalosporin allergies. However, it does not cover anaerobic

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species, meaning it would not effectively treat an infection with *B. fragilis*.

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Question # 34

A 48-year-old woman comes to the physician because of a 6-month history of excessive fatigue and a 1-month history of progressively increasing generalized pruritus. She has hypothyroidism, for which she receives thyroid replacement therapy. Physical examination shows jaundice. The liver is palpated 4 cm below the right costal margin. Serum studies show a direct bilirubin concentration of 2.9 mg/dL, alkaline phosphatase activity of 580 U/L, and increased titers of antimitochondrial antibodies and anti-thyroid peroxidase antibodies. Which of the following is the most likely cause of this patient's condition?

	Answer	Image
A	Hepatocellular accumulation of copper	
B	Idiopathic hepatocellular accumulation of fat	
C	Neoplasia of the ampulla of Vater	
D	Destruction of intrahepatic bile ducts	
E	Autoimmune-mediated destruction of hepatocytes	
F	Inflammation and fibrosis of the biliary tree	

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Hint

Elevated antimitochondrial antibodies and signs of cholestasis (pruritus, jaundice, and increased ALP and bilirubin concentration) in a middle-aged woman suggest primary biliary cholangitis.

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Correct Answer

A - Hepatocellular accumulation of copper

Explanation Why

Copper accumulation in the body (including hepatocellular copper accumulation) is the underlying mechanism of Wilson disease. Although Wilson disease leads to hepatic damage, which can present with hepatomegaly and cholestasis, affected individuals generally present at a younger age with a broad spectrum of neurologic manifestations (e.g., extrapyramidal symptoms) and Kayser-Fleischer rings. Moreover, Wilson disease would not explain this patient's positive testing for antimitochondrial antibodies.

B - Idiopathic hepatocellular accumulation of fat

Explanation Why

Idiopathic hepatocellular accumulation of fat is the underlying mechanism of non-alcoholic steatohepatitis (NASH). Individuals with NASH generally do not exhibit signs of hepatic disease in early stages of NASH, but progression to cirrhosis can occur, which can present with hepatomegaly and cholestasis. However, this patient does not have risk factors for NASH, such as obesity and diabetes mellitus. Moreover, NASH would not explain this patient's positive testing for antimitochondrial antibodies.

C - Neoplasia of the ampulla of Vater

Explanation Why

Neoplasia of the ampulla of Vater can manifest with fatigue, painless jaundice, and pruritus secondary to cholestasis. However, this patient lacks other typical features of an underlying malignancy, such as a history of weight loss and/or anorexia. Moreover, periampullary carcinoma would not explain this patient's positive testing for antimitochondrial antibodies.

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D - Destruction of intrahepatic bile ducts

Explanation But

Other autoimmune conditions associated with PBC include Sjögren syndrome, CREST syndrome, and rheumatoid arthritis.

Explanation Why

Destruction of intrahepatic bile ducts is the underlying mechanism of primary biliary cholangitis (PBC). As a result, chronic cholestasis with ensuing secondary hepatic damage and liver cirrhosis can develop. While most patients are asymptomatic in the early stages of the disease, affected individuals can develop cholestatic pruritus, as seen here. Antimitochondrial antibodies are found in 95% of patients with PBC. This patient's hypothyroidism is most likely due to Hashimoto thyroiditis (elevated anti-thyroid peroxidase antibodies), which is commonly associated with PBC.

E - Autoimmune-mediated destruction of hepatocytes

Explanation Why

Autoimmune-mediated destruction of hepatocytes is the underlying mechanism of autoimmune hepatitis. While patients with autoimmune hepatitis can also present with jaundice, pruritus, hepatomegaly, and a history of autoimmune thyroid disease, this patient lacks other typical features of the disease, such as weight loss, abdominal pain, anti-smooth muscle antibodies, and hypergammaglobulinemia. Moreover, autoimmune hepatitis is not usually associated with positive testing for antimitochondrial antibodies.

F - Inflammation and fibrosis of the biliary tree

Explanation Why

Inflammation and fibrosis of the biliary tree is the underlying mechanism of primary sclerosing cholangitis. While patients with primary sclerosing cholangitis can present with fatigue, cholestasis,

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and hepatomegaly, this condition more commonly occurs in men and is associated with inflammatory bowel disease. Moreover, primary sclerosing cholangitis would be associated with the development of pANCA, not antimitochondrial antibodies.

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Question # 35

A 34-year-old woman comes to the emergency department because of decreased appetite, nausea, vomiting, and episodic abdominal pain for the past two months. The pain is sharp, colicky, and lasts about an hour after meals. Her stools are light in appearance and difficult to flush. Physical examination shows tenderness in the right upper quadrant. Without treatment, this patient is at greatest risk for developing which of the following?

	Answer	Image
A	Glossitis	
B	Megaloblastic anemia	
C	Low bone mineral density	
D	Delayed wound healing	
E	Steatohepatitis	

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Hint

This patient's presenting symptoms suggest cholelithiasis. The floating, light-colored stool likely results from fat malabsorption due to bile acid deficiency. Therefore, this patient is prone to developing fat-soluble vitamin deficiencies.

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Correct Answer

A - Glossitis

Explanation Why

Deficiency of various water-soluble vitamins may cause glossitis. It would not be caused by malabsorption of fat-soluble vitamins (though a range of deficiencies can co-occur in some malabsorption conditions). The cholelithiasis and bile acid deficiency seen in this patient would not cause glossitis.

B - Megaloblastic anemia

Explanation Why

Megaloblastic anemia can be caused by vitamin B1 (thiamine), vitamin B9 (folic acid), or vitamin B12 (cobalamin) deficiencies, all of which are water-soluble vitamins. Fat malabsorption itself should not affect water-soluble vitamins, though some conditions include deficiency in both (e.g., concomitant B, D, and iron deficiency in celiac disease). Folic acid deficiency, for instance, can occur with a decreased intestinal surface area to absorb nutrients, increased physical demand (pregnancy), or decreased dietary intake. Pernicious anemia (vitamin B12 deficiency) can be due to intestinal malabsorption or lack of intrinsic factor. Thiamine deficiency is commonly observed in individuals with alcohol use disorder or diets reliant on polished rice and milled white cereals. Check for other malabsorption syndromes as a differential diagnosis.

C - Low bone mineral density

Explanation Why

Low bone mineral density is observed in patients with vitamin D deficiency, which can occur secondary to fat malabsorption (as in this patient), decreased intake, reduced sun exposure, decreased endogenous synthesis, or end-organ resistance to vitamin D. This patient is prone to developing other fat-soluble vitamin deficiencies (A ,E ,K), as well.

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D - Delayed wound healing

Explanation Why

Impaired wound healing is observed in vitamin C deficiency and zinc deficiency, which result from inadequate dietary intake rather than fat malabsorption. Wound healing is also delayed in megaloblastic anemia and microcytic anemia. These can occur together with vitamin D deficiency in intestinal malabsorptive conditions. However, in a patient with fat malabsorption resulting from bile acid deficiency, delayed wound healing is not expected.

E - Steatohepatitis

Explanation Why

Hepatic steatosis can be alcohol or non-alcohol related. It may be observed in patients with surplus nutritional intake, protein malnutrition, toxin-induced liver damage, or other underlying diseases. A dysbalance in fatty acid metabolism or peripheral fat absorption traps triglycerides and other fatty acids in the liver. Decreased apolipoprotein and very low-density lipoprotein (VLDL) synthesis can play a role. It is not expected in patients with fat malabsorption due to bile acid deficiency.

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Question # 36

A 31-year-old man comes to the physician because of a 2-day history of nausea, abdominal discomfort, and yellow discoloration of the eyes. Six weeks ago, he had an episode of fever, joint pain, swollen lymph nodes, and an itchy rash on his trunk and extremities that persisted for 1 to 2 days. He returned from a backpacking trip to Colombia two months ago. His temperature is 39°C (101.8°F). Physical examination shows scleral icterus. Infection with which of the following agents is the most likely cause of this patient's findings?

	Answer	Image
A	Hepatitis B	
B	Enterotoxigenic E. coli	
C	Borrelia burgdorferi	
D	Hepatitis A	
E	Campylobacter jejuni	

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Hint

This patient's current condition (jaundice, nausea) suggest liver pathology and his medical history suggests a serum sickness-like reaction (fever, arthritis, itchy rash).

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Correct Answer

A - Hepatitis B

Explanation Why

Hepatitis B is associated with a serum sickness-like reaction, which typically occurs during the prodromal period of the infection 1-2 weeks after antigen exposure and is thought to be mediated by immune complex formation. Symptoms of serum sickness-like reaction usually resolve within a few weeks, but symptoms from acute HBV infection may persist for longer, as seen in this patient. Other causes of serum sickness-like reaction include antibiotics (cefaclor, penicillin), streptococcal infection, and vaccines.

B - Enterotoxigenic E. coli

Explanation Why

Enterotoxigenic *E. coli* (ETEC) infection is a common cause of traveler's diarrhea that can cause nausea, abdominal cramping, and fever, similar to the symptoms seen in this patient. However, this patient's history of rash and current jaundice would not be explained by ETEC. Furthermore, he is lacking the acute, watery diarrhea that is characteristic of ETEC infection.

C - Borrelia burgdorferi

Explanation Why

Borrelia burgdorferi is a tick-borne pathogen that causes Lyme disease. Patients with Lyme disease may present with fever, lymphadenopathy, transient arthritis, and jaundice. However, Lyme disease would typically present with erythema migrans, not an itchy rash involving the trunk and extremities.

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D - Hepatitis A

Explanation Why

Hepatitis A is a common cause of acute hepatitis in the US and up to 50% of cases are acquired while traveling abroad. However, hepatitis A is not a known cause of serum sickness-like reactions, and would therefore not present with fever, arthritis, and an itchy rash in the prodromal phase.

E - Campylobacter jejuni

Explanation Why

Campylobacter jejuni is a gram-negative, oxidase-positive bacterium that classically causes bloody diarrhea but can also cause reactive arthritis, which may present similarly to this patient. However, it is not known to cause liver pathology and this patient is missing the classic symptoms of conjunctivitis and urethritis typically seen in reactive arthritis.

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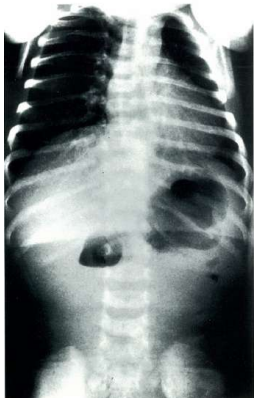
Question # 37

A 15-month-old girl is brought to the physician by her mother for grossly bloody diarrhea for 2 days. The girl has had a few episodes of blood-tinged stools over the past 3 weeks. She has not had pain, nausea, or vomiting. She is at the 55th percentile for height and 55th percentile for weight. Examination shows conjunctival pallor. The abdomen is soft and nontender. There is a small amount of dark red blood in the diaper. Her hemoglobin concentration is 9.5 g/dL, mean corpuscular volume is 68 μm^3, and platelet count is 300,000/$mm^{3.}$ Further evaluation is most likely to show which of the following findings?

	Answer	Image
A	Double bubble sign on abdominal x-ray	
B	Cobblestone mucosa on colonoscopy	
C	Neutrophil infiltrated crypts on colonic biopsy	
D	Absent ganglionic cells on rectal suction biopsy	

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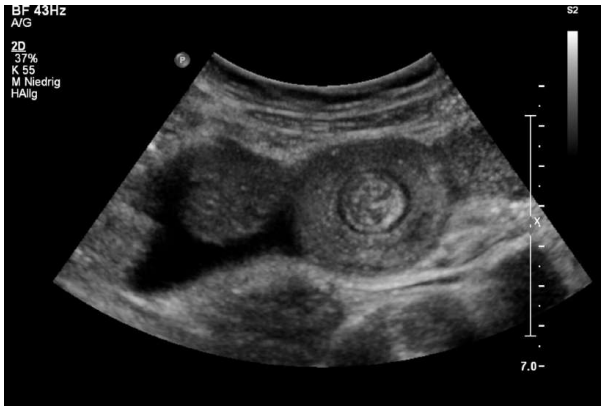
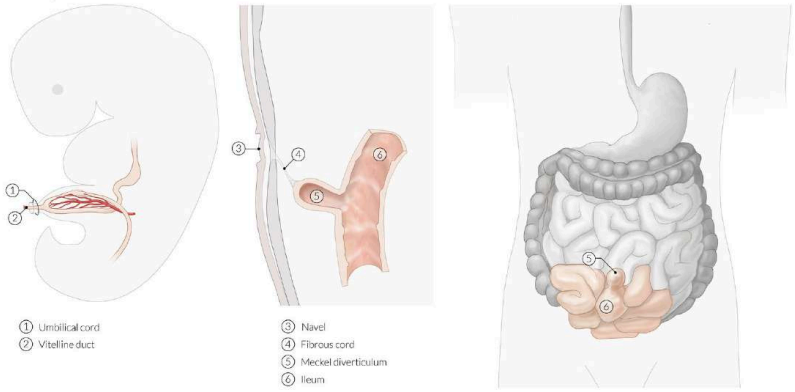
	Answer	Image
E	Target sign on abdominal ultrasound	
F	Ectopic gastric mucosa on Technetium-99m pertechnetate scan	

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Hint

This young girl presents with painless lower gastrointestinal bleeding and resultant microcytic anemia (likely due to iron deficiency from chronic blood loss), which is the characteristic presentation of Meckel diverticulum.

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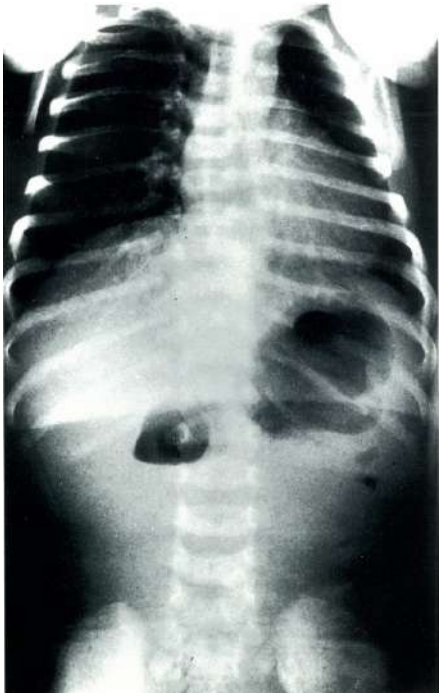
Correct Answer

A - Double bubble sign on abdominal x-ray

Image



Explanation Why

Plain abdominal x-ray showing double bubble sign is suggestive of duodenal atresia. This girl does not present with bilious vomiting or abdominal distention, which would be expected in this condition. Additionally, she is 15 months old and therefore past the window in which duodenal atresia would manifest (24–48 hours after birth).

B - Cobblestone mucosa on colonoscopy

Explanation Why

Cobblestone mucosa (due to linear ulcerations of the mucosa) is a classical colonoscopic finding of

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Crohn disease (CD). Although intestinal blood loss in CD can cause iron deficiency anemia and a low MCV, as seen in this patient, this condition is associated with further symptoms such as nonbloody chronic diarrhea, abdominal pain, and failure to thrive. Moreover, since the peak incidence of CD is 15–35 years, it is unlikely in this 15-month old patient.

C - Neutrophil infiltrated crypts on colonic biopsy

Explanation Why

A colonic biopsy showing neutrophil infiltrated crypts can be seen in ulcerative colitis (UC). This disease can manifest with lower gastrointestinal bleeding and subsequent microcytic anemia, as seen in this patient. However, UC is also associated with abdominal pain, tenesmus, failure to thrive, and extraintestinal manifestations (e.g., uveitis, arthritis, erythema nodosum). Furthermore, the peak incidence of UC is 15–35 years; and therefore, it is unlikely in this 15-month-old patient.

D - Absent ganglionic cells on rectal suction biopsy

Explanation Why

Rectal suction biopsy showing absent ganglionic cells is diagnostic of Hirschsprung's disease. This disease can manifest in neonates with bilious vomiting, abdominal distention, and delayed meconium passage, or at a later stage of childhood with chronic or recurrent constipation. However, it is not associated with the painless lower gastrointestinal bleeding seen in this girl.

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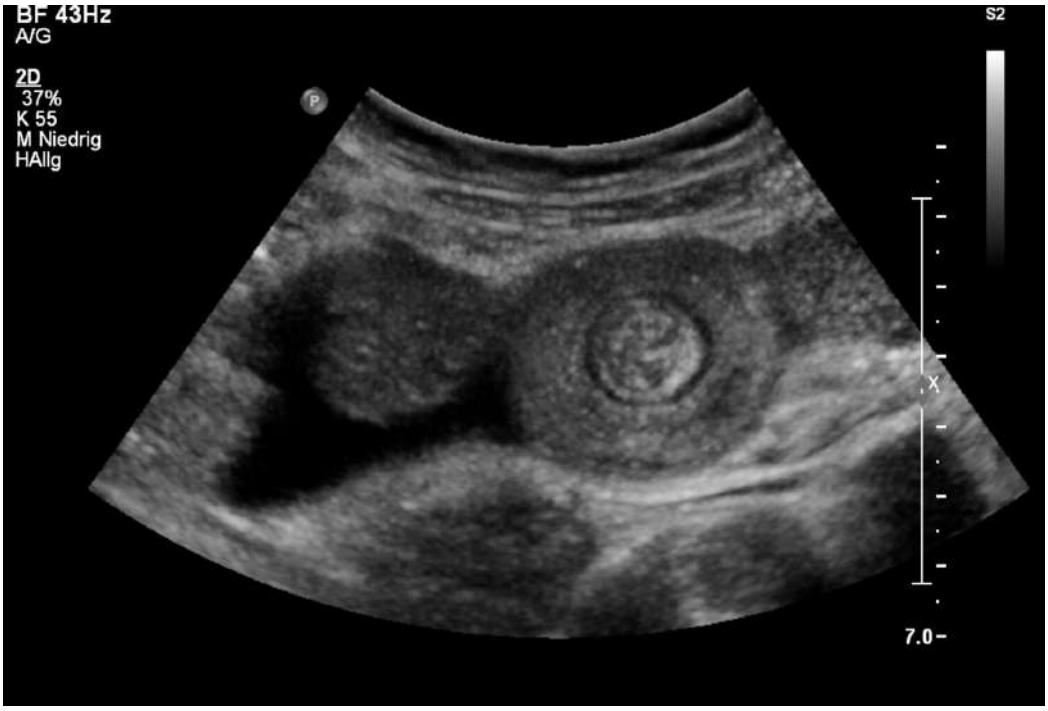
E - Target sign on abdominal ultrasound

Image



Explanation But

Meckel diverticulum can act as a pathological lead point and therefore predisposes to intussusception.

Explanation Why

In young children, abdominal ultrasound showing a target sign is suggestive of intussusception. While intussusception can cause lower gastrointestinal bleeding, it usually presents with acute cyclical colicky abdominal pain, vomiting, and abdominal tenderness. This patient has a benign abdominal exam and no concomitant symptoms, making intussusception unlikely.

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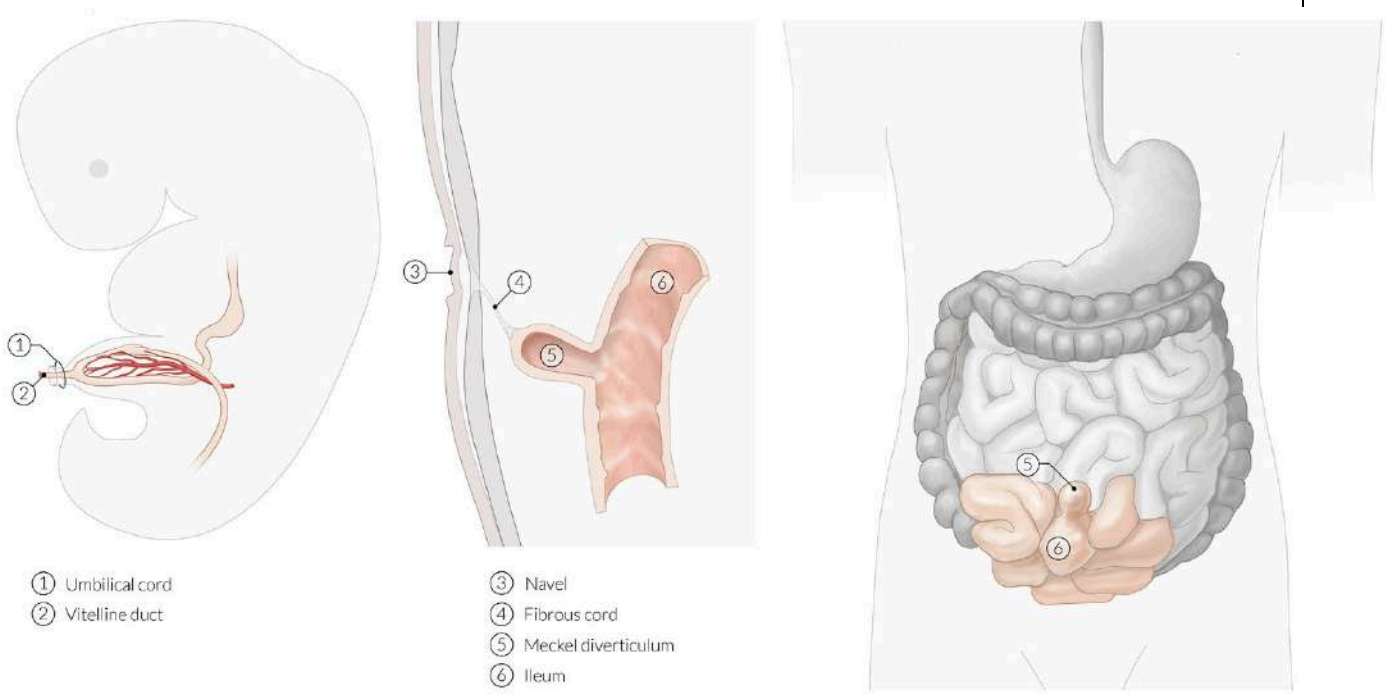
F - Ectopic gastric mucosa on Technetium-99m pertechnetate scan

Image



Explanation But

The sensitivity of technetium-99m pertechnetate scan is lower in adults because the adult population tends to have a higher percentage of Meckel diverticulum that lacks ectopic gastric mucosa. False positives may be seen in intussusception and inflammatory bowel disease.

Explanation Why

Technetium-99m pertechnetate scan showing ectopic gastric mucosa in the small bowel is diagnostic of Meckel diverticulum in children. Meckel diverticulum is a true diverticulum that may contain ectopic gastric mucosa and/or pancreatic tissue. Acid-secretion by gastric mucosa within the diverticulum results in ileal ulceration and subsequent bleeding. Consequently, chronic blood loss can lead to iron deficiency anemia, and thus a low MCV, as seen in this patient.

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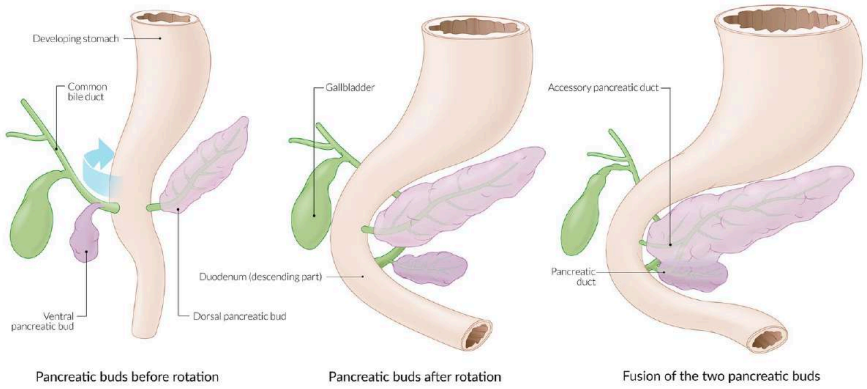
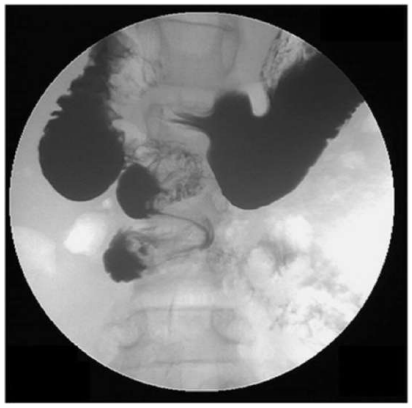
Question # 38

A 34-year-old woman comes to the emergency department because of a 2-hour history of abdominal pain, nausea, and vomiting that began an hour after she finished lunch. Examination shows abdominal guarding and rigidity; bowel sounds are reduced. Magnetic resonance cholangiopancreatography shows the dorsal pancreatic duct draining into the minor papilla and a separate smaller duct draining into the major papilla. The spleen is located anterior to the left kidney. A disruption of which of the following embryological processes is the most likely cause of this patient's imaging findings?

	Answer	Image
A	Fusion of the pancreatic buds	
B	Fusion of visceral and parietal peritoneum	
C	Rotation of the midgut	

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	Answer	Image
D	Proliferation of mesenchyme in the dorsal mesentery	
E	Differentiation of the proximal hepatic diverticulum	
F	Rotation of the ventral splenic bud	

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Hint

The dorsal pancreatic duct normally drains into the major duodenal papilla.

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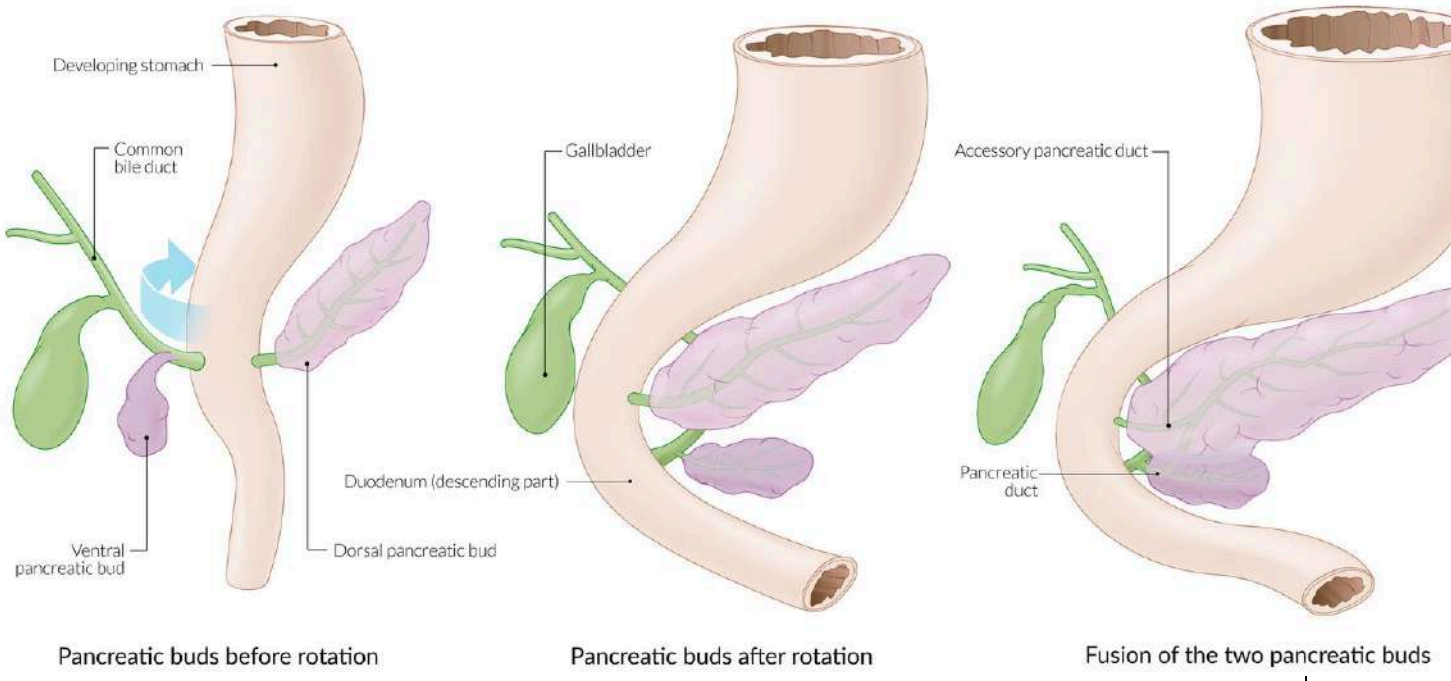
Correct Answer

A - Fusion of the pancreatic buds

Image



Explanation Why

Fusion of the dorsal and ventral pancreatic buds normally occurs during the 8th week of embryological development. Subsequently, the distal portion of the dorsal pancreatic duct fuses with the ventral pancreatic duct, which drains into the major duodenal papilla via the Ampulla of Vater. The proximal portion of the dorsal pancreatic duct would degenerate or persist as an accessory pancreatic duct that drains into the minor duodenal papilla. If the pancreatic buds fail to fuse (pancreas divisum), the dorsal and ventral pancreatic duct would drain separately into the duodenum with the dorsal pancreatic duct draining via the minor duodenal papilla, as seen on this patient's MRCP. Most individuals with pancreas divisum are asymptomatic, but a small percentage will present with chronic abdominal pain or pancreatitis, as is the case here.

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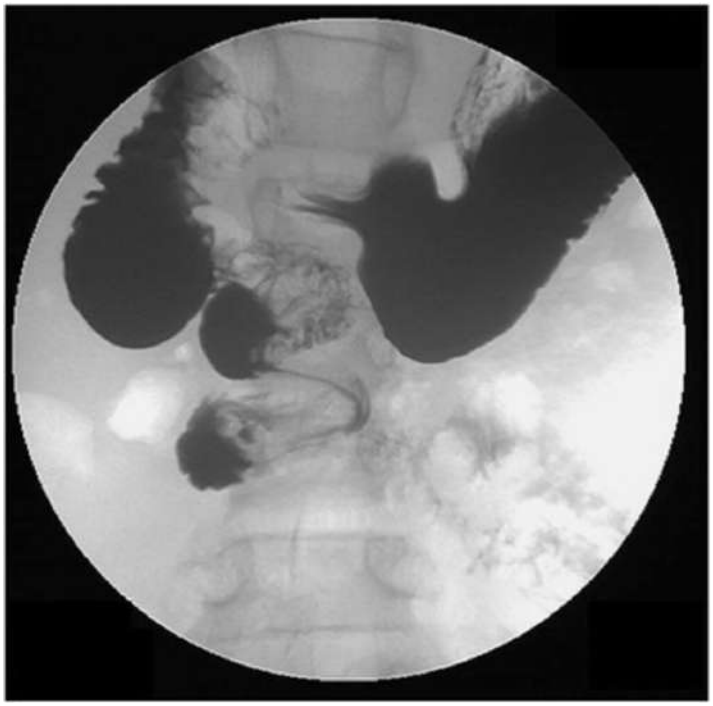
B - Fusion of visceral and parietal peritoneum

Explanation Why

Fusion of the visceral and parietal peritoneum ensures that the pancreas becomes a retroperitoneal structure (secondary retroperitonealization). In the event that this fusion does not occur, the pancreas may remain intraperitoneal. This anomaly is not known to cause any clinical signs or symptoms.

C - Rotation of the midgut

Image



Explanation Why

Rotation of the midgut is important for proper positioning of the intestines. In cases of malrotation, the formation of fibrous bands (Ladd bands) may lead to volvulus or acute intestinal obstruction. Imaging typically shows small bowel sequestered on the right side of the abdomen and large bowel on the left. Anomalies of the pancreatic duct would not be explained by this diagnosis.

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D - Proliferation of mesenchyme in the dorsal mesentery

Explanation Why

Proliferation of mesenchyme in the dorsal mesentery is the process by which the spleen develops. This patient's spleen is situated in the normal anatomical position (anterior to the left kidney) and does not have congenital abnormalities that are evident on imaging.

E - Differentiation of the proximal hepatic diverticulum

Explanation Why

Differentiation of the proximal region of the hepatic diverticulum is the process by which the biliary system develops. In this patient, the pancreatic ducts are abnormal but the biliary system itself shows no evidence of congenital abnormalities.

F - Rotation of the ventral splenic bud

Explanation But

Abnormal rotation of the ventral pancreatic bud can result in an annular pancreas, which can cause nausea and vomiting due to narrowing of the duodenum. However, abdominal guarding and rigidity would not be expected with duodenal obstruction and MRCP would show an annular duct draining into the major duodenal papilla.

Explanation Why

The splenic bud is located in the dorsal mesentery; a ventral splenic bud does not exist. Failure of fusion of the dorsal primordial splenic buds can lead to supernumerary (accessory) spleen formation, which occurs in up to 10% of the population. However, it is most often diagnosed incidentally on abdominal imaging and is rarely symptomatic.

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Question # 39

A 34-year-old man comes to the physician because of a 3-week history of colicky abdominal pain and diarrhea. He has bowel movements 10–12 times daily; the stool contains blood and mucus. He constantly has the urge to defecate. His vital signs are within normal limits. Examination of the abdomen shows diffuse tenderness to palpation. Serum concentration of C-reactive protein is 20 mg/L (N<10). Colonoscopy shows a bleeding, ulcerated rectal mucosa with several pseudopolyps. Which of the following is this patient at greatest risk of developing?

	Answer	Image
A	Hemolytic uremic syndrome	
B	Oral ulcers	
C	Colorectal cancer	
D	Colonic granulomas	
E	Gastric cancer	
F	Pancreatic cancer	

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Hint

The patient presents with colicky abdominal pain and bloody, mucoid diarrhea. Serum studies show an elevated inflammatory marker, and colonoscopy shows a bleeding, ulcerated rectal mucosa with several pseudopolyps. These symptoms and findings are consistent with a diagnosis of ulcerative colitis, an inflammatory bowel disease.

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Correct Answer

A - Hemolytic uremic syndrome

Explanation Why

Hemolytic uremic syndrome (HUS) is a thrombotic microangiopathy caused by bacterial toxins, most commonly the Shiga-like toxin of enterohemorrhagic *Escherichia coli* (*E. coli*) O157:H7. HUS mainly occurs in children < 5 years of age with a classic triad of thrombocytopenia, microangiopathic hemolytic anemia, and impaired renal function all occurring 5–10 days after the onset of a diarrheal illness. It is not a complication of ulcerative colitis.

B - Oral ulcers

Explanation Why

Oral ulcers are an extraintestinal symptom of Crohn disease, an inflammatory bowel disease that also causes abdominal cramping and diarrhea. Unlike ulcerative colitis, which only affects the colon and rectum, Crohn disease can involve any part of the gastrointestinal tract from mouth to anus (most commonly involved site is the terminal ileum). However, Crohn disease usually spares the rectum and typically features grossly nonbloody diarrhea (although stool is often positive for occult blood). In addition, ileocolonoscopy in a patient with active Crohn disease would more likely show linear ulcers, pinpoint lesions, a characteristic cobblestone appearance of the mucosa, and perianal fissures or fistulas.

C - Colorectal cancer

Explanation But

Colorectal cancer in ulcerative colitis patients is more likely to arise from non-polypoid lesions and to be multifocal.

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Explanation Why

Patients with ulcerative colitis have an increased risk of colorectal cancer, with the extent, duration, and histologic severity of the disease correlating with the degree of risk. Eight to ten years after the initial diagnosis of ulcerative colitis, patients should receive colonoscopies with biopsies every 1–3 years to screen for colorectal cancer.

D - Colonic granulomas

Explanation Why

Colonic granulomas are often seen in Crohn disease, an inflammatory bowel disease that also causes abdominal cramping and diarrhea. Unlike ulcerative colitis, which only affects the colon and rectum, Crohn disease can involve any part of the gastrointestinal tract from mouth to anus (most commonly involved site is the terminal ileum). However, Crohn disease usually spares the rectum and typically features grossly nonbloody diarrhea (although stool is often positive for occult blood). In addition, ileocolonoscopy in a patient with active Crohn disease would more likely show linear ulcers, pinpoint lesions, a characteristic cobblestone appearance of the mucosa, and perianal fissures or fistulas.

E - Gastric cancer

Explanation Why

Gastric cancer has multiple risk factors, but ulcerative colitis is not among them. Risk factors for gastric cancer include a diet rich in nitrates and salt, alcohol use, *H. pylori* infection, and gastroesophageal reflux disease (GERD).

F - Pancreatic cancer

Explanation Why

Pancreatic cancer has multiple risk factors, but ulcerative colitis is not among them. Risk factors for

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pancreatic cancer include smoking, chronic pancreatitis, high alcohol consumption, type 2 diabetes mellitus, and inherited genetic syndromes.

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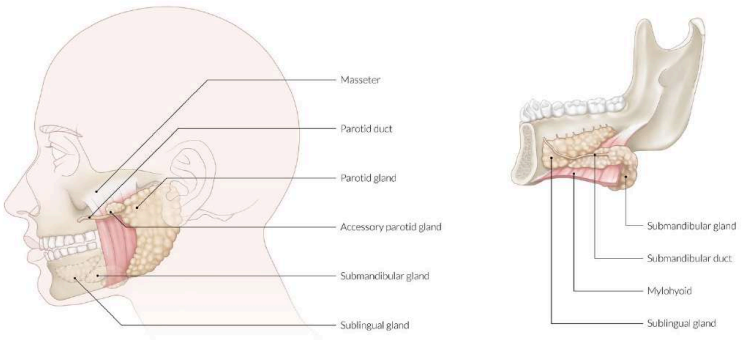
Question # 40

A 55-year-old woman comes to the physician because of a 2-week history of painful swelling on the right side of her face. The pain worsens when she eats. Examination of the face shows a right-sided, firm swelling that is tender to palpation. Oral examination shows no abnormalities. Ultrasonography shows a stone located in a duct that runs anterior to the masseter muscle and passes through the buccinator muscle. Sialoendoscopy is performed to remove the stone. At which of the following sites is the endoscope most likely to be inserted during the procedure?

	Answer	Image
A	Lateral to the superior labial frenulum	
B	Lateral to the lingual frenulum	
C	Into the foramen cecum	
D	Lateral to the second upper molar tooth	
E	Into the floor of the mouth	

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	Answer	Image
F	Into the mandibular foramen	

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Hint

Ultrasonography shows that the stone is located in the parotid duct.

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Correct Answer

A - Lateral to the superior labial frenulum

Explanation Why

There is no salivary duct that opens into the oral cavity lateral to the superior labial frenulum.

B - Lateral to the lingual frenulum

Explanation Why

The submandibular duct arises from the deep part of the submandibular gland and opens into the oral cavity lateral to the lingual frenulum. Although ~ 80% of salivary stones are located in the submandibular gland or duct, this patient's ultrasonography findings suggest that the stone is located in the parotid duct.

C - Into the foramen cecum

Explanation Why

The foramen cecum is a small, midline indentation in the posterior aspect of the tongue, and it is the embryologic remnant of the thyroglossal duct. If the duct fails to obliterate, midline neck cysts or fistulas can develop. There is no salivary gland that drains into the foramen cecum.

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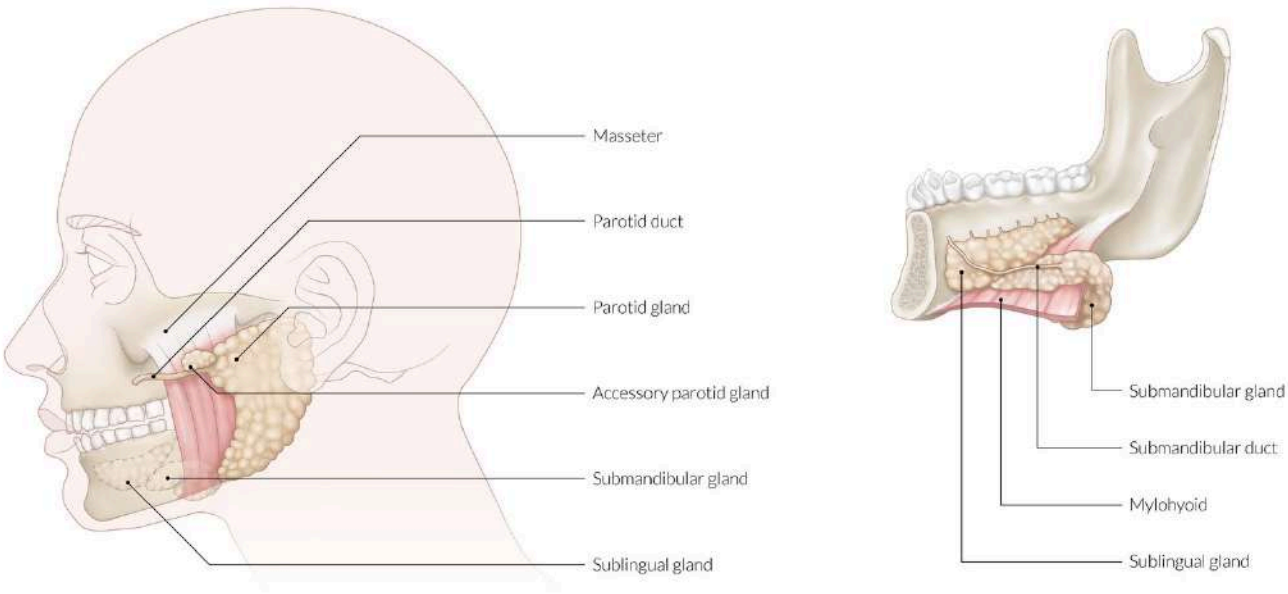
D - Lateral to the second upper molar tooth

Image



Explanation Why

The parotid duct emerges from the anterior edge of the parotid gland, turns medially at the anterior edge of the masseter muscle, and, after piercing through the buccinator muscle, enters the oral cavity lateral to the second upper molar. Sialolithiasis, which affects the parotid gland or duct in approx. 20% of cases, typically manifests with acute pain while eating and tender swelling of the affected gland, both of which are seen here. Risk factors include dehydration, certain medications (e.g., anticholinergics), and trauma. Sialolithiasis is usually treated conservatively, e.g., with NSAIDs and stimulation of salivary flow by gland massage or warm compresses. In severe cases or if conservative treatment fails, salivary stones can be removed via sialoendoscopy or open surgical procedures.

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E - Into the floor of the mouth

Explanation Why

The sublingual gland is drained by numerous ducts, the largest of which joins the submandibular duct while the remaining small ducts drain into the floor of the mouth. Although salivary stones are sometimes located in the sublingual gland or ducts, this patient's ultrasonography findings suggest that the stone is located in the parotid duct.

F - Into the mandibular foramen

Explanation Why

The mandibular foramen is an opening on the internal surface of the ramus of the mandible. Vessels and nerves pass through this opening; however, there is no salivary gland that drains into the mandibular foramen.

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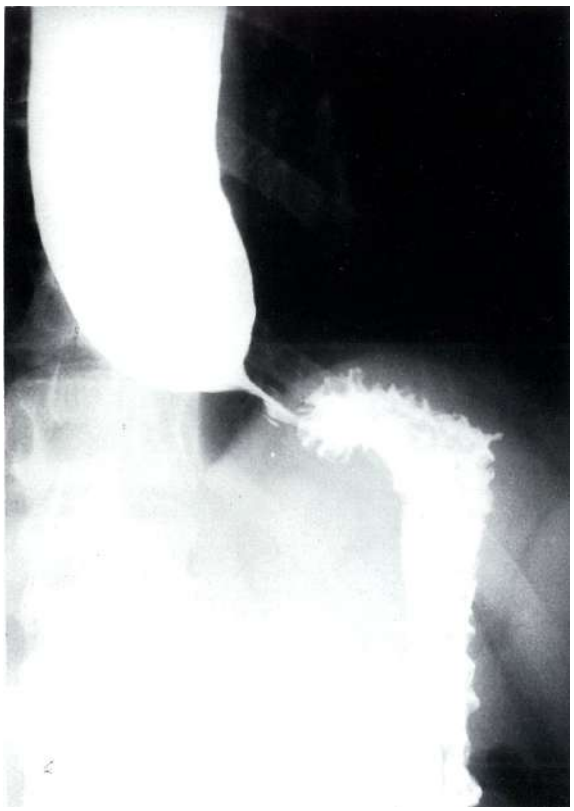
Question # 1

A 45-year-old woman comes to the physician because of progressive difficulty swallowing solids and liquids over the past 4 months. She has lost 4 kg (9 lb) during this period. There is no history of serious illness. She emigrated to the US from Panama 7 years ago. She does not smoke cigarettes or drink alcohol. Cardiopulmonary examination shows a systolic murmur and an S3 gallop. A barium radiograph of the chest is shown. Endoscopic biopsy of the distal esophagus is most likely to show which of the following?



	Answer	Image
A	Atrophy of esophageal smooth muscle cells	
B	Presence of intranuclear basophilic inclusions	
C	Infiltration of eosinophils in the epithelium	

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	Answer	Image
D	Absence of myenteric plexus neurons	
E	Presence of metaplastic columnar epithelium	

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Hint

Clinical features of dilated cardiomyopathy (e.g., systolic murmur due to mitral regurgitation, S3 gallop) in a patient from Central America is suggestive of Chagas disease.

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Correct Answer

A - Atrophy of esophageal smooth muscle cells

Explanation Why

Loss of esophageal smooth muscle is commonly seen in patients with diffuse or limited systemic sclerosis. Loss of muscle results in esophageal hypomotility and lower esophageal sphincter incompetence, which can manifest as progressive dysphagia and dilation of the esophagus on a barium esophagram. However, the gastro-esophageal junction would be open rather than narrowed. Moreover, this patient does not have features of systemic sclerosis (e.g., thickened skin, sclerodactyly, mask-like facies).

B - Presence of intranuclear basophilic inclusions

Explanation Why

Intranuclear basophilic inclusions are aggregates of viral replication-associated proteins commonly seen in CMV infections. CMV esophagitis can cause dysphagia, which is seen in this patient. However, CMV would not cause achalasia and only rarely leads to cardiomyopathy. Furthermore, most patients presenting with CMV esophagitis are immunocompromised, with CD4 counts ≤ 50. This patient's relatively unremarkable medical history suggests that she is immunocompetent.

C - Infiltration of eosinophils in the epithelium

Explanation Why

Infiltration of eosinophils in the epithelium is the hallmark of eosinophilic esophagitis, which is often seen in patients with atopic tendency. It is characterized by mucosal fragility and inflammation, which can manifest with dysphagia. A barium esophagram or endoscopy may reveal formed rings or small strictures arranged in consequent ridges/furrows ("corrugated esophagus"), but not esophageal dilation. Furthermore, eosinophilic esophagitis is not associated with dilated cardiomyopathy.

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D - Absence of myenteric plexus neurons

Explanation Why

Chagas disease is caused by *Trypanosoma cruzi* infection, a parasite endemic to regions of Central and South America. In addition to dilated cardiomyopathy, *T. cruzi* infection can lead to denervation and destruction of myenteric plexus neurons anywhere along the gastrointestinal tract. This results in an inability to relax the lower esophageal sphincter (achalasia), which manifests as progressive dysphagia, weight loss, and a bird-beak sign on barium swallow.

E - Presence of metaplastic columnar epithelium

Explanation Why

The presence of metaplastic columnar epithelium in the distal esophagus is a hallmark of Barrett esophagus. This condition is characterized by the transformation of stratified squamous epithelium to metaplastic columnar epithelium after the esophageal mucosa is chronically exposed to stomach acid in GERD. This patient has no history of retrosternal pain (heartburn), which would potentially indicate GERD. Furthermore, Barrett esophagus is not typically associated with cardiomyopathy.

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Question # 2

A 28-year-old man comes to the physician for the evaluation of a progressively worsening tremor in his hands and multiple falls over the past 3 months. The tremor occurs both at rest and with movement. He also reports decreased concentration and a loss of interest in his normal activities over this time period. He has no history of serious medical illness and takes no medications. He drinks two alcoholic beverages daily and does not use illicit drugs. Vital signs are within normal limits. Physical exam shows mild jaundice, a flapping tremor, and a broad-based gait. Serum studies show:

Aspartate aminotransferase	554 U/L
Hepatitis B surface antibody	positive
Hepatitis B surface antigen	negative
Ceruloplasmin	5.5 mg/dL (normal: 19.0-31.0 mg/dL)

Which of the following is the most appropriate pharmacotherapy for this patient?

	Answer	Image
A	Tenofovir	
B	Prednisolone	
C	Levodopa	
D	Deferoxamine	

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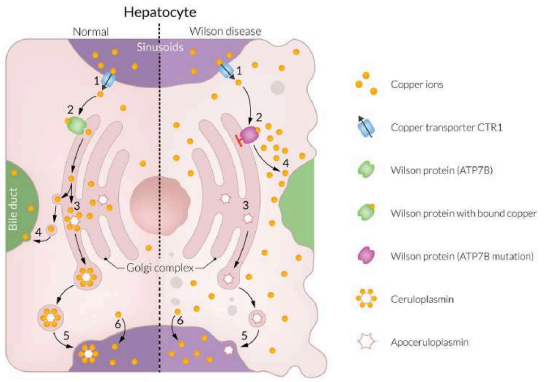
	Answer	Image
E	Penicillamine	

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Hint

This young patient presents with extrapyramidal symptoms, jaundice, and a low ceruloplasmin level, which is consistent with Wilson disease.

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Correct Answer

A - Tenofovir

Explanation Why

Tenofovir is the first-line therapy for hepatitis B infection. This patient has a positive hepatitis B surface antibody and a negative hepatitis B surface antigen, which is indicative of either prior vaccination or a resolved prior infection, neither of which would require treatment.

B - Prednisolone

Explanation Why

Prednisolone can be used for the management of severe alcoholic hepatitis, which can also present with jaundice and elevated AST. A patient abusing alcohol could present with an ataxic gait (due to Wernicke encephalopathy) and/or asterixis (secondary to alcohol withdrawal or hepatic encephalopathy), findings which are similar to the tremor and gait disturbances seen in this patient. However, this patient's alcohol consumption is within the CDC guidelines for moderate alcohol consumption (14 drinks/week for men). Additionally, alcoholic hepatitis would not explain a low ceruloplasmin level.

C - Levodopa

Explanation Why

Levodopa is used for the treatment of Parkinson disease, which can also present with extrapyramidal symptoms (flapping tremor, broad-based gait). However, Parkinson does not affect the liver and would not cause jaundice, increased AST, or decreased ceruloplasmin.

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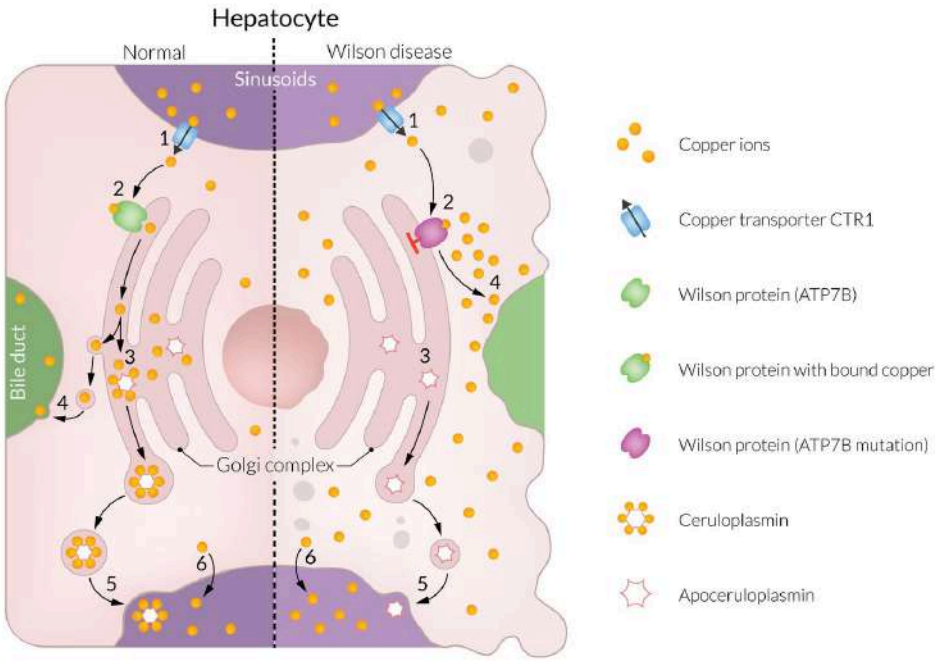
D - Deferoxamine

Explanation Why

Deferoxamine is used to treat hemochromatosis, a disease characterized by chronic iron overload, leading to iron accumulates, especially in the liver (increased risk of HCC), pancreas, skin ("bronze diabetes"), heart, pituitary, and joints. Although hemochromatosis can also cause liver disease with an elevated AST and jaundice, it does not result in extrapyramidal symptoms or a low ceruloplasmin level. Also, it most commonly presents after age 40.

E - Penicillamine

Image



Explanation Why

Penicillamine facilitates renal excretion of copper and is considered a first-line treatment for Wilson disease. Trientine hydrochloride and zinc salts can be used as alternative therapies. Treatment with a

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chelating agent should be administered gradually over the course of 3–6 months, as mobilizing the copper stored in tissues too rapidly may exacerbate neurological symptoms.

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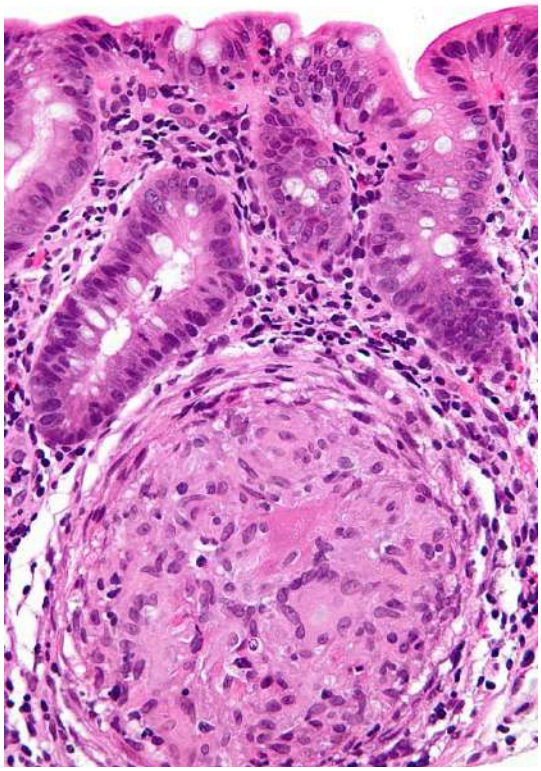
Question # 3

A 63-year-old man comes to the physician with a 4-week history of fatigue, crampy abdominal pain, watery diarrhea, and pain in his mouth and gums. He returned from a 2-week trip to the Dominican Republic 2 months ago. He has smoked one pack of cigarettes daily for 45 years. Examination shows three 1.5-cm, painful ulcers in the mouth. Abdominal examination shows mild tenderness to palpation in the right lower quadrant without guarding or rebound. His hemoglobin concentration is 11.2 g/dL, mean corpuscular volume is 75 fL, and leukocyte count is 11,900 mm^3. Colonoscopy shows a cobblestone mucosa. A photomicrograph of a biopsy specimen is shown. Which of the following is the most likely diagnosis?



	Answer	Image
A	Tropical sprue	
B	Behcet disease	

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	Answer	Image
C	Crohn disease	
D	Whipple disease	
E	Ulcerative colitis	

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Hint

Colonoscopy findings in patients with this condition can also show transmural inflammation, linear ulcers, fistulas, and aphthous hemorrhagic mucosa.

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Correct Answer

A - Tropical sprue

Explanation Why

Tropical sprue is more commonly seen in the tropics or in travelers returning from tropical destinations. Although this patient recently traveled to the Dominican Republic, where tropical sprue is endemic, it is usually only seen in patients who have lived in an endemic area for more than one month. Moreover, tropical sprue presents with malabsorption, steatorrhea, and megaloblastic anemia (due to deficiency of vitamin B12 and folate), which is not consistent with this patient's presentation. Biopsy of the small bowel typically shows villous atrophy and elongated crypts, in contrast to this patient's findings.

B - Behcet disease

Explanation Why

Behcet disease can present with painful oral ulcers, abdominal pain, and diarrhea. It is more common in patients from the Mediterranean region to eastern Asia, with the highest prevalence observed in Turkey. Genital ulcers, which are another typical finding, are not present in this patient. In addition, this patient lacks lesions of the skin (e.g., erythema nodosum), eye (e.g., anterior uveitis, retinal vasculitis), or vasculature (e.g., phlebitis, DVT), which would be typical of Behcet disease. Moreover, granulomatous inflammation would not be expected.

C - Crohn disease

Explanation Why

Crohn disease (CD) has a bimodal distribution and can develop in older patients around the age of 60 years. CD typically presents with chronic, watery, nonbloody diarrhea and abdominal pain, mainly in the right lower quadrant (RLQ). Extraintestinal manifestations, such as the oral aphthae in this patient, are often also seen. Laboratory findings include microcytic anemia and leukocytosis. CD is strongly associated with a history of smoking. Biopsy results showing granulomatous inflammation

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of the colonic mucosa are diagnostic of Crohn disease.

D - Whipple disease

Explanation Why

Whipple disease is a rare disease that mainly occurs in male patients 30–60 years of age. Gastrointestinal manifestations include abdominal pain, bloating diarrhea, and malabsorption. Extraintestinal involvement is common and includes arthritis, sacroiliitis, and cardiac and neurological symptoms. However, oral ulcers would not be expected. Furthermore, biopsy shows PAS-positive macrophages (within the small intestine), in contrast to this patient's granulomatous inflammation of the colon.

E - Ulcerative colitis

Explanation Why

Ulcerative colitis (US) may occur in patients around 60 years of age and also presents with chronic diarrhea and abdominal pain. While neutrophilic cryptitis is also seen in UC, the granulomas seen on this biopsy are not consistent with UC. Moreover, oral ulcers are not seen in UC and diarrhea in UC is typically bloody. Furthermore, smoking has a protective effect on the development of UC, whereas it is a known risk factor for another inflammatory bowel disease.

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Question # 4

A 45-year-old man comes to the emergency department because of a 1-day history of black, tarry stools. He has also had upper abdominal pain that occurs immediately after eating and a 4.4-kg (9.7-lb) weight loss in the past 6 months. He has no history of major medical illness but drinks 3 beers daily. His only medication is acetaminophen. He is a financial consultant and travels often for work. Physical examination shows pallor and mild epigastric pain. Esophagogastroduodenoscopy shows a bleeding 15-mm ulcer in the antrum of the stomach. Which of the following is the strongest predisposing factor for this patient's condition?

	Answer	Image
A	Age above 40 years	
B	Alcohol consumption	
C	Acetaminophen use	
D	Work-related stress	
E	Helicobacter pylori infection	

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Hint

Melena, anemia, unintentional weight loss, and a history of upper abdominal pain that worsens with food intake should raise concern for a peptic ulcer disease. The endoscopy results confirm this diagnosis.

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Correct Answer

A - Age above 40 years

Explanation Why

Although age is a predisposing factor for PUD, the risk is significantly higher in individuals over the age of 65 years, it would only be marginally increased in a 45-year-old patient.

B - Alcohol consumption

Explanation Why

Alcohol consumption increases the risk of PUD by causing chemical gastritis, which predisposes individuals to ulcer development and prolongs ulcer healing. However, alcohol consumption is not the strongest predisposing factor for PUD in this patient.

C - Acetaminophen use

Explanation Why

Acetaminophen is a commonly used non-opioid analgesic. Although it can cause gastrointestinal side effects such as nausea and vomiting, it does not increase the risk of PUD or gastrointestinal bleeding. In comparison, NSAIDs, another class of commonly used non-opioid analgesic, can increase the risk of PUD 5-fold.

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D - Work-related stress

Explanation Why

Stress has been associated with increased gastric acid production and development of PUD, although the exact underlying mechanism is poorly understood and causality has not yet been defined. A different predisposing factor is more likely in this patient.

E - Helicobacter pylori infection

Explanation But

H. pylori infection increases the risk of gastric cancer and MALT lymphoma.

Explanation Why

Helicobacter pylori infection is the strongest predisposing factor for this patient's peptic ulcer disease (PUD). *H. pylori* infection accounts for up to 80% of gastric ulcers and 90% of duodenal ulcers. The most common sites for ulcer development are the lesser curvature and the antrum of the stomach and the duodenal bulb, and diagnosis of *H. pylori* infection can be confirmed on biopsy. In addition to controlling bleeding, treatment of his peptic ulcer should include Helicobacter pylori eradication therapy.

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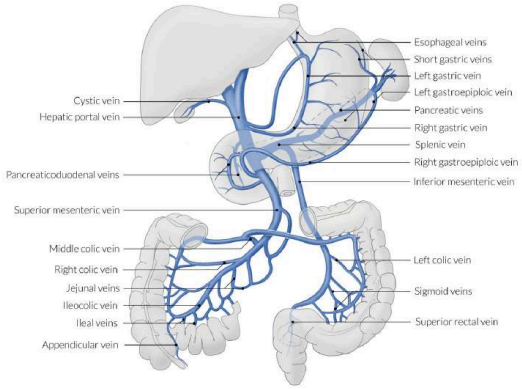
Question # 5

A previously healthy 47-year-old woman comes to the emergency department because of a 2-week history of fatigue, abdominal distention, and vomiting. She drinks 6 beers daily. Physical examination shows pallor and scleral icterus. A fluid wave and shifting dullness are present on abdominal examination. The intravascular pressure in which of the following vessels is most likely to be increased?

	Answer	Image
A	Short gastric vein	
B	Splenic artery	
C	Inferior epigastric vein	
D	Azygos vein	
E	Gastroduodenal artery	

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Hint

Given this patient's heavy alcohol consumption, her symptoms of vomiting, fatigue, ascites, and jaundice are highly suggestive of alcoholic cirrhosis.

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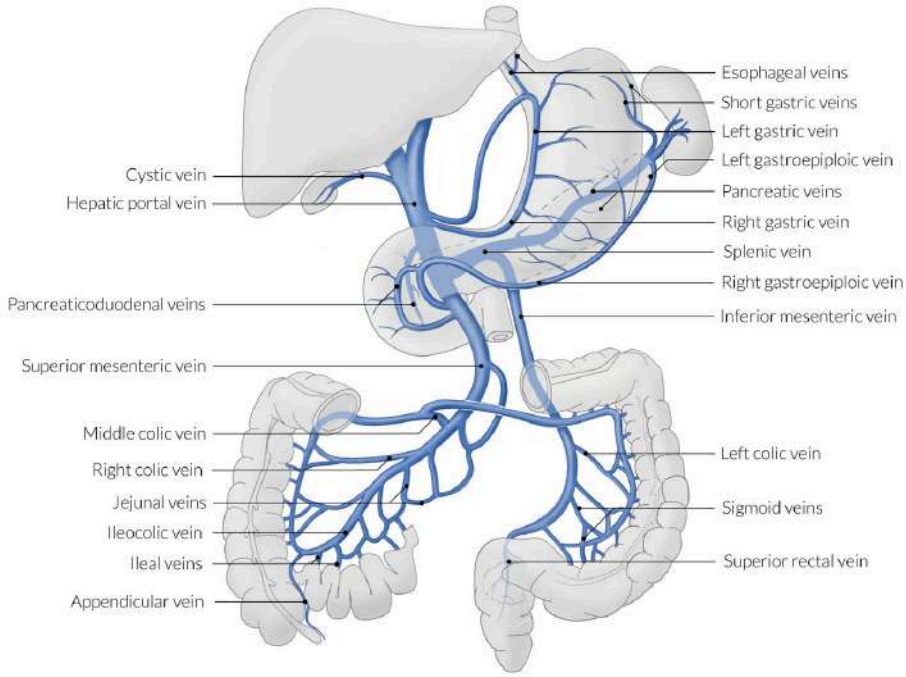
Correct Answer

A - Short gastric vein

Image



Explanation Why

The short gastric veins drain into the splenic vein, which joins the superior mesenteric vein to form the hepatic portal vein. In patients with liver cirrhosis, the increased intraluminal pressure from portal hypertension causes engorgement of these vessels. This can result in gastric varices that can be complicated by life-threatening upper gastrointestinal bleeding.

B - Splenic artery

Explanation Why

The splenic artery, which is a branch of the celiac trunk, supplies blood to the spleen, pancreas as

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well as the fundus and upper greater curvature of the stomach. However, as arteries carry blood to rather than drain blood from organs, they are not involved in portal hypertension.

C - Inferior epigastric vein

Explanation Why

The inferior epigastric vein, which drains into the external iliac vein, is a part of the systemic circulation. Increased blood flow through the inferior epigastric vein can occur in patients with portal hypertension as a result of portosystemic shunting via paraumbilical veins and result in caput medusae. However, since the inferior epigastric vein is not a part of the portal system, the blood pressure is more likely to be increased in a different vessel that is part of the portal system before it is increased in inferior epigastric vein.

D - Azygos vein

Explanation Why

The azygos vein, which drains into the superior vena cava, is part of the systemic circulation. Increased blood flow through the azygos vein can occur in patients with portal hypertension as a result of portosystemic shunting via the esophageal vein. However, since the azygos vein is not a part of the portal system, the blood pressure is more likely to be increased in a different vessel that is part of the portal system before it is increased in the azygos vein.

E - Gastroduodenal artery

Explanation Why

The gastroduodenal artery, which is a branch of the common hepatic artery, carries blood to the pylorus of the stomach, the duodenum, and the head of the pancreas (via the superior pancreaticoduodenal arteries). However, as arteries carry blood to rather than drain blood from organs, they are not involved in portal hypertension.

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Question # 6

A 49-year-old man with alcohol use disorder is brought to the emergency department immediately after two episodes of coffee-ground emesis. His pulse is 116/min and blood pressure is 92/54 mm Hg. Physical examination shows a distended abdomen with shifting dullness. Skin examination shows jaundice, erythematous palms, and dilated veins in the anterior abdominal wall. After fluid resuscitation, he is given a drug that decreases portal venous pressure. The drug works by inhibiting the secretion of splanchnic vasodilatory hormones as well as blocking glucagon and insulin release. This drug is a synthetic analog of a substance normally produced in which of the following cells?

	Answer	Image
A	S cells	
B	G cells	
C	K cells	
D	D cells	
E	I cells	

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Hint

This patient with alcohol use disorder and signs of liver dysfunction (jaundice, ascites, caput medusae) is now presenting with hematemesis and hemodynamic instability, which is seen in ruptured esophageal varices. Treatment includes hemodynamic resuscitation and octreotide.

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Correct Answer

A - S cells

Explanation Why

S cells are secretin-producing cells located in the duodenum. Secretin increases pancreatic bicarbonate secretion and bile secretion into the duodenum and decreases gastric acid secretion. Secretin is not an analog of octreotide.

B - G cells

Explanation Why

G cells are gastrin-producing cells located in the antrum of the stomach and the duodenum. Gastrin increases gastric H^+ release and gastric motility and stimulates growth of the gastric mucosa. Gastrin is not an analog of octreotide.

C - K cells

Explanation Why

K cells produce glucose-dependent insulinotropic peptide (also known as gastric inhibitory peptide, or GIP) and are located in the duodenum and jejunum. GIP decreases gastric acid secretion and increases insulin release. GIP is not an analog of octreotide.

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D - D cells

Explanation But

Octreotide is also used in the treatment of carcinoid syndrome, acromegaly, and gigantism.

Explanation Why

D cells are somatostatin-producing cells located in the gastrointestinal mucosa and in pancreatic islets. This patient shows signs of esophageal bleeding and has been given octreotide, which is a synthetic analog of somatostatin with a longer half-life. Both substances inhibit secretion of vasodilatory hormones, which indirectly leads to splanchnic vasoconstriction and reduced splanchnic blood flow.

E - I cells

Explanation Why

I cells are cholecystokinin-producing cells located in the duodenum and jejunum. Cholecystokinin increases pancreatic secretions, gallbladder contraction, and sphincter of Oddi relaxation. It also decreases gastric emptying. Cholecystokinin is not an analog of octreotide.

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Question # 7

A 65-year-old man comes to the physician because of a 2-week history of dizziness, fatigue, and shortness of breath. He has noticed increased straining with bowel movements and decreased caliber of his stools over the past 3 months. He has no history of medical illness and takes no medications. He appears pale. Physical examination shows mild tachycardia and conjunctival pallor. Test of the stool for occult blood is positive. His hemoglobin concentration is 6.4 g/dL, and mean corpuscular volume is 74 μm^3. A double-contrast barium enema study in this patient is most likely to show which of the following?

	Answer	Image
A	Thumbprint sign of the transverse colon	
B	Lead pipe sign of the descending colon	
C	Diverticula in the sigmoid colon	
D	Protruding mass in the proximal ileum	
E	Filling defect of the rectosigmoid colon	
F	String sign in the terminal ileum	

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Hint

This patient has manifestations of iron deficiency anemia (e.g., fatigue, pallor, tachycardia, decreased mean corpuscular volume) and a positive fecal occult blood test, most likely due to underlying colorectal carcinoma.

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Correct Answer

A - Thumbprint sign of the transverse colon

Explanation Why

Thumbprint sign is caused by bowel wall thickening and associated with several conditions, including ischemic colitis and inflammatory bowel disease. These conditions typically cause abdominal pain and diarrhea, which this patient does not have. Moreover, ischemic colitis does not cause obstructive symptoms (e.g., straining during defecation, decrease in stool caliber). Patients with recurrent exacerbations of Crohn disease can develop obstructive symptoms due to stricture formation, but the development of these complications in a patient with no prior history of Crohn disease exacerbations is unlikely.

B - Lead pipe sign of the descending colon

Explanation Why

Lead pipe sign on double-contrast barium enema is a characteristic finding in patients with ulcerative colitis. This condition can develop in older adults and cause iron deficiency anemia due to chronic bleeding. However, this patient lacks classic manifestations of ulcerative colitis such as bloody diarrhea with mucus, abdominal pain, and tenesmus. Moreover, this condition does not typically cause obstructive symptoms (e.g., straining during defecation, decrease in stool caliber).

C - Diverticula in the sigmoid colon

Explanation Why

Diverticular disease, which typically arises in the sigmoid colon, commonly affects older adults. Diverticulosis can cause iron deficiency anemia due to chronic bleeding, and patients with recurrent diverticulitis can develop obstructive symptoms (e.g., straining during defecation, decrease in stool caliber) due to inflammatory stenosis and subsequent stricture formation. However, this patient has no history of diverticulitis, which typically manifests with fever, left lower quadrant pain, and leukocytosis.

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D - Protruding mass in the proximal ileum

Explanation Why

A protruding mass in the proximal ileum raises concern for small bowel cancer, which can cause a positive fecal occult blood test and iron deficiency anemia due to chronic bleeding. However, small bowel cancer does not typically cause obstructive symptoms (e.g., straining during defecation, decrease in stool caliber).

E - Filling defect of the rectosigmoid colon

Explanation Why

The rectosigmoid colon is the most commonly involved site of colorectal carcinoma, followed by the ascending colon and then the descending colon. Lumen constriction caused by circumferential tumor growth results in a characteristic apple core lesion filling defect on double-contrast barium enema study. Colorectal carcinoma should be suspected as an underlying cause of iron deficiency anemia in men > 50 years of age and postmenopausal women. Left-sided colorectal carcinomas, which involve the rectosigmoid colon and/or the descending colon, are more likely to cause obstructive symptoms (e.g., straining during defecation, decrease in stool caliber) than right-sided colorectal carcinomas, which involve the ascending colon.

F - String sign in the terminal ileum

Explanation Why

A string sign in the distal ileum (which can be seen on a barium swallow study, not a double-contrast barium enema study) is a characteristic finding in patients with Crohn disease. This condition can develop in older adults and cause iron deficiency anemia due to chronic bleeding. However, this patient lacks classic manifestations of Crohn disease such as diarrhea and abdominal pain. Patients with recurrent exacerbations of Crohn disease can develop obstructive symptoms (e.g., straining during defecation, decrease in stool caliber) due to stricture formation. However, the development of these complications in a patient with no prior history of Crohn disease exacerbations is unlikely.

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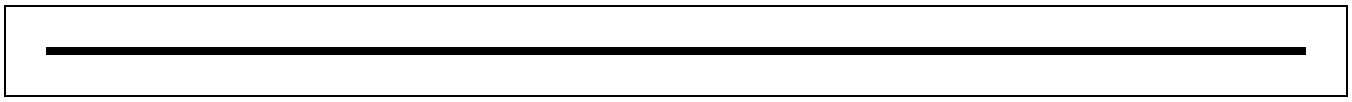

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Question # 8

A 30-year-old woman comes to the physician because of a 1-month history of intermittent abdominal pain, flatulence, and watery diarrhea. The episodes typically occur 2–3 hours after meals, particularly following ingestion of ice cream, cheese, and pizza. She is administered 50 g of lactose orally. Which of the following changes is most likely to be observed in this patient?

	Answer	Image
A	Increased stool pH	
B	Decreased urinary D-xylose concentration	
C	Increased serum glucose concentration	
D	Increased stool osmotic gap	
E	Decreased fecal fat content	
F	Decreased breath hydrogen content	

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Hint

A presentation of abdominal pain, flatulence, and diarrhea occurring after the ingestion of dairy products is suggestive of lactose intolerance. Symptoms are caused by malabsorption of lactose in the small bowel, which leads to increased intestinal filling and bacterial fermentation of undigested lactose in the colon.

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Correct Answer

A - Increased stool pH

Explanation Why

An increased stool pH would not be expected in this patient, as those with lactose intolerance present with acidic stool (pH < 6). Lactose reaches the large intestine due to insufficient hydrolysis by lactase. There, it serves as a fermentation substrate for colonic bacterial flora. Hydrogen and fatty acids are generated during fermentation, resulting in a decreased stool pH.

B - Decreased urinary D-xylose concentration

Explanation Why

A decreased urinary D-xylose concentration would be expected in patients with malabsorptive disorders because xylose is absorbed in the proximal small intestine and excreted through the kidneys. Diminished absorption (e.g., in the setting of celiac disease, which can underlie lactose intolerance) would lead to decreased urinary D-xylose levels. However, this patient was given oral lactose, not xylose. A statement cannot yet be made regarding urinary D-xylose excretion.

C - Increased serum glucose concentration

Explanation Why

In individuals with lactose intolerance, lactose is not sufficiently cleaved into the absorbable monosaccharides (galactose and glucose) that would raise serum glucose concentration in tolerant individuals. Instead, lactose is transferred to the colon without being absorbed. Therefore, serum glucose levels fail to rise after administration of lactose.

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D - Increased stool osmotic gap

Explanation But

An increased stool osmotic gap is not specific to lactose intolerance and occurs in all forms of osmotic diarrhea (e.g., laxative abuse)

Explanation Why

Calculation of the stool osmotic gap relies on the assumption that total stool osmolality stays constant and comes mainly from stool electrolyte concentrations. The remaining contribution to stool osmolality, i.e. the stool osmotic gap, depends on nonelectrolyte substances. In lactose intolerance, unabsorbed lactose and its fermented metabolites contribute significantly to stool osmolality, meaning an increased stool osmotic gap.

E - Decreased fecal fat content

Explanation Why

Lactose intolerance does not affect fat absorption, though it can occur in the setting of other malabsorption disorders with elevated fecal fat content. Giving this patient an oral load of lactose will likely induce diarrhea, which may be accompanied by a slightly increased, not decreased, fecal fat content, as diarrhea generally impedes fat absorption.

F - Decreased breath hydrogen content

Explanation Why

Unabsorbed lactose undergoes fermentation by bacteria in the colon, a process that produces fatty acids and hydrogen. Hydrogen is then absorbed into the bloodstream, transported to the lungs, and exhaled. Therefore, increased, rather than decreased, breath hydrogen content would be expected in this patient. The hydrogen breath test is routinely used for patients with suspected lactose intolerance.

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Question # 9

An otherwise healthy 45-year-old woman comes to the physician because of a 1-year history of episodic abdominal cramps, bloating, and flatulence. The symptoms worsen when she has pizza or ice cream and have become more frequent over the past 4 months. Lactose intolerance is suspected. Which of the following findings would most strongly support the diagnosis of lactose intolerance?

	Answer	Image
A	Partial villous atrophy with eosinophilic infiltrates	
B	Periodic acid-Schiff-positive foamy macrophages	
C	Crypt abscesses and colonic ulcerations	
D	Tall villi with focal collections of goblet cells	
E	Duodenal epithelium with dense staining for chromogranin A	
F	Villous atrophy and crypt hyperplasia	
G	Noncaseating granulomas with lymphoid aggregates	

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Hint

Lactose intolerance does not cause bowel wall inflammation, so normal histological architecture is expected on biopsy.

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Correct Answer

A - Partial villous atrophy with eosinophilic infiltrates

Explanation Why

Partial villous atrophy with eosinophilic infiltrates is not found in lactose intolerance but is one of the characteristic histological findings in cases of cow's milk allergy. This condition can manifest with abdominal pain and bloating, but is virtually exclusively seen in infants and also involves diarrhea. In contemporary practice, the diagnosis is most commonly made following an oral milk challenge or with identification of serum cow milk-specific IgE.

B - Periodic acid-Schiff-positive foamy macrophages

Explanation Why

Periodic acid-Schiff-positive foamy macrophages are not found in lactose intolerance but occur in Whipple disease, caused by *Tropheryma whipplei* infection. This condition is very rare and most often manifests with chronic malabsorptive diarrhea and abdominal pain. It also causes weight loss, migratory nondeforming arthritis, lymphadenopathy, and a low-grade fever. The absence of these features suggests a different diagnosis.

C - Crypt abscesses and colonic ulcerations

Explanation Why

Crypt abscesses and colonic ulcerations are not found in lactose intolerance but are histological hallmarks of ulcerative colitis. Important gross morphological changes that are commonly observed include inflammation limited to mucosa and submucosa, easily friable mucosa, and continuous ulcers that consistently involve the rectum. While ulcerative colitis may present with episodic abdominal pain, frequent bloody diarrhea is an important part of the history. The absence of bloody diarrhea makes this diagnosis much less likely.

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D - Tall villi with focal collections of goblet cells

Explanation Why

Tall villi lined by simple columnar epithelium and crypts with interspaced goblet cells (crypts of Lieberkühn) and Paneth cells describes normal jejunal architecture. Patients with lactose intolerance are deficient in lactase, permitting osmotically active lactose to pass undigested to the large bowel. The molecule subsequently binds water and acts as a substrate for colonic bacteria, leading to symptoms of flatulence, bloating, and abdominal pain. Biopsy shows normal histological findings, but samples will also show decreased activity of lactase.

E - Duodenal epithelium with dense staining for chromogranin A

Explanation Why

Duodenal epithelium with dense staining for chromogranin A is inconsistent with lactose intolerance but is found in a subset of patients with irritable bowel syndrome. This condition also manifests with episodic abdominal cramps, bloating, and flatulence, as in this patient. Changes in stool frequency and stool form or appearance are also common. The diagnosis is most often made using the ROME IV criteria with biopsy reserved for unusual cases.

F - Villous atrophy and crypt hyperplasia

Explanation Why

Villous atrophy and crypt hyperplasia are not found in lactose intolerance but are characteristic biopsy findings in celiac disease. The underlying pathophysiology derives from intestinal hypersensitivity to gliadin. The clinical presentation is variable, ranging from solely gastrointestinal symptoms (e.g., cramps, bloating, and steatorrhea, some of which are observed in this patient) to more systemic involvement (e.g., vitamin deficiencies and anemia, depression, dermatitis herpetiformis, fertility complications, and osteoporosis). This patient lacks diarrhea/steatorrhea or systemic signs typical of the disease and is significantly older than the typical age of first onset (usually teenage or young adulthood).

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G - Noncaseating granulomas with lymphoid aggregates

Explanation Why

Noncaseating granulomas with lymphoid aggregates are not found in lactose intolerance but are classic histological findings of Crohn disease; gross findings can include cobblestone mucosa and discontinuous linear ulcers (“skip” ulcers), especially in the terminal ileum. This condition causes abdominal pain, diarrhea (which may be bloody), and extraintestinal symptoms involving the skin (pyoderma gangrenosum, erythema nodosum), the eyes (uveitis), and joints (arthritis), to name a few. This patient has none of these clinical features, and she is older than the typical age of onset (usually teenager or young adult).

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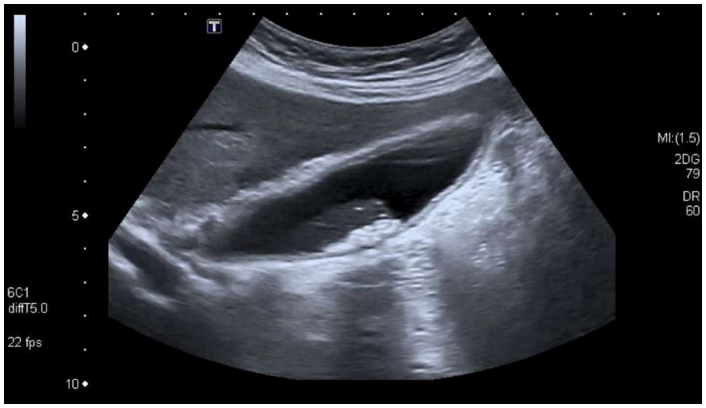
Question # 10

A 52-year-old woman comes to the emergency department because of epigastric abdominal pain that started after her last meal and has become progressively worse over the past 6 hours. She has had intermittent pain similar to this before, but it has never lasted this long. Her temperature is 39°C (102.2°F). Examination shows a soft abdomen with normal bowel sounds. The patient has sudden inspiratory arrest during right upper quadrant palpation. Her alkaline phosphatase, total bilirubin, amylase, and aspartate aminotransferase levels are within the reference ranges. Abdominal imaging is most likely to show which of the following findings?

	Answer	Image
A	Dilated common bile duct with intrahepatic biliary dilatation	
B	Gas in the gallbladder wall	
C	Gallstone in the cystic duct	
D	Fistula formation between the gallbladder and bowel	
E	Decreased echogenicity of the liver	

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	Answer	Image
F	Enlargement of the pancreas with peripancreatic fluid	

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Hint

This middle-aged woman presents with post-prandial epigastric abdominal pain, fever, and a positive Murphy sign, suggesting a diagnosis of acute cholecystitis.

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Correct Answer

A - Dilated common bile duct with intrahepatic biliary dilatation

Explanation Why

The presence of a dilated common bile duct and intrahepatic biliary dilatation in the setting of acute abdominal pain would be consistent with choledocholithiasis. Choledocholithiasis typically manifests with RUQ pain, nausea, and occasionally jaundice. Elevation in serum ALP and bilirubin is common. Fever would be unusual and is typically only seen in patients with complications of choledocholithiasis (e.g., acute pancreatitis or acute cholangitis).

B - Gas in the gallbladder wall

Explanation Why

Gas within the gallbladder wall, also referred to as emphysematous cholecystitis, suggests either gallbladder necrosis or infection with gas-forming bacteria. It is typically a complication of untreated cholecystitis (including acalculous cholecystitis) and can be visualized on both ultrasound and CT. However, this patient is not critically ill and her abdominal pain is acute, making this an unlikely diagnosis here.

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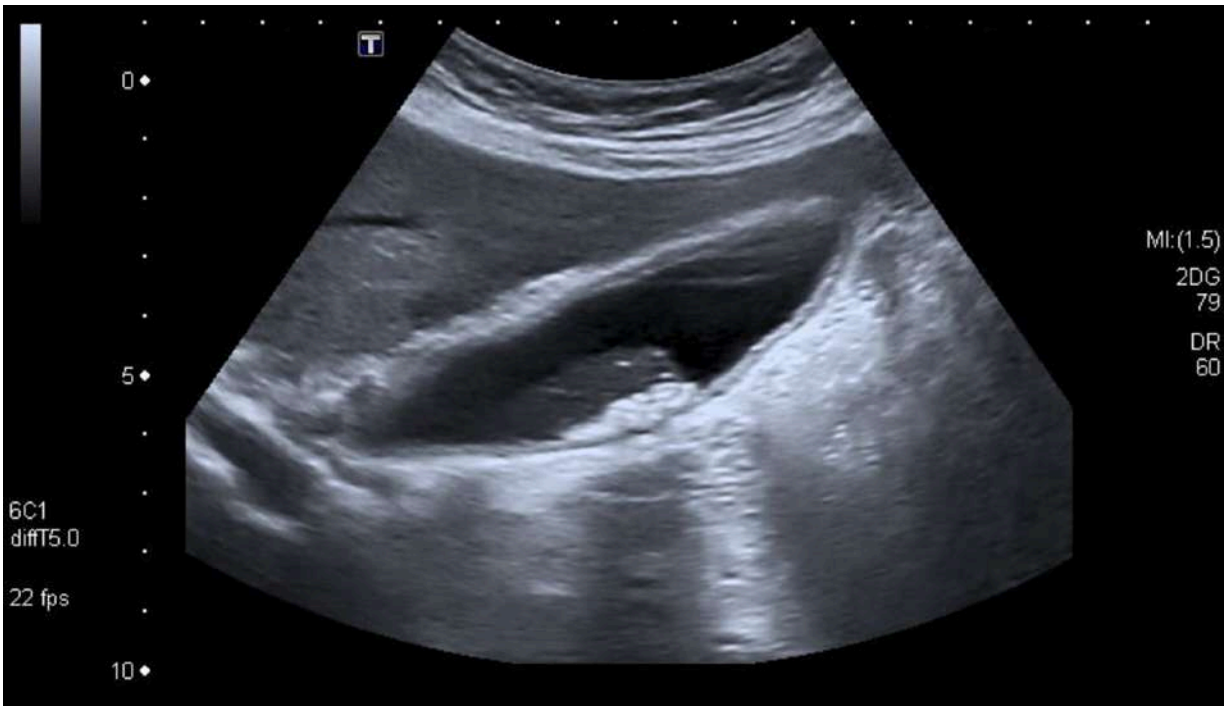
C - Gallstone in the cystic duct

Image



Explanation But

Biliary colic is a more benign condition that can be difficult to distinguish from cholecystitis. It usually occurs after a fatty meal, but it is not usually associated with peritoneal signs, and symptoms typically resolve on their own within a few hours.

Explanation Why

The vast majority of cases of acute cholecystitis are due to obstructing gallstones in the cystic duct. In a patient with clinical features of acute cholecystitis (e.g., RUQ/epigastric pain lasting over 6 hours, fever, and positive Murphy sign), ultrasonography of the RUQ is indicated. Findings that support the diagnosis include gallbladder wall thickening, gallbladder wall edema, obstructing gallstone, and/or a positive Murphy sign on ultrasound. Gallstones are a common incidental finding on ultrasound but in this setting would also suggest acute cholecystitis.

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D - Fistula formation between the gallbladder and bowel

Explanation Why

Gallstone ileus is a very rare complication of gallstone cholecystitis and occurs when a biliary-enteric fistula is formed that leads to a gallstone entering the small intestine and obstructing the ileum. Patients can present with symptoms of small bowel obstruction, including nausea, vomiting (often bilious), crampy abdominal pain, and obstipation. Physical examination would show abdominal distention and high-pitched (tympanic) bowel sounds. CT is the preferred imaging modality and classically shows bowel obstruction with a biliary-enteric fistula and/or pneumobilia.

E - Decreased echogenicity of the liver

Explanation Why

Decreased echogenicity of the liver on ultrasound is a nonspecific finding seen in patients with acute liver inflammation (e.g., due to acute viral hepatitis, alcoholic hepatitis, etc). While acute hepatitis may also manifest with RUQ abdominal pain, nausea, and vomiting, expected findings would include jaundice and tender hepatomegaly. Liver transaminases (AST and ALT) are usually elevated, making this diagnosis unlikely in this patient.

F - Enlargement of the pancreas with peripancreatic fluid

Explanation Why

Edema of the pancreas on either ultrasound or CT is suggestive of acute pancreatitis. Patients with pancreatitis often present with abdominal pain and nausea that may be worse after meals. However, pain from pancreatitis classically radiates to the back and is not associated with the Murphy sign, which is seen in this patient. Elevations in serum amylase would also be expected in acute pancreatitis.

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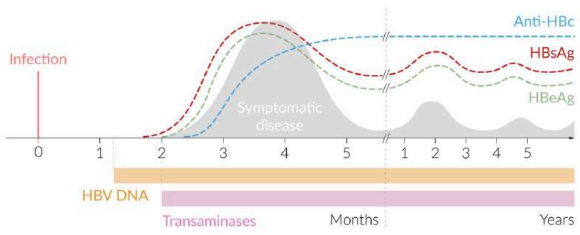
Question # 11

A 32-year-old man comes to the physician for a pre-employment examination. He recently traveled to Guatemala. He feels well but has not seen a physician in several years, and his immunization records are unavailable. Physical examination shows no abnormalities. Serum studies show:

Anti-HAV IgM	Positive
Anti-HAV IgG	Negative
HBsAg	Negative
Anti-HBs	Positive
HBcAg	Negative
Anti-HBc	Negative
HBeAg	Negative
Anti-HBe	Negative
Anti-HCV	Negative

Which of the following best explains this patient's laboratory findings?

	Answer	Image
A	Active hepatitis B infection	

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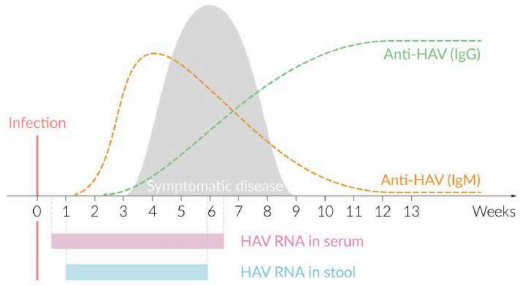
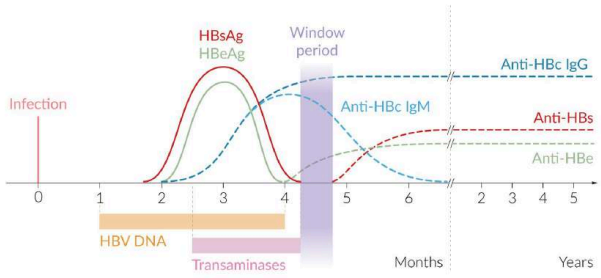
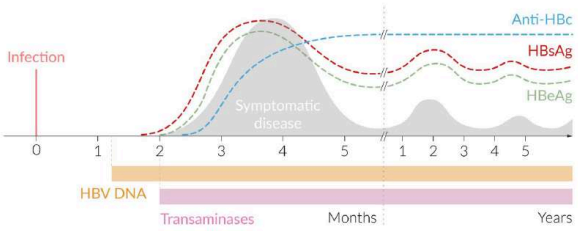
	Answer	Image
B	Active hepatitis A infection	
C	Previous hepatitis B infection	
D	Previous hepatitis A infection	
E	Chronic hepatitis B infection	

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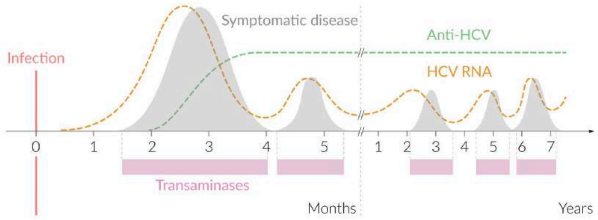
	Answer	Image
F	Chronic hepatitis C infection	
G	Hepatitis A vaccination	

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Hint

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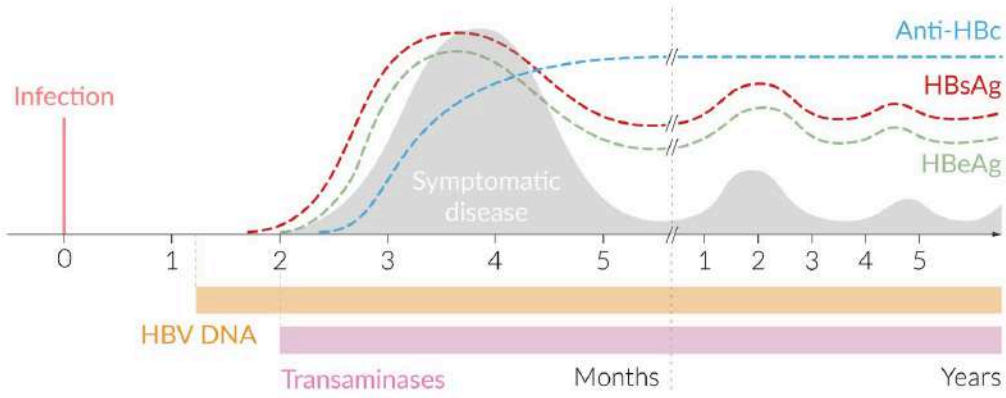
Correct Answer

A - Active hepatitis B infection

Image



Explanation Why

In patients with active hepatitis B infection, serum studies for HBeAg and HBcAg would be positive. Either anti-HBc IgM (acute active infection) or anti-HBc IgG (chronic active infection) would also be positive. In addition, this patient tests positive for anti-HBs antibodies, which would prevent infection.

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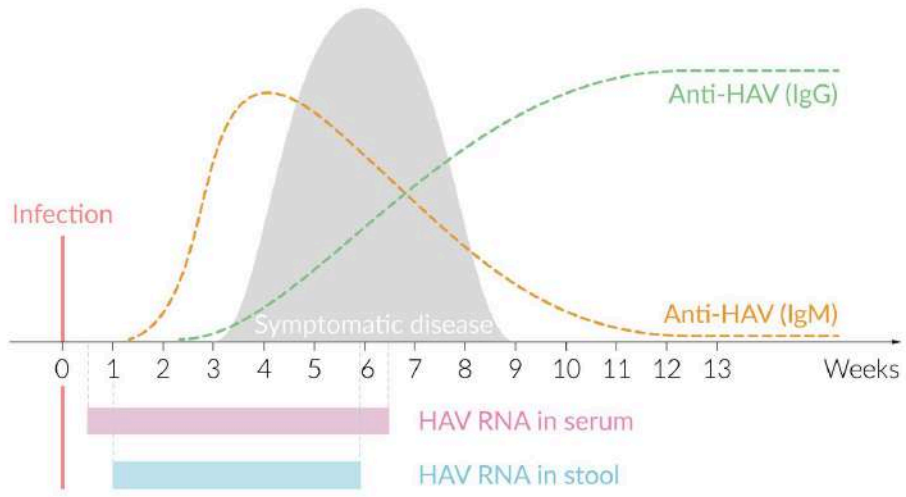
B - Active hepatitis A infection

Image



Explanation But

Unlike hepatitis B and hepatitis C, hepatitis A does not have a carrier state. The presence of anti-HAV IgG antibodies on serology would indicate prior hepatitis A infection or immunization. This patient tests positive for anti-HBs antibodies and negative for anti-HBc antibodies, which indicates that he has been immunized against hepatitis B.

Explanation Why

Active hepatitis A infection is confirmed in this patient by the presence of IgM antibodies against the hepatitis A virus (anti-HAV IgM antibodies) on serology. Anti-HAV IgM antibodies appear approx. 1 week after onset of infection and persist for 3–6 months. This patient is asymptomatic because his infection is very mild or because the disease is still in the incubation period, which lasts 2–6 weeks. Hepatitis A is more prevalent in developing countries (e.g., Guatemala).

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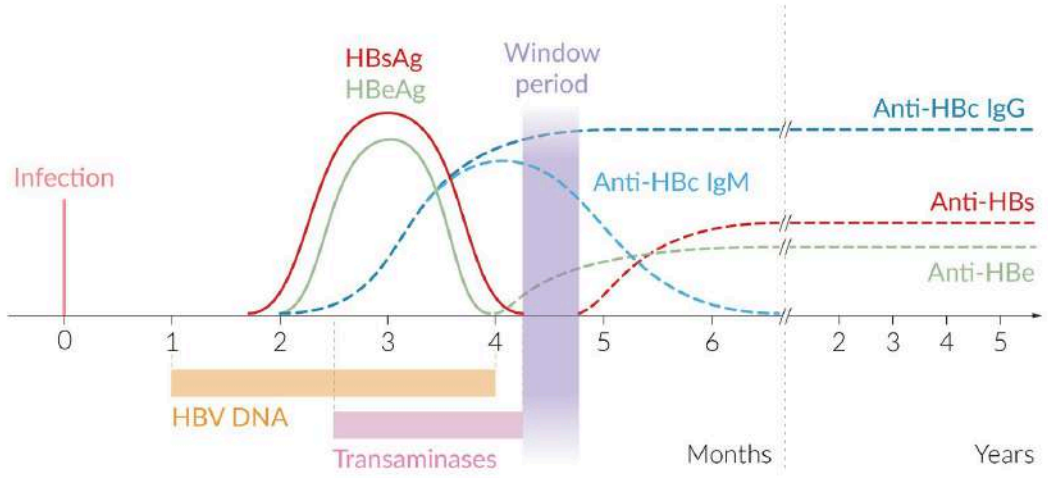
C - Previous hepatitis B infection

Image



Explanation Why

In patients with previous hepatitis B infection, serum studies for anti-HBs antibodies are positive, as in this case. However, anti-HBe antibodies and anti-HBc IgG antibodies would also be present. The presence of anti-HBs antibodies on serology in the absence of other hepatitis B markers indicates that this patient has been immunized against hepatitis B.

D - Previous hepatitis A infection

Explanation Why

In patients with previous hepatitis A infection, serum studies for anti-HAV IgG antibodies would be positive. These antibodies appear about 1–2 weeks after infection and persist for life.

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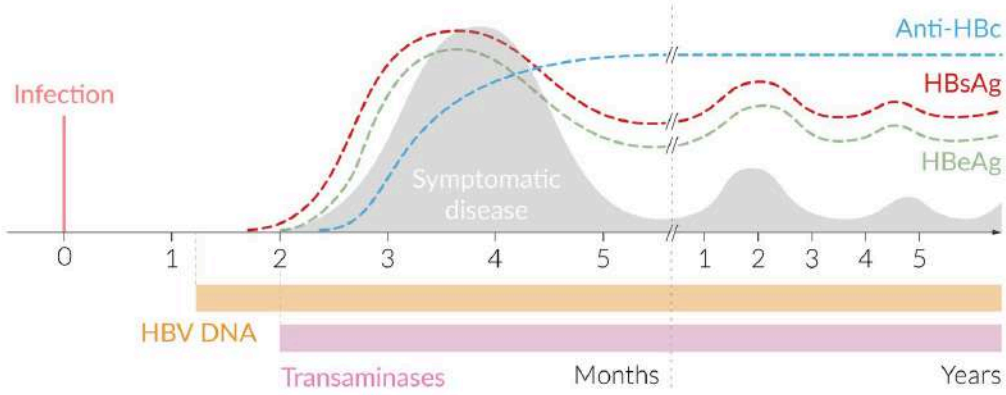
E - Chronic hepatitis B infection

Image



Explanation Why

In patients with chronic hepatitis B infection, serum studies for HBsAg, HBeAg, and anti-HBc IgG antibodies would be positive. In addition, this patient tests positive for anti-HBs antibodies, which would prevent infection.

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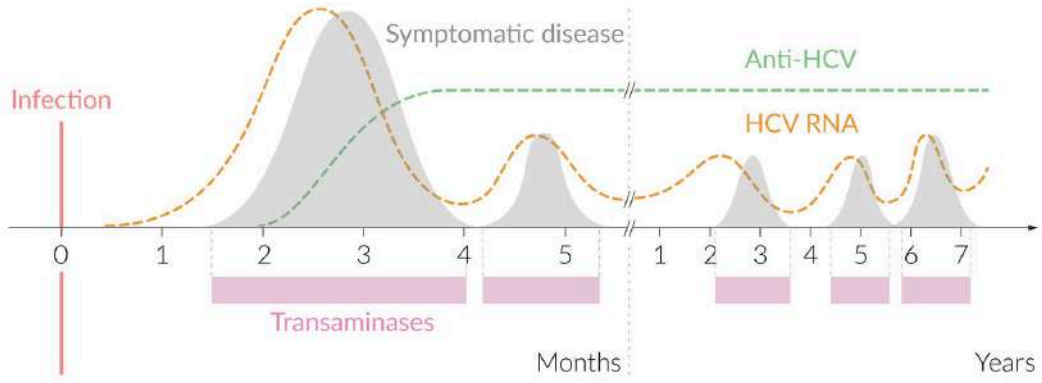
F - Chronic hepatitis C infection

Image



Explanation Why

In patients with chronic hepatitis C infection, serum studies for anti-HCV antibodies would be positive.

G - Hepatitis A vaccination

Explanation Why

In patients who have been vaccinated against hepatitis A, serum studies for anti-HAV IgG antibodies would be positive.

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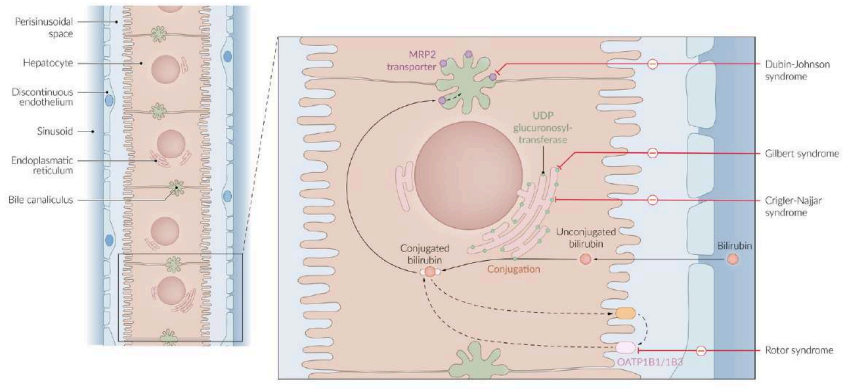
Question # 12

A 3-day-old girl is brought to the physician by her mother because of difficulty feeding and lethargy for 1 day. She had jaundice after birth and was scheduled for a follow-up visit the next day. Her hemoglobin is 18.5 g/dL, total bilirubin is 38.1 mg/dL, and direct bilirubin is 0.1 mg/dL. Despite appropriate measures, the infant dies. At autopsy, examination of the brain shows deep yellow staining of the basal ganglia and subthalamic nuclei bilaterally. Which of the following is the most likely cause of this infant's findings?

	Answer	Image
A	Defective intracellular bilirubin transport	
B	Increased degradation of red blood cells	
C	Extrahepatic obliteration of the biliary tree	
D	Impaired glucuronidation of bilirubin	
E	Decreased bilirubin uptake in hepatocytes	

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Hint

This patient's symptoms and autopsy findings of deep yellow staining in the basal ganglia are highly suggestive of kernicterus due to unconjugated hyperbilirubinemia.

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Correct Answer

A - Defective intracellular bilirubin transport

Explanation Why

Defective intracellular bilirubin transport, seen in both Dubin Johnson and Rotor syndrome, presents with conjugated hyperbilirubinemia, with mild clinical conditions typically manifesting with occasional scleral icterus. This patient presented with elevated unconjugated bilirubin and severe symptoms three days after delivery, making this diagnosis unlikely.

B - Increased degradation of red blood cells

Explanation Why

Increased degradation of red blood cells, seen in hemolytic anemias such as hereditary spherocytosis and sickle cell disease, can present at birth with unconjugated hyperbilirubinemia. However, as this patient had normal hemoglobin levels, hemolytic anemia is an unlikely diagnosis.

C - Extrahepatic obliteration of the biliary tree

Explanation Why

Extrahepatic obliteration of the biliary tree presents with cholestasis in the neonatal period and is also called biliary atresia. Although jaundice is one of the first symptoms, patients usually also present with pale stool and dark urine, which this patient did not have. Moreover, biliary atresia shows elevated conjugated bilirubin, whereas this patient has elevated unconjugated bilirubin but normal conjugated bilirubin. Conjugated bilirubin does not cross the blood-brain barrier and, therefore, does not cause kernicterus.

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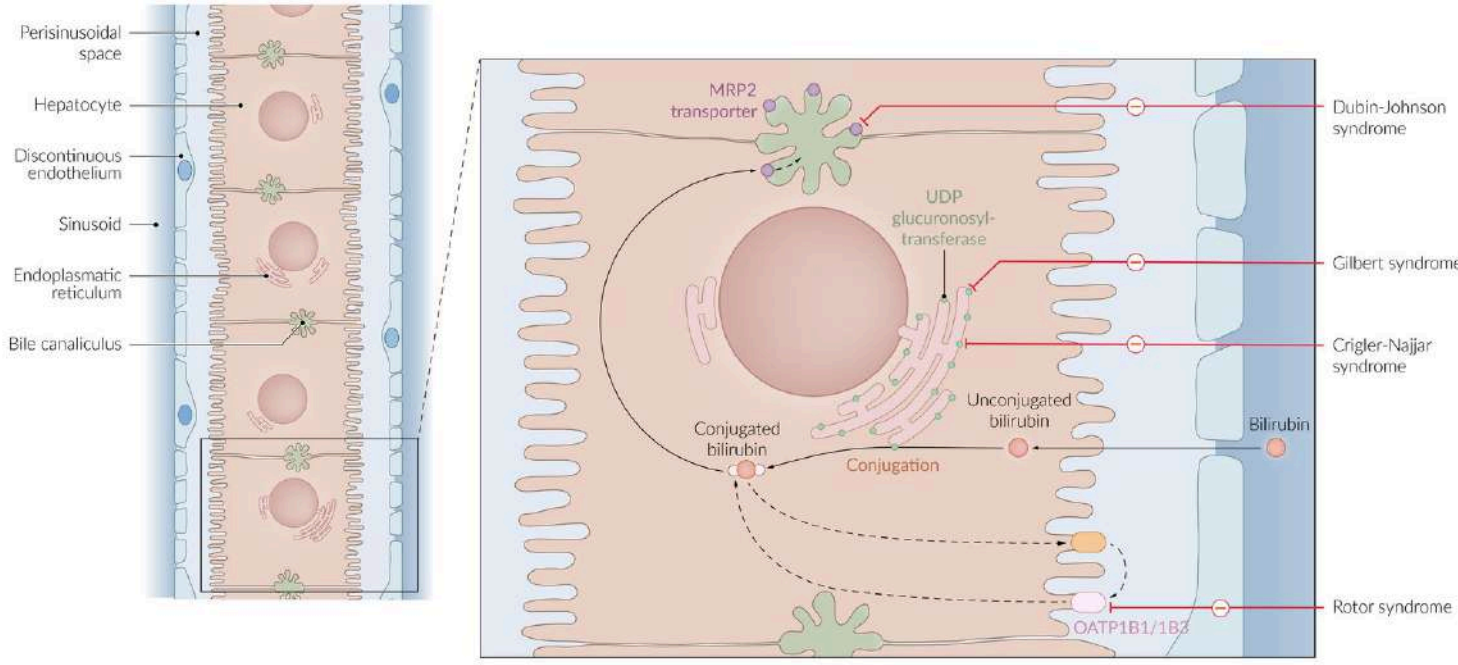
D - Impaired glucuronidation of bilirubin

Image



Explanation Why

Impaired glucuronidation of bilirubin leads to elevated unconjugated bilirubin. Concurrent with pathological neonatal jaundice, normal conjugated bilirubin levels and the absence of anemia, the patient's condition is highly suggestive of type 1 Crigler-Najjar syndrome, in which unconjugated bilirubin crosses the blood-brain barrier, leading to kernicterus and, potentially, death.

E - Decreased bilirubin uptake in hepatocytes

Explanation Why

Although decreased bilirubin uptake in hepatocytes, as seen in Gilbert syndrome, causes unconjugated hyperbilirubinemia, as seen in this patient, it is rarely present at birth. Most cases are asymptomatic and mild, with increased bilirubinemia during times of stress, often not requiring

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treatment.

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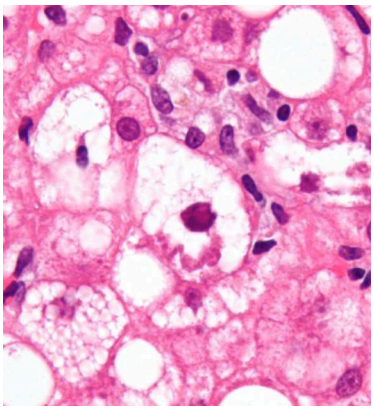
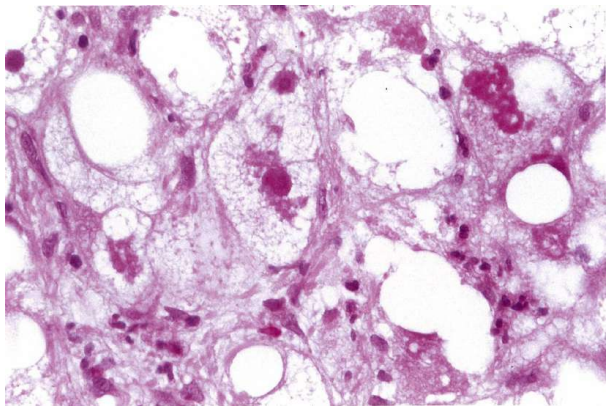
Question # 13

A 38-year-old woman comes to the physician because of a 1-month history of fatigue and pruritus. Examination of the abdomen shows an enlarged, nontender liver. Serum studies show an alkaline phosphatase level of 200 U/L, aspartate aminotransferase activity of 28 U/L, and alanine aminotransferase activity of 29 U/L. Serum antimitochondrial antibody titers are elevated. A biopsy specimen of this patient's liver is most likely to show which of the following findings?

	Answer	Image
A	Fibrous, concentric obliteration of small and large bile ducts	
B	Intracytoplasmic eosinophilic inclusions in hepatocytes and cellular swelling	
C	Macrovesicular fatty infiltration and necrosis of hepatocytes	
D	Ballooning degeneration and apoptosis of hepatocytes	

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	Answer	Image
E	Lymphocytic infiltration of portal areas and periductal granulomas	

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Hint

Fatigue, pruritus, hepatomegaly, elevated alkaline phosphatase, and elevated antimitochondrial antibodies (AMA) titers suggest primary biliary cholangitis (formerly primary biliary cirrhosis).

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Correct Answer

A - Fibrous, concentric obliteration of small and large bile ducts

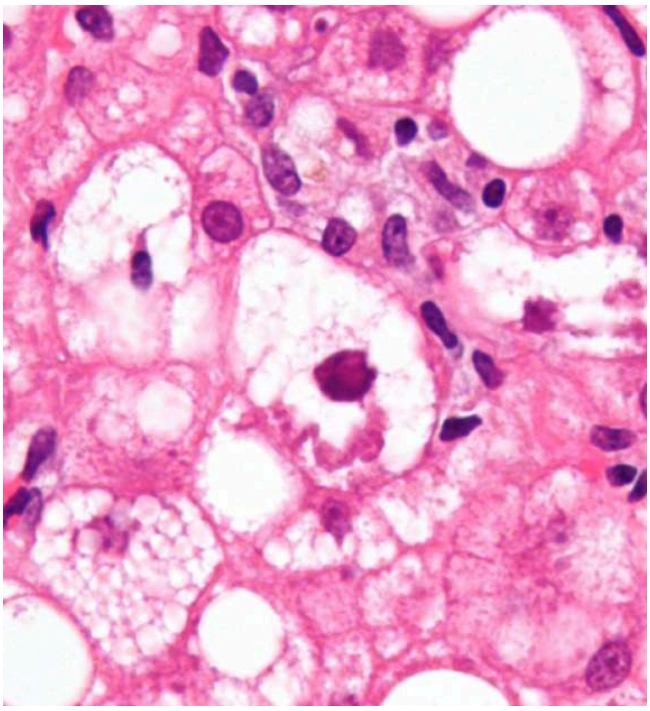
Explanation Why

Fibrous, concentric obliteration of small and large bile ducts (e.g., “onion-skin” fibrosis) is characteristic of primary sclerosing cholangitis (PSC), which is associated with elevations in anti-neutrophil cytoplasmic antibodies rather than antimitochondrial antibodies. PSC is more common in men and is associated with ulcerative colitis, as well as with an increased risk of developing cholangiocarcinoma.

B -

Intracytoplasmic eosinophilic inclusions in hepatocytes and cellular swelling

Image



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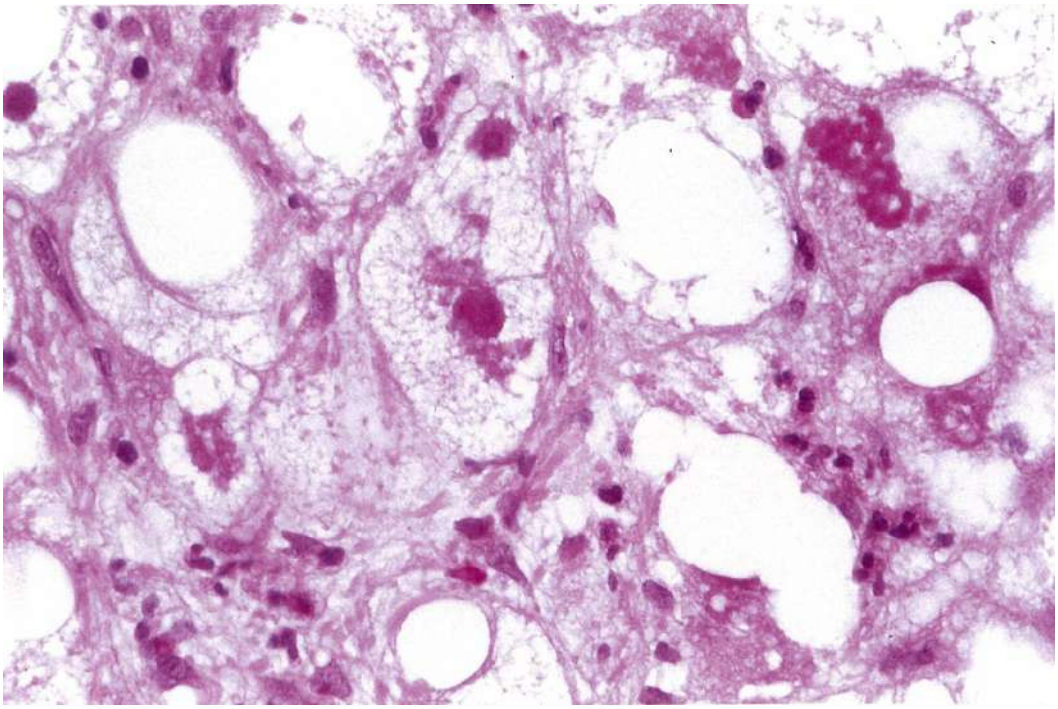
Explanation Why

Intracytoplasmic eosinophilic inclusions in hepatocytes (Mallory bodies) and cellular swelling are most commonly seen in alcoholic hepatitis. Alcoholic hepatitis usually manifests with elevated transaminases (AST > ALT), which is not present here. Mallory bodies are also seen in other conditions, including nonalcoholic fatty liver disease, Wilson disease, and hepatocellular carcinoma. However, none of these conditions would explain this patient's elevated AMA titers. Occasionally, Mallory bodies are found in patients with PBC; however, a different pathologic finding is more characteristic of PBC and therefore more likely to be found in this patient.

C - Macrovesicular fatty infiltration and necrosis of hepatocytes

Image



Explanation Why

Macrovesicular fatty infiltration and necrosis of hepatocytes are characteristic findings in steatohepatitis, which is most commonly related to obesity or metabolic syndrome (nonalcoholic fatty liver disease) but can also be caused by alcohol use. This patient's pruritus and elevated AMA titers are more suggestive of a different etiology, making this finding unlikely.

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D - Ballooning degeneration and apoptosis of hepatocytes

Explanation Why

Ballooning degeneration and apoptosis of hepatocytes is a specific type of apoptotic hepatocyte degeneration that is characteristic of steatohepatitis. It is most often seen in nonalcoholic fatty liver disease, alcoholic hepatitis, and acute viral hepatitis, which usually also manifests with lymphocytic infiltration in the lobules and surrounding the sinuses. In a patient with steatohepatitis, elevated transaminases would be expected, however.

E - Lymphocytic infiltration of portal areas and periductal granulomas

Explanation Why

Primary biliary cholangitis (PBC) most commonly affects middle-aged women and is characterized by lymphocytic inflammation of the portal area with periductal granulomatous changes and eventual bile duct destruction. Symptoms include fatigue, hyperpigmentation, and pruritus. PBC is typically diagnosed through elevated serum alkaline phosphatase levels and normal serum total bilirubin levels. Antimitochondrial antibodies (AMAs) are present in 90%–95% of patients. For patients with undetectable serum AMA levels, a liver biopsy is required for diagnosis.

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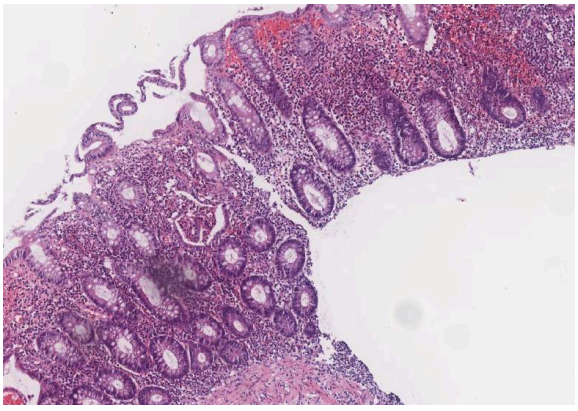
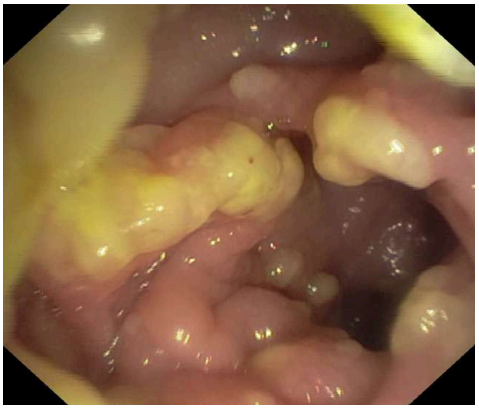
Question # 14

A previously healthy, 24-year-old man comes to the physician because of a 6-week history of loose, nonbloody stools. He also reports abdominal pain, intermittent nausea, and fever. He has not had vomiting, tenesmus, or rectal pain. His vital signs are within normal limits. Abdominal examination reveals tenderness of the right lower abdomen without rebound tenderness. Rectal exam is unremarkable. Laboratory studies show a leukocyte count of 14,800/mm^3 and an erythrocyte sedimentation rate of 51 mm/h. Test of the stool for occult blood and stool studies for infection are negative. A CT scan of the abdomen shows transmural thickening and surrounding fat stranding of discrete regions of the terminal ileum and transverse colon. A colonoscopy is performed and biopsy specimens of the affected areas of the colon are taken. Which of the following findings is most specific for this patient's condition?

	Answer	Image
A	Neutrophilic inflammation of the crypts	
B	Neutrophil-rich pseudomembranes	

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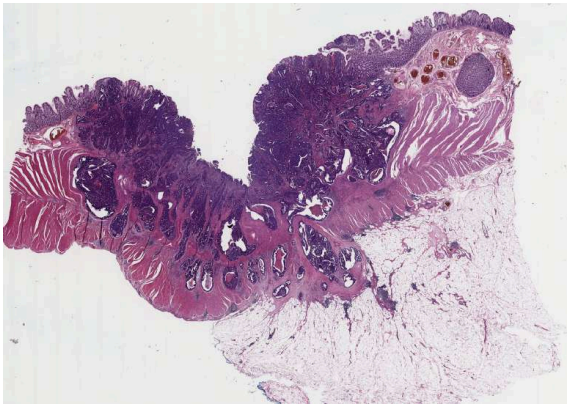
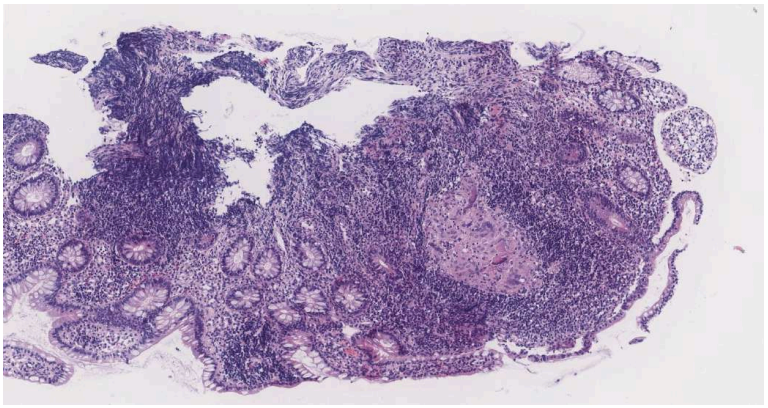
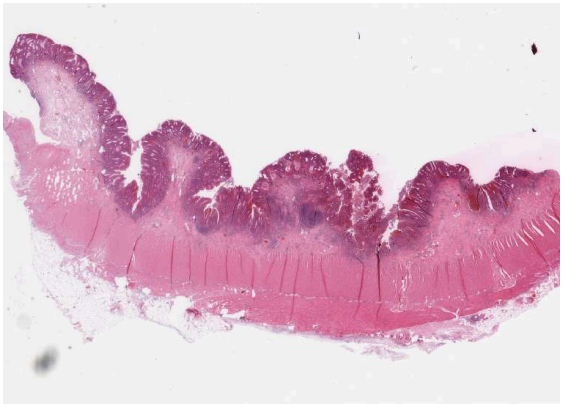
	Answer	Image
C	Poorly differentiated gland-forming cells with desmoplasia	
D	Inflammation of the terminal ileum	
E	Formation of noncaseating granulomas	
F	Inflammation limited to the mucosa and submucosa	
G	Presence of pseudopolyps	

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Hint

This young man has abdominal pain, diarrhea, fever, laboratory evidence of inflammation, and a CT scan of the abdomen showing skip lesions in the colon with transmural inflammation and sparing of the rectum. Given that the infectious workup was negative, autoimmune enteritis is high on the differential. Crohn disease is more likely than ulcerative colitis based on the CT scan and the absence of tenesmus, gross bleeding, and rectal pain.

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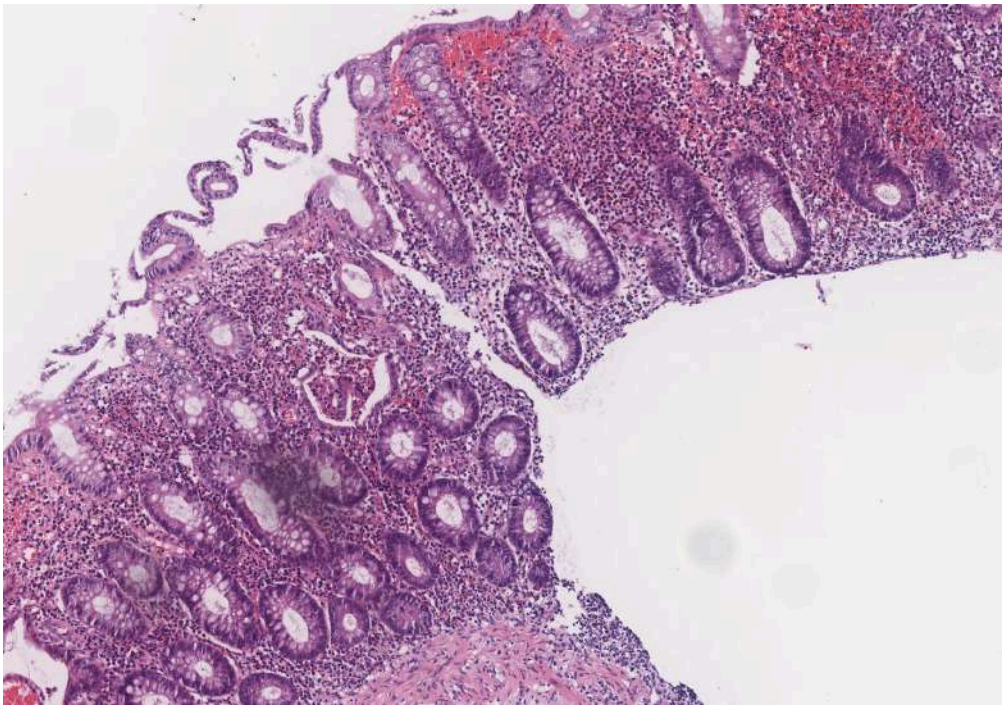
Correct Answer

A - Neutrophilic inflammation of the crypts

Image



Explanation Why

Neutrophilic inflammation of the crypts is a histopathologic finding in approximately 20% of patients with Crohn disease, but it is relatively nonspecific. Approximately 40% of patients with ulcerative colitis (UC) also have this finding. UC may also present with abdominal pain, loose stools, nausea, and fever. However, stool in UC is typically grossly bloody and contains mucus. A CT scan of the abdomen would most likely show continuous inflammation starting in the rectum, in contrast to the discrete regions of inflammation in this patient.

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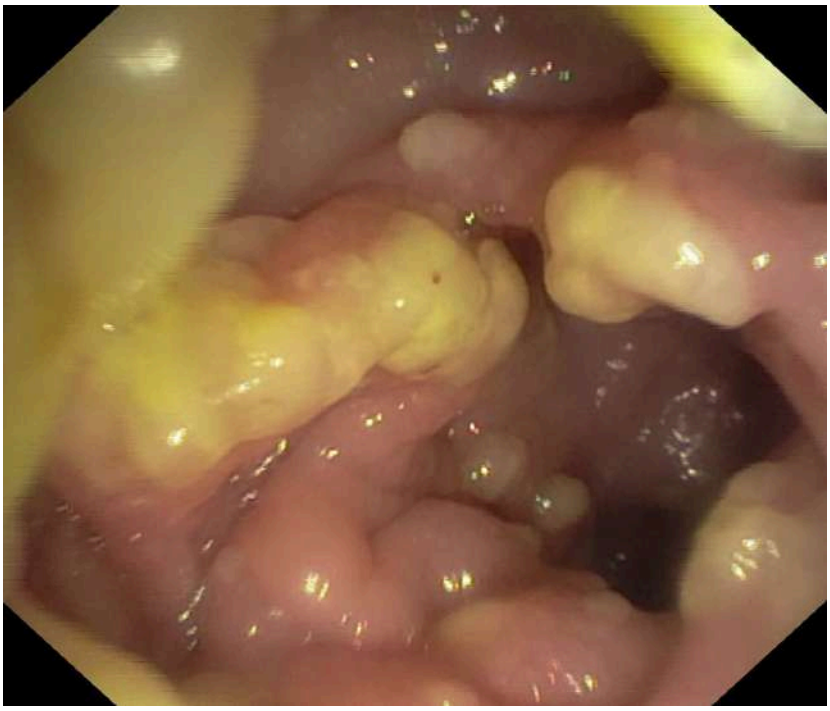
B - Neutrophil-rich pseudomembranes

Image



Explanation Why

Neutrophil-rich pseudomembranes are a histopathologic finding of clostridium enterocolitis, which may also present with abdominal pain, loose stools, nausea, and fevers. However, clostridium enterocolitis typically presents following antibiotic treatment, which facilitates overgrowth of *Clostridioides difficile* in the intestinal tract. Unlike in this patient, the loose stools are usually watery and characteristically foul-smelling. Inflammation of the colonic mucosa causes fibrinous exudate, which manifests as pseudomembranes.

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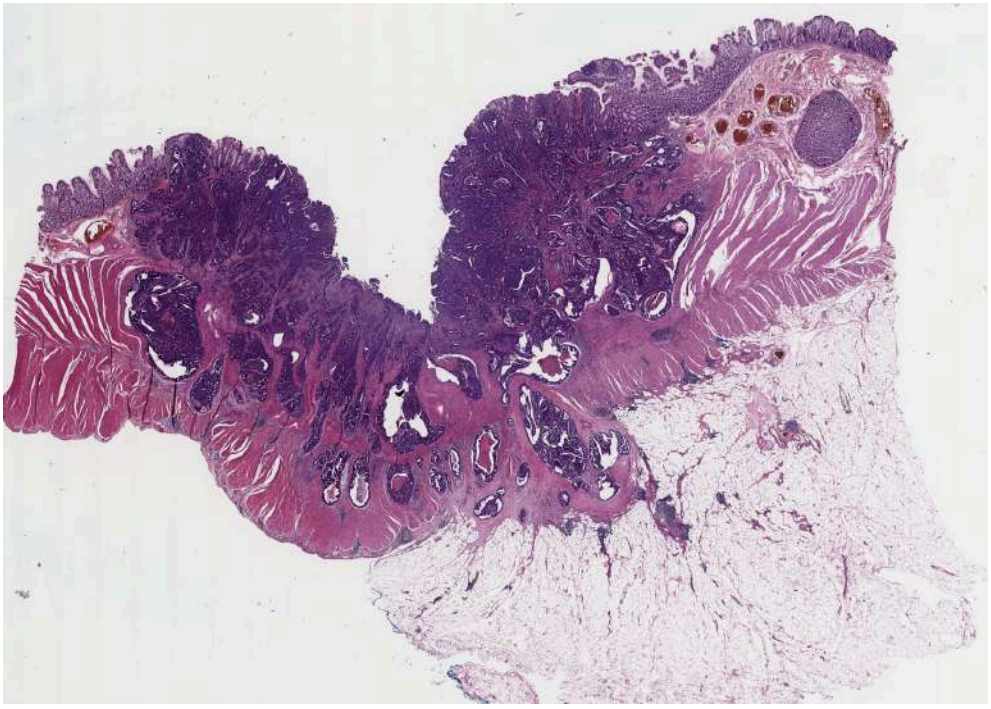
C - Poorly differentiated gland-forming cells with desmoplasia

Image



Explanation Why

Poorly differentiated gland-forming cells with desmoplasia of the surrounding connective tissue is a histopathologic finding of colon cancer, which may also present with abdominal pain, loose stools, and nausea. However, colon cancer would be unlikely in a 24-year-old patient without a significant family history. Moreover, it would have likely appeared as a soft tissue density narrowing the bowel lumen on abdominal CT scan.

D - Inflammation of the terminal ileum

Explanation Why

The terminal ileum is the most commonly affected region of the small bowel in patients with Crohn disease (CD). However, inflammation of the ileum is not specific to CD and can also occur in other

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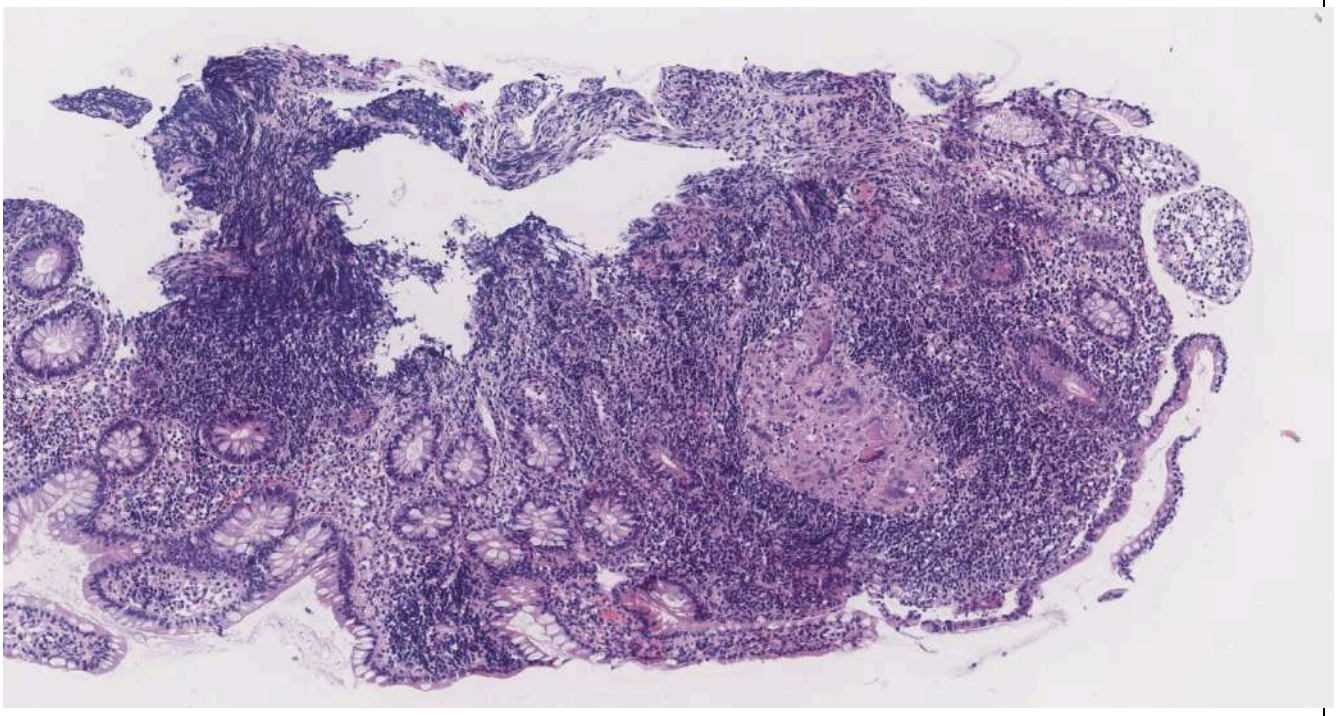
conditions, including ulcerative colitis (UC). While UC is limited to the colon in most cases, approximately 10–20% of patients have concomitant inflammation of the terminal ileum (backwash ileitis), making it difficult to differentiate from CD.

E - Formation of noncaseating granulomas

Image



Explanation But

Some intestinal infections, including tuberculosis and yersiniosis, may also present with granulomatous inflammation. However, intestinal tuberculosis and yersiniosis would present with caseating (central necrotizing) granulomas. Moreover, intestinal granulomas are also seen in patients with intestinal sarcoidosis or lymphomas.

Explanation Why

Formation of noncaseating granulomas is a histopathological finding in ~ 30% of patients with Crohn disease (CD). While the absence of granulomas does not rule out CD, their presence helps to distinguish CD from ulcerative colitis. This distinction can be challenging, especially in CD involving the colon. Distinguishing between the two conditions is crucial, however, as their management differs significantly. On biopsy, the presence of granulomatous inflammation,

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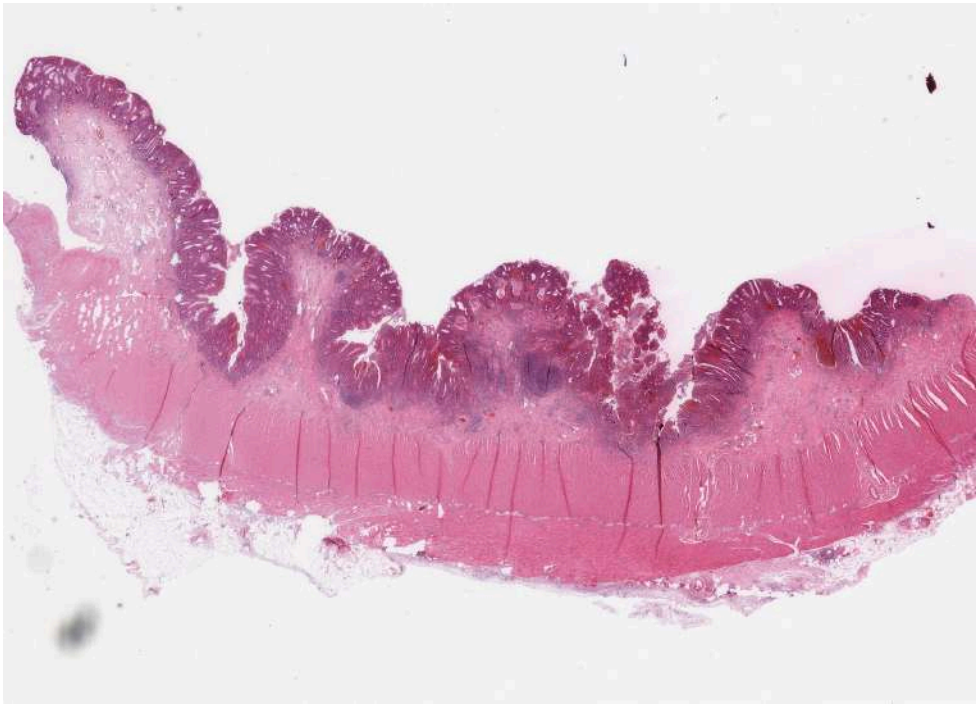
transmural inflammation, fissures, and aphthous ulcers would strongly suggest CD.

F - Inflammation limited to the mucosa and submucosa

Image



Explanation Why

Inflammation limited to the mucosa and submucosa is a histopathologic finding of ulcerative colitis (UC), which may also present with abdominal pain, loose stools, nausea, and fever. However, stool in UC is typically grossly bloody and contains mucus. Additionally, a CT scan of the abdomen would most likely show continuous inflammation starting in the rectum, in contrast to the discrete regions of inflammation in this patient.

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G - Presence of pseudopolyps

Explanation Why

Pseudopolyps can be found in Crohn disease (CD), but they are not specific to the condition. In fact, they are more commonly associated with ulcerative colitis (UC). UC may also present with abdominal pain, loose stools, nausea, and fever. However, stool in UC is typically grossly bloody and contains mucus. A CT scan of the abdomen would most likely show continuous inflammation starting in the rectum, in contrast to the discrete regions of inflammation in this patient.

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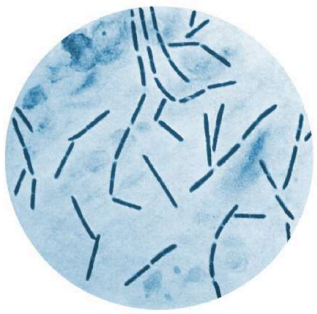
Question # 15

A 30-year-old woman comes to the emergency department because of fever, watery diarrhea, and abdominal cramping for the past 24 hours. She recently went to an international food fair. Her temperature is 39°C (102.2°F). Physical examination shows increased bowel sounds. Stool cultures grow gram-positive, spore-forming, anaerobic rods that produce alpha toxin. The responsible organism also causes which of the following physical examination findings?

	Answer	Image
A	Diffuse, flaccid bullae	
B	Facial paralysis	
C	Subcutaneous crepitus	
D	Rose spots	
E	Petechial rash	

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Hint

This patient's symptoms and stool culture are consistent with *Clostridium perfringens* enterocolitis.

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Correct Answer

A - Diffuse, flaccid bullae

Explanation Why

Diffuse, flaccid bullae are seen in staphylococcal scalded skin syndrome (SSSS), which is caused by *Staphylococcus aureus*. While these bacteria are a common cause of acute gastroenteritis, *Staphylococcus aureus* is a β-hemolytic, catalase-positive, gram-positive coccus that grows in clusters.

B - Facial paralysis

Explanation Why

Facial paralysis can be observed in Guillain Barré syndrome, which may occur as a complication of *Campylobacter jejuni* enteritis, the most common pathogen responsible for foodborne gastroenteritis in the US. While this infection also manifests with diarrhea, it most often causes bloody diarrhea, not the watery diarrhea seen in this patient. Moreover, *Campylobacter jejuni* is a comma-shaped, gram-negative rod, while this patient's culture has grown gram-positive, spore-forming, anaerobic rods.

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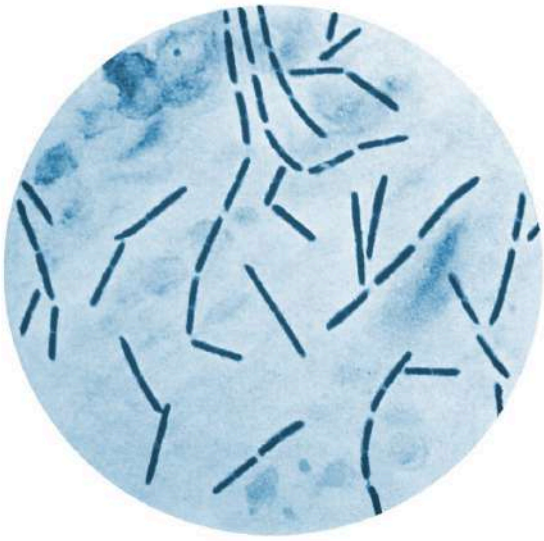
C - Subcutaneous crepitus

Image



Explanation Why

Clostridium perfringens, the organism responsible for this patient's symptoms, can also cause gas gangrene, which classically presents with subcutaneous emphysema and palpable crepitus. The spores of these obligate anaerobic rods survive in undercooked food; when ingested, bacteria release heat-labile enterotoxins that cause food poisoning with watery diarrhea and severe abdominal cramping. This condition is rarely complicated by a syndrome that resembles necrotizing enteritis.

D - Rose spots

Explanation Why

Rose spots can be caused by infection with *Salmonella typhi* or *Salmonella paratyphi*, which are transmitted via the fecal-oral route. While these organisms can cause diarrhea, (para)typhoid fever

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typically progresses over the course of weeks. Moreover, these organisms are gram-negative and non-spore-forming, which would not be consistent with the gram-positive, spore-forming bacteria seen in this patient's culture.

E - Petechial rash

Explanation Why

A petechial rash can be observed in hemolytic uremic syndrome (HUS), which is most commonly caused by enterohemorrhagic *E. coli* (EHEC). However, EHEC typically causes bloody diarrhea, which is not present in this patient. The only type of *E. coli* that causes watery diarrhea is enterotoxigenic *E. coli* (ETEC), the most frequent cause of traveler's diarrhea. Since this patient has no history of recent travel, this diagnosis is also unlikely.

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Question # 16

A 3-year-old girl is brought to the emergency department because of abdominal pain and watery diarrhea for the past 2 days. This morning, her stool had a red tint. She and her parents visited a circus 1 week ago. The patient attends day care. Her immunizations are up-to-date. Her temperature is 38°C (100.4°F), pulse is 140/min, and blood pressure is 80/45 mm Hg. Abdominal examination shows a soft abdomen that is tender to palpation in the right lower quadrant with rebound. A stool culture grows *Yersinia enterocolitica*. Consumption of which of the following is most likely to cause the infection seen in this patient?

	Answer	Image
A	Undercooked pork	
B	Undercooked eggs	
C	Undercooked poultry	
D	Reheated rice	
E	Home-canned food	
F	Unwashed vegetables	
G	Undercooked seafood	
H	Deli meats	

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Hint

This patient presents with gastroenteritis, signs of pseudoappendicitis (right lower quadrant pain), and has stool cultures growing *Yersinia enterocolitica*. Humans are considered to be incidental hosts.

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Correct Answer

A - Undercooked pork

Explanation Why

Yersinia enterocolitica is usually transmitted via contaminated raw pork, unpasteurized milk products, unfiltered water, or pet feces. In day-care centers, where children might not be toilet trained or follow personal hygiene practices (e.g., handwashing), person-to-person fecal-oral transmission of *Y. enterocolitica* is possible. After an incubation period of typically 4–6 days, yersiniosis causes inflammatory diarrhea, nausea, low-grade fever, and possibly RLQ tenderness that may mimic appendicitis ("pseudoappendicitis").

B - Undercooked eggs

Explanation Why

Consuming undercooked eggs is especially a risk factor for developing salmonellosis, which can also present with watery-bloody diarrhea and fever. Consuming undercooked eggs is not a known risk factor for transmission of *Yersinia enterocolitica*.

C - Undercooked poultry

Explanation Why

Consuming undercooked poultry is especially a risk factor for infection with *Salmonella enteritidis* or *Campylobacter jejuni*, both of which could cause similar symptoms. *Campylobacter* is the most common cause of bacterial diarrhea in the US and is transmitted either through food or direct contact with infected animals (e.g., puppies). Undercooked poultry is not associated with transmission of *Yersinia enterocolitica*.

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D - Reheated rice

Explanation Why

Consuming reheated rice is a risk factor for the direct ingestion of the heat-stable cereulide toxin of *Bacillus cereus*. This toxin causes an emetic syndrome that progresses to diarrhea in approximately one-third of exposed patients. However, the watery diarrheal syndrome (without emesis) associated with *Bacillus cereus* would only result from the consumption of contaminated meats, vegetables, and sauces (not rice). Reheated rice is not associated with transmission of *Yersinia enterocolitica*.

E - Home-canned food

Explanation Why

Consuming home-canned fruits, vegetables, and packed meats is especially a risk factor for infection with *Clostridium botulinum*, the pathogen that causes botulism. Botulism classically presents with mydriasis, flaccid paralysis that progresses caudally, and cranial nerve involvement (e.g., slurred speech, dysphagia). Consuming canned food is not a known risk factor for transmission of *Yersinia enterocolitica*.

F - Unwashed vegetables

Explanation Why

Consuming unwashed vegetables is especially a risk factor for infection with *Shigella dysenteriae*, which can also cause bloody diarrhea. Shigella has an incubation period of up to 2 days and is usually accompanied by high fever and tenesmus. Consuming unwashed vegetables is not a known risk factor for transmission of *Yersinia enterocolitica*.

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G - Undercooked seafood

Explanation Why

Consuming undercooked seafood and raw oysters are especially risk factors for infection with *Vibrio* species or hepatitis A, both of which can present similarly to this patient. Undercooked seafood is not associated with transmission of *Yersinia enterocolitica*.

H - Deli meats

Explanation Why

Consuming deli meats (precooked cold cuts) is a risk factor for infection with *Listeria monocytogenes*, which is usually asymptomatic but may cause gastroenteritis and/or meningitis in newborns, pregnant women, and immunocompromised patients. Consuming deli meats is not a known risk factor for the transmission of *Yersinia enterocolitica*.

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Question # 17

A previously healthy 5-year-old girl is brought to the emergency department by her parents because of a severe headache, nausea, and vomiting for 6 hours. Last week she had fever, myalgias, and a sore throat for several days that resolved with over-the-counter medication. She is oriented only to person. Examination shows bilateral optic disc swelling. Serum studies show:

Glucose	61 mg/dL
Aspartate aminotransferase (AST)	198 U/L
Alanine aminotransferase (ALT)	166 U/L
Prothrombin time	18 sec

Which of the following is the most likely cause of this patient's symptoms?

	Answer	Image
A	Autoimmune destruction of beta cells	
B	Acute viral hepatitis	
C	Hepatic mitochondrial injury	
D	Bacterial meningitis	

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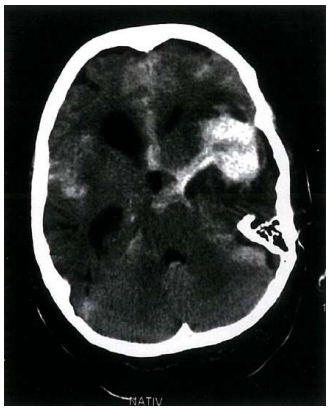
	Answer	Image
E	Ruptured berry aneurysm	
F	Ethylene glycol poisoning	

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Hint

The patient was likely given over-the-counter aspirin for her flu-like symptoms, which should be avoided in pediatric patients because of a rare, life-threatening adverse effect.

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Correct Answer

A - Autoimmune destruction of beta cells

Explanation Why

Autoimmune destruction of pancreatic beta cells occurs in type 1 diabetes mellitus, which may also present with altered mental status and vomiting if it first manifests as diabetic ketoacidosis (DKA). However, DKA is characterized by very high blood glucose levels and would not explain this patient's elevated transaminases.

B - Acute viral hepatitis

Explanation Why

Acute infection with hepatitis A virus may lead to fever, vomiting, and high levels of serum transaminases. However, elevated ICP (as evidenced by bilateral optic disc swelling) and hypoglycemia are not consistent with this diagnosis.

C - Hepatic mitochondrial injury

Explanation But

Acetaminophen should be used as an antipyretic instead of aspirin in children with febrile illness to avoid Reye syndrome!

Explanation Why

Reye syndrome is caused by hepatic mitochondrial injury that can develop in children 3–5 days after aspirin treatment of a febrile viral illness (most commonly with VZV or influenza B). It initially presents as hepatic encephalopathy that manifests with profuse vomiting (due to ↑ ICP) and lethargy, which progresses to delirium, seizures, and coma. Other typical findings include hepatomegaly, elevated AST and ALT, hypoglycemia, elevated INR, and metabolic acidosis. Liver biopsy is only

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performed in doubtful cases and shows microvesicular hepatic steatosis (fatty degenerative liver).

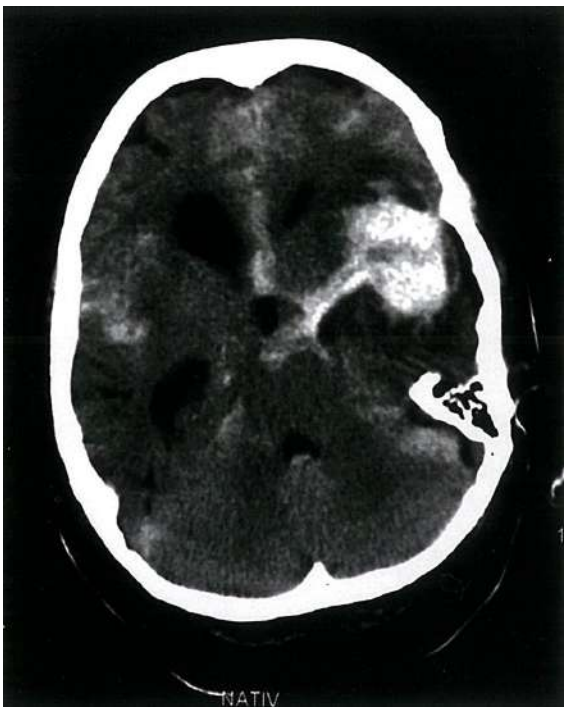
D - Bacterial meningitis

Explanation Why

Patients with meningitis typically present with fever, headache, vomiting, and altered mental status. Infection with *Neisseria meningitidis* is the most common cause of meningitis in this patient's age group and may also occur after a pharyngitis or sinusitis. However, this patient does not have any of the physical exam findings typical of meningitis, such as neck stiffness (nuchal rigidity), a positive Kernig sign, or a positive Brudzinski sign. Additionally, meningitis would not account for this patient's abnormally elevated serum transaminases or elevated prothrombin time.

E - Ruptured berry aneurysm

Image



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Explanation Why

In pediatric patients, a ruptured berry aneurysm in the circle of Willis and subsequent subarachnoid hemorrhage may also present with a severe headache, impaired consciousness, bilateral optic disc swelling, and fever. However, a ruptured aneurysm is unlikely to cause elevated serum transaminases or an elevated prothrombin time.

F - Ethylene glycol poisoning

Explanation Why

Toxicity from ingestion of antifreeze, which contains ethylene glycol, may present with altered mental status, vomiting, and signs of hepatocellular injury. However, patients typically also present with sweet-smelling breath, hallucinations, seizures, tetany, dyspnea, flank pain, and hematuria due to calcium oxalate deposition in the kidneys, all of which are absent in this patient.

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Question # 18

A 12-year-old girl is brought to the physician because of a 2-hour history of severe epigastric pain, nausea, and vomiting. Her father has a history of similar episodes of abdominal pain and developed diabetes mellitus at the age of 30 years. Abdominal examination shows guarding and rigidity. Ultrasonography of the abdomen shows diffuse enlargement of the pancreas; no gallstones are visualized. Which of the following is the most likely underlying cause of this patient's condition?

	Answer	Image
A	Defective bilirubin glucuronidation	
B	Elevated serum amylase levels	
C	Increased β-glucuronidase activity	
D	Premature activation of trypsinogen	
E	Defective elastase inhibitor	
F	Impaired cellular copper transport	

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Hint

The patient's severe epigastric pain and ultrasonography showing diffuse enlargement of the pancreas suggest acute pancreatitis, which usually occurs in older patients with a history of gallstones or longstanding alcohol use disorder. The absence of these risk factors, the atypical age of presentation, and the family history of similar episodes suggests there is a hereditary component to this patient's disease.

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Correct Answer

A - Defective bilirubin glucuronidation

Explanation Why

Defective glucuronidation of bilirubin is seen in Gilbert syndrome and Crigler-Najjar syndrome, which are genetic disorders characterized by unconjugated hyperbilirubinemia. Unconjugated hyperbilirubinemia predisposes to the development of black or brown pigment gallstones, which are a risk factor for acute pancreatitis. However, this patient has no history of recurrent episodes of jaundice and there are no gallstones visualized on abdominal ultrasonography.

B - Elevated serum amylase levels

Explanation Why

Elevated serum amylase levels greater than three times the baseline in a patient with acute epigastric pain is diagnostic of acute pancreatitis. Amylase is an intracellular enzyme, and elevated serum levels indicate pancreatic acinar injury. Hyperamylasemia is, therefore, a result of acute pancreatitis, not a cause of it.

C - Increased β-glucuronidase activity

Explanation Why

Increased β-glucuronidase activity is a result of bacterial infections of the biliary tract. β-glucuronidase deconjugates direct bilirubin, resulting in excessive unconjugated bilirubin in the biliary tract that precipitates with calcium to form brown pigment gallstones. This can cause acute pancreatitis. However, gallstone pancreatitis would typically manifest in older individuals (> 40 years of age). Moreover, there are no gallstones visualized on abdominal ultrasonography of this patient.

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D - Premature activation of trypsinogen

Explanation But

Other genetic variants associated with chronic pancreatitis are mutations in *SPINK 1* and *CFTR* genes.

Explanation Why

Premature activation of trypsinogen to trypsin within the pancreas activates the pancreatic digestive enzymes (lipase, amylase, and protease) that cause pancreatic autodigestion and inflammation. This enzymatic pathway is the underlying pathophysiology of acute pancreatitis, regardless of the etiology (e.g., pancreatic ductal blockage in gallstone pancreatitis, pancreatic acinar injury in alcohol-induced pancreatitis). Hereditary pancreatitis, which this patient most likely has, is usually caused by a mutated *PRSS1* gene that promotes intrapancreatic trypsinogen activation.

E - Defective elastase inhibitor

Explanation Why

α1 antitrypsin inhibits the enzyme elastase, which breaks down elastin. A defect or deficiency in α1 antitrypsin causes unopposed elastase activity, which predisposes to the development of lung emphysema and liver cirrhosis. The pancreas, however, is usually not affected in α1 antitrypsin deficiency. It was previously thought that α1 antitrypsin deficiency is a cause of chronic pancreatitis. However, recent studies show that there is no concrete link between the two conditions.

F - Impaired cellular copper transport

Explanation Why

Impaired hepatocellular copper transport and subsequent accumulation of copper in various organs of the body is seen in Wilson disease, which can become symptomatic in childhood. Pancreatitis is an uncommon manifestation of Wilson disease but can occur due to an intrapancreatic accumulation of

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copper. However, Wilson disease typically first manifests with signs of liver disease (e.g., jaundice, hepatomegaly, ascites) in early childhood and neurological manifestations (e.g., dysarthria, ataxia, parkinsonism) in late childhood/adulthood.

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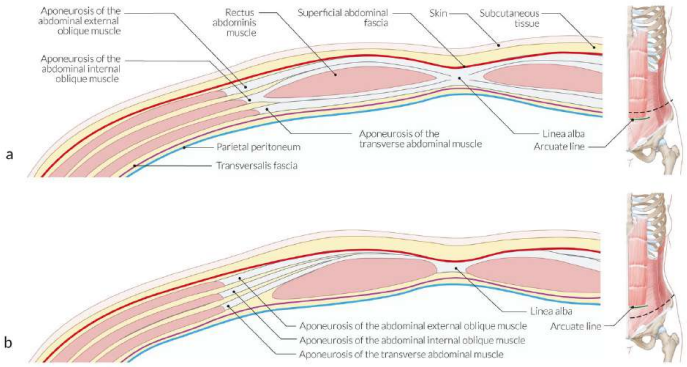
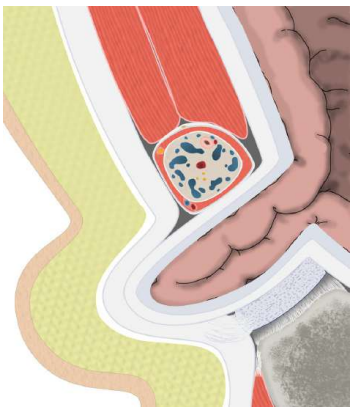
Question # 19

A 67-year-old woman is brought to the emergency department by her husband because of a 1-hour history of severe groin pain, nausea, and vomiting. She has had a groin swelling that worsens with standing, coughing, and straining for the past 3 months. Her pulse is 120/min. Examination shows pallor; there is swelling, erythema, and tenderness to palpation of the right groin that is centered below the inguinal ligament. The most likely cause of this patient's condition is entrapment of an organ between which of the following structures?

	Answer	Image
A	Linea alba and conjoint tendon	
B	Inferior epigastric artery and rectus sheath	
C	Conjoint tendon and inguinal ligament	
D	Medial and median umbilical ligaments	

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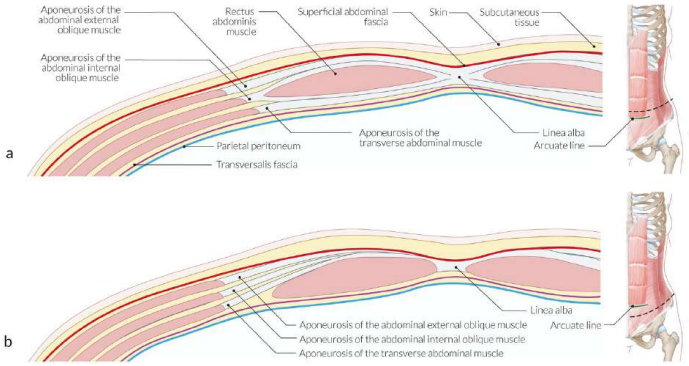
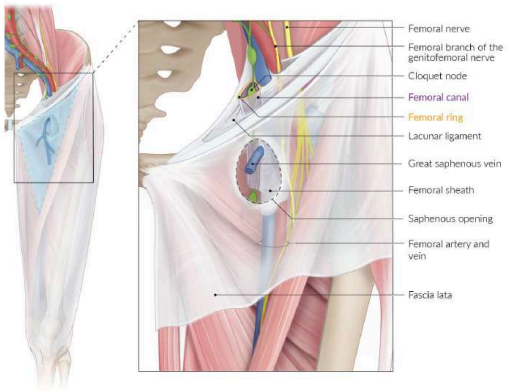
	Answer	Image
E	Transversalis fascia and internal oblique aponeurosis	
F	Lacunar ligament and femoral vein	

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Hint

A groin swelling that worsens with standing, coughing, and straining is suggestive of a hernia. In a patient with a hernia, severe pain and features of bowel obstruction (e.g., nausea, vomiting) indicate strangulation. As the swelling is located below the midpoint of the inguinal canal, a femoral hernia is the most likely diagnosis.

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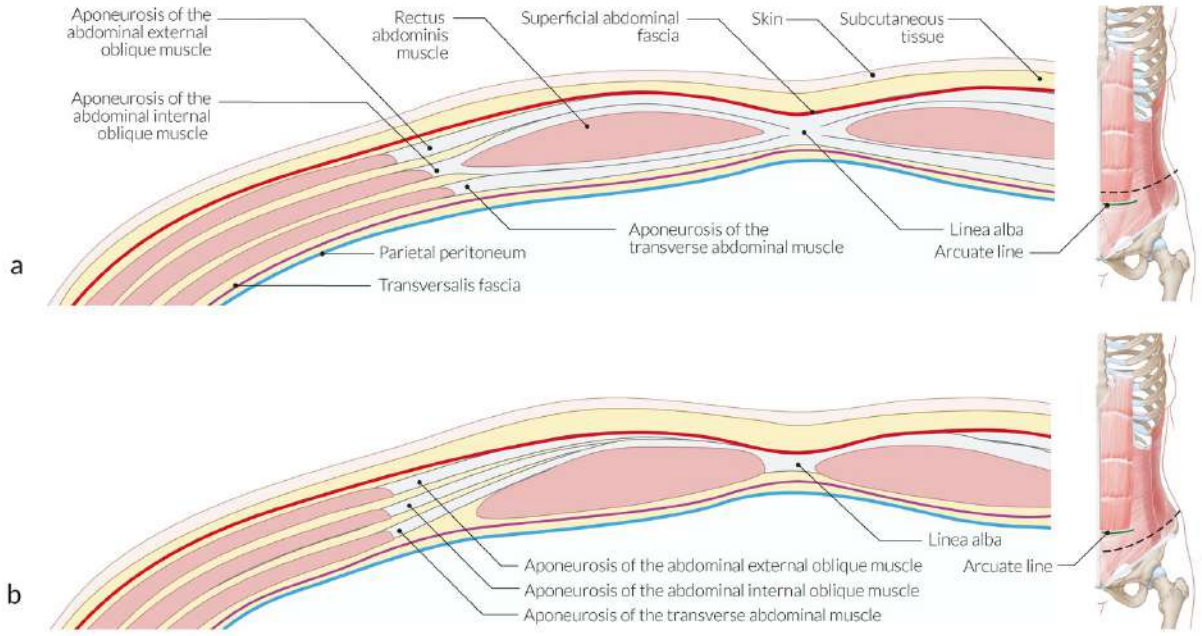
Correct Answer

A - Linea alba and conjoint tendon

Image



Explanation Why

The linea alba is a longitudinal band in the anterior abdomen extending from the xiphoid process to the pubic symphysis. The conjoint tendon lies in the inferior quadrant of the abdomen, attached medially to the pubic tubercle. Ventral hernias (e.g., epigastric hernias) occur when intra-abdominal contents herniate through the linea alba. This patient, however, presents with pain and swelling below the inguinal ligament.

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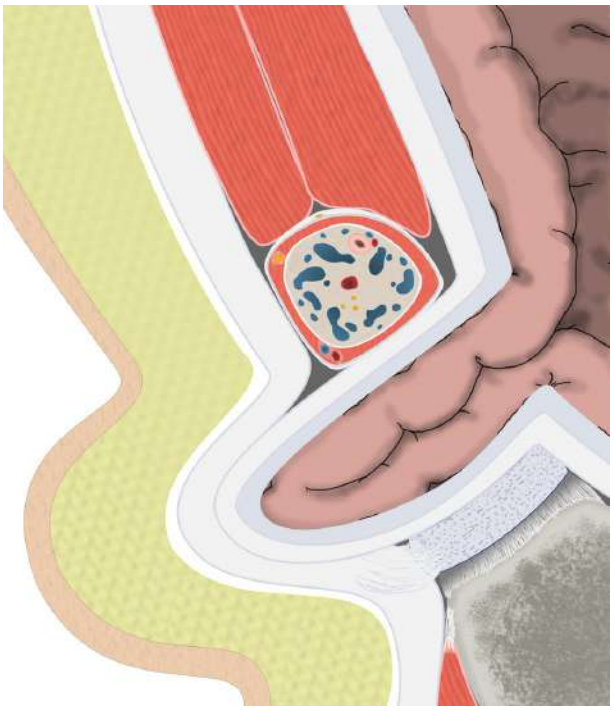
B - Inferior epigastric artery and rectus sheath

Image



Explanation Why

The inferior epigastric artery and the lateral edge of the rectus sheath form the lateral and medial borders of the Hesselbach triangle. Contents of a direct inguinal hernia pass between these two structures. A direct inguinal hernia would appear as a mass above the inguinal ligament, unlike the mass below the inguinal ligament seen here. Moreover, direct inguinal hernias are less prone to strangulation or incarceration when compared to other hernias because the neck of a direct hernia is wide.

C - Conjoint tendon and inguinal ligament

Explanation Why

The inguinal canal is bounded superiorly by the conjoint tendon and inferiorly by the inguinal

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ligament. In the case of an indirect inguinal hernia, intra-abdominal contents pass through the deep inguinal ring and lie within the inguinal canal. However, an indirect inguinal hernia would appear as a mass above the inguinal ligament, unlike the mass below the inguinal ligament seen here. Moreover, indirect inguinal hernias occur typically among men; they are uncommon among women.

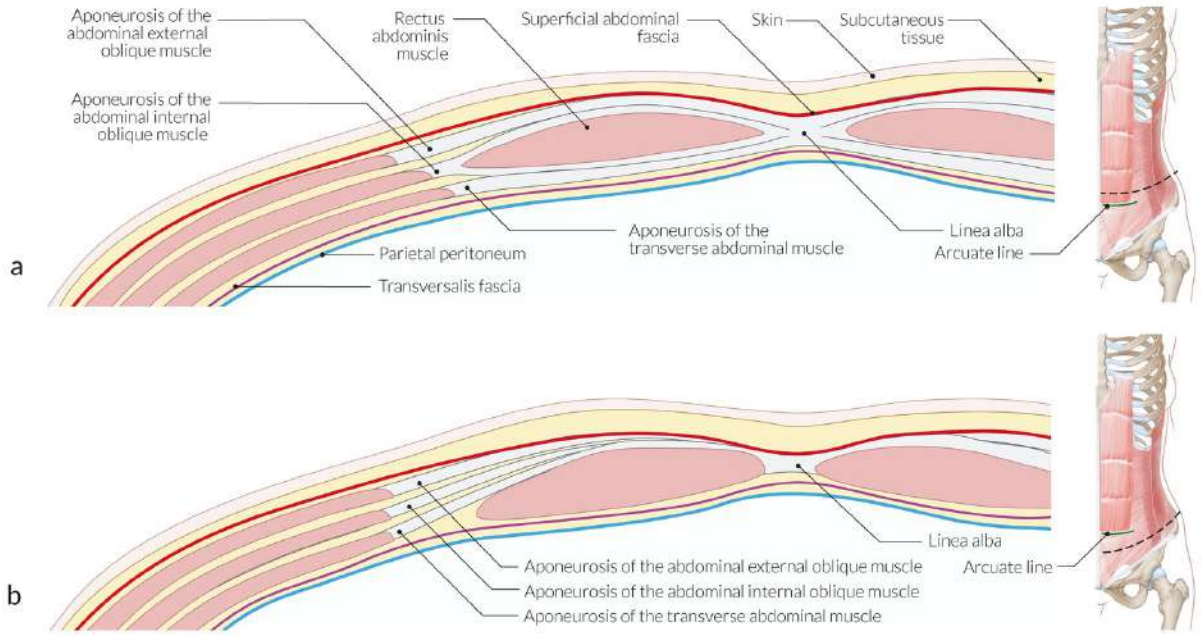
D - Medial and median umbilical ligaments

Explanation Why

The supravesical fossae lie between the median umbilical ligament and medial umbilical ligaments on either side. Rarely, bowel may herniate into the supravesical fossae (internal hernia), in which case, examination would show tenderness in the suprapubic region, usually without a palpable mass. This patient, however, presents with a tender mass below the inguinal ligament.

E - Transversalis fascia and internal oblique aponeurosis

Image



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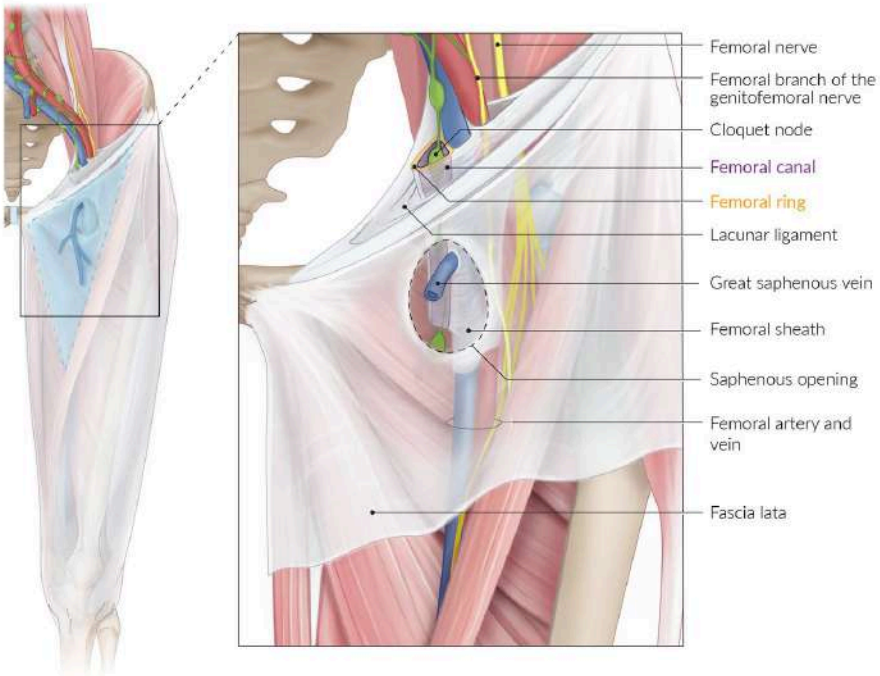
Explanation Why

The transversalis fascia and internal oblique aponeurosis contribute to the formation of the rectus sheath, the fascial covering of the spermatic cord, and the conjoint tendon, which forms the medial part of the posterior wall of the inguinal canal. Weakness of the posterior wall of the inguinal canal results in a direct inguinal hernia, which would appear as a mass above the inguinal ligament, unlike the mass below the inguinal ligament seen here. Moreover, direct inguinal hernias are less prone to strangulation or incarceration when compared to other hernias because the neck of a direct hernia is wide.

F - Lacunar ligament and femoral vein

Image



Explanation Why

In the case of a femoral hernia, intra-abdominal contents (e.g., bowel, mesentery) pass into the femoral canal, which is bounded medially by the lacunar ligament and laterally by the femoral vein. Femoral hernias are more common in women and are likely to strangulate because the femoral canal is narrow.

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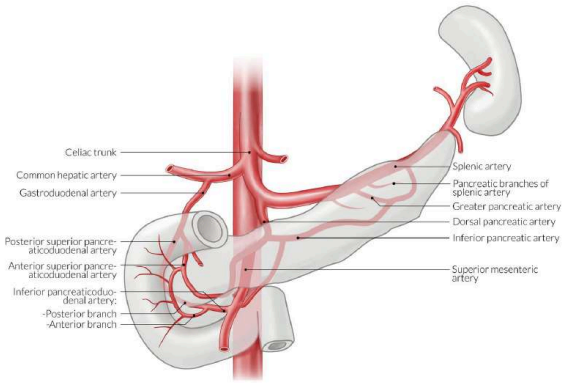
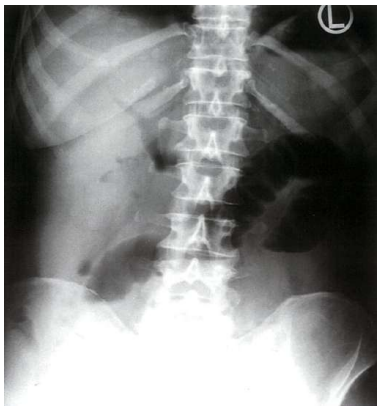
Question # 20

A 67-year-old woman comes to the physician because of a 5-day history of episodic abdominal pain, nausea, and vomiting. She has coronary artery disease and type 2 diabetes mellitus. She takes aspirin, metoprolol, and metformin. She is 163 cm (5 ft 4 in) tall and weighs 91 kg (200 lb); her BMI is 34 kg/m^2. Her temperature is 38.1°C (100.6°F). Physical examination shows dry mucous membranes, abdominal distension, and hyperactive bowel sounds. Ultrasonography of the abdomen shows air in the biliary tract. This patient's symptoms are most likely caused by obstruction at which of the following locations?

	Answer	Image
A	Third part of the duodenum	
B	Distal ileum	
C	Hepatic duct	
D	Proximal jejunum	

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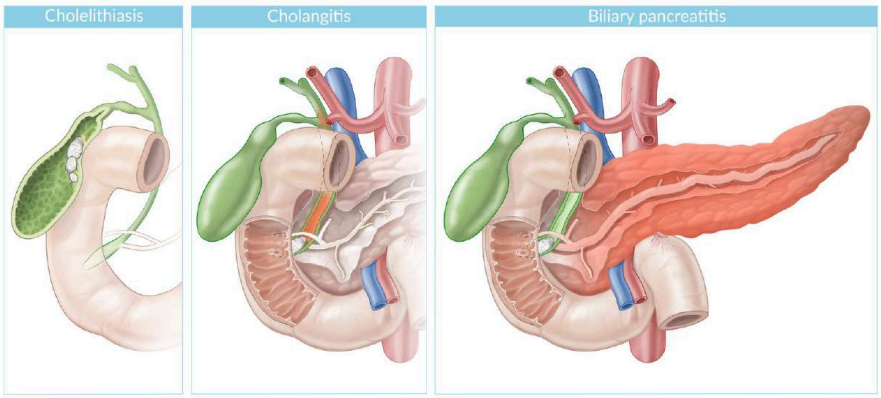
	Answer	Image
E	Pancreatic duct	

Hint

This patient has risk factors for gallstone disease (e.g., obesity, age > 40, female gender). In a patient with signs of intestinal obstruction (e.g., vomiting, abdominal pain, abdominal distension, hyperactive bowel sounds), the presence of pneumobilia is highly suggestive of gallstone ileus.

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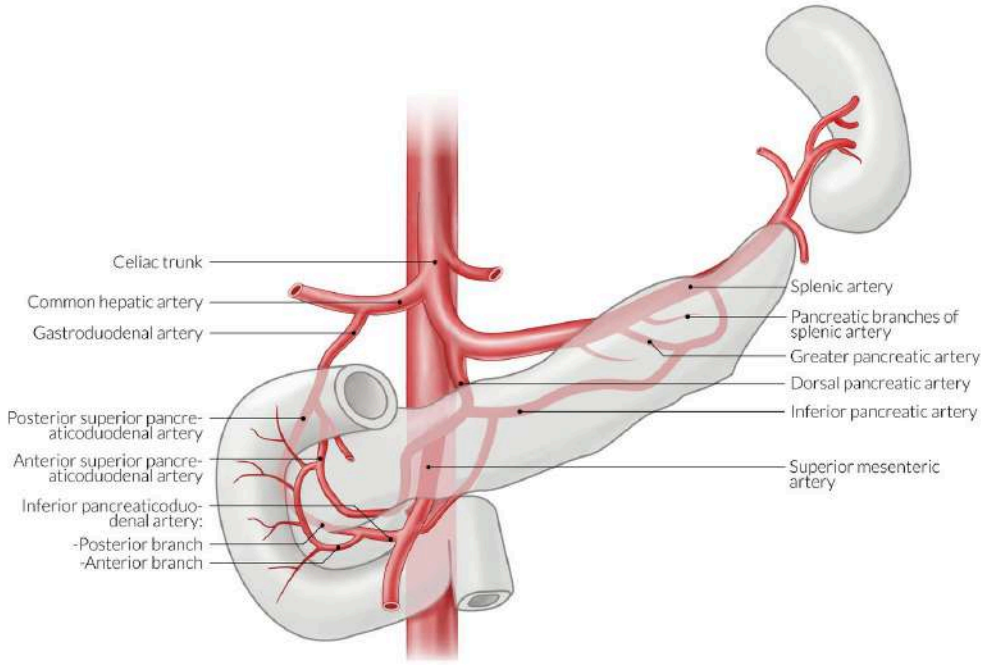
Correct Answer

A - Third part of the duodenum

Image



Explanation Why

The third part of the duodenum lies posterior to the superior mesenteric artery. In duodenal obstruction due to superior mesenteric artery syndrome, narrowing of the aortomesenteric angle causes compression of the inferior portion of the duodenum, leading to nausea, vomiting, and symptoms of small bowel obstruction, which are seen in this patient. However, superior mesenteric artery syndrome would not explain this patient's pneumobilia.

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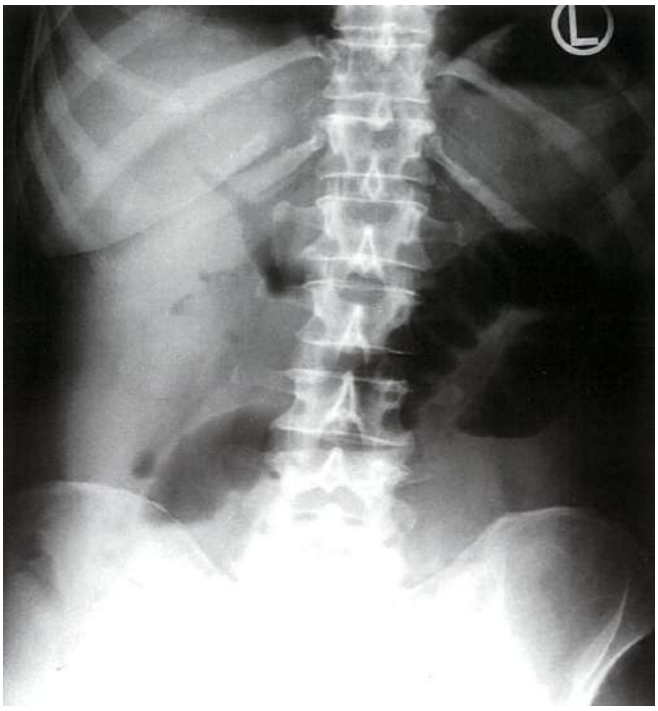
B - Distal ileum

Image



Explanation Why

Gallstone ileus is a rare complication of cholecystitis in which a cholecystoenteric fistula forms, through which air can enter the biliary tree. Gallstones can also pass through into the bowel lumen, leading to bowel obstruction and gallstone ileus. The distal ileum is separated from the large intestine by the ileocecal valve, which is the narrowest part of the small intestine and hence the most likely location for gallstone obstruction. Other causes of distal ileal obstruction include fecaliths, Meckel diverticulum, and intussusception.

C - Hepatic duct

Explanation Why

The hepatic duct joins the cystic duct to drain bile from the liver into the intestines. The common

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hepatic duct can be obstructed by an impacted gallstone in a condition known as Mirizzi syndrome, leading to the development of abdominal pain, fever, nausea, vomiting. However, due to biliary obstruction, Mirizzi syndrome typically manifests with jaundice, which is not seen in this patient. Moreover, signs of intestinal obstruction (ileus) would not be expected.

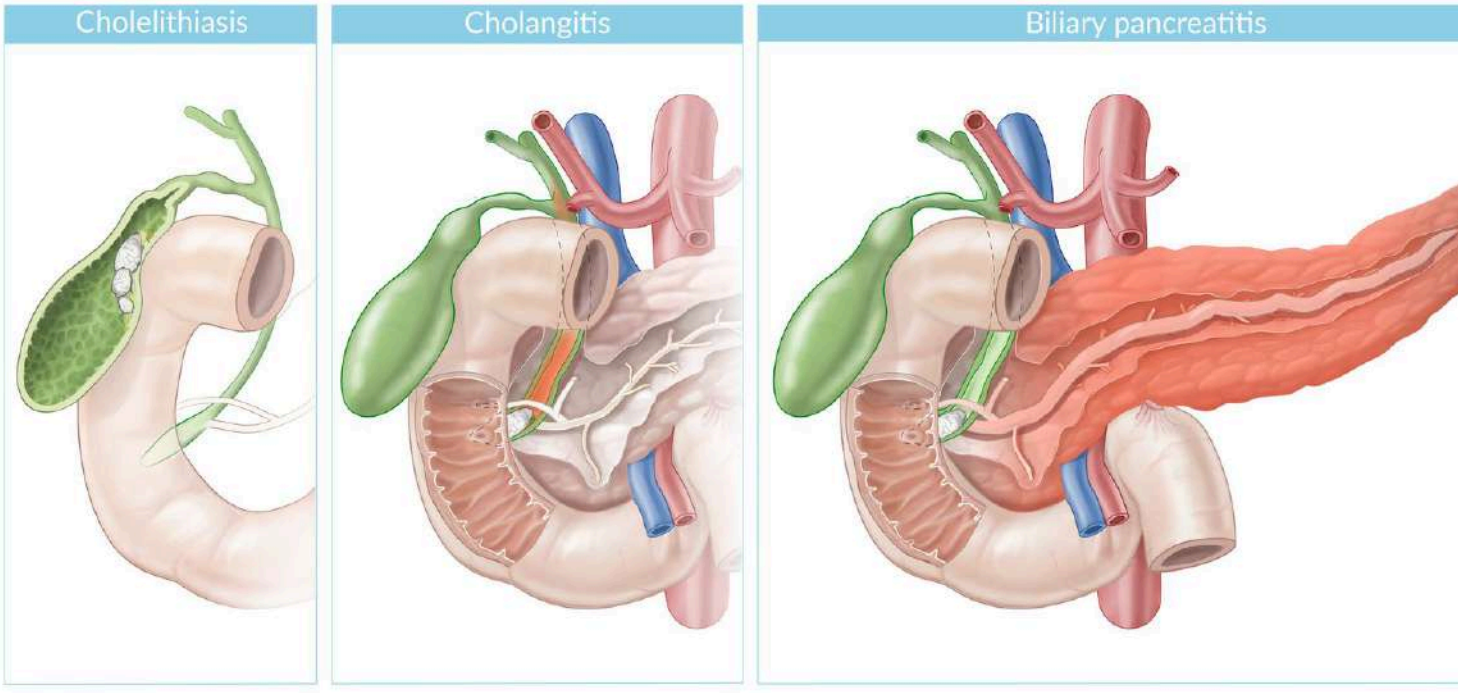
D - Proximal jejunum

Explanation Why

The jejunum is the section of bowel between the duodenum and the ileum. Jejunal obstruction would lead to abdominal pain, nausea, vomiting, and fever, which are seen in this patient. However, jejunal obstruction is typically caused by bowel adhesions or intussusception, not gallstones. This patient's history does not include risk factors for adhesions (e.g., prior abdominal surgery), and she is outside of the typical age range for intussusception (children), making jejunal obstruction unlikely.

E - Pancreatic duct

Image



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Explanation Why

The pancreatic duct extends from the tail to the head of the pancreas and drains pancreatic fluid into the common bile duct. Pancreatic duct obstruction by a gallstone can cause acute pancreatitis with abdominal pain, nausea, vomiting, and fever, which are symptoms seen in this patient. However, because pancreatic duct obstruction occurs upstream of the small bowel, symptoms of small bowel obstruction (e.g., hyperactive bowel sounds) would not be expected. In addition, pancreatitis would not cause pneumobilia.

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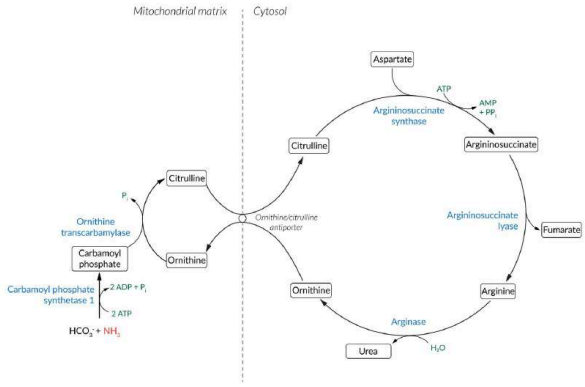
Question # 21

A 4-day-old boy is brought to the physician because of somnolence, poor feeding, and vomiting after his first few breast feedings. He appears lethargic. His respiratory rate is 73/min. Serum ammonia is markedly increased. Genetic analysis shows deficiency in N-acetylglutamate synthase. The activity of which of the following enzymes is most likely directly affected by this genetic defect?

	Answer	Image
A	Carbamoyl phosphate synthetase I	
B	Ornithine translocase	
C	Ornithine transcarbamylase	
D	Argininosuccinate synthetase	
E	Argininosuccinase	
F	Arginase	

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Hint

N-acetylglutamate synthase produces N-acetylglutamate, which serves as an allosteric activator for one of the two enzymatic reactions of the urea cycle that take place in the mitochondria.

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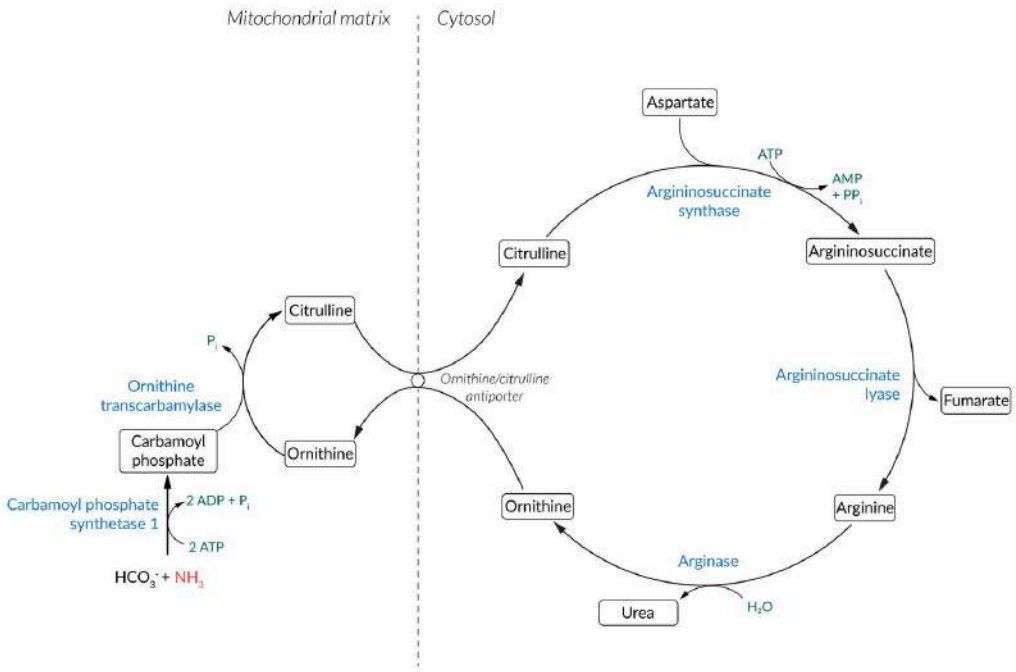
Correct Answer

A - Carbamoyl phosphate synthetase I

Image



Explanation But

The two most common hereditary defects in the urea cycle are ornithine transcarbamylase deficiency (OTC deficiency) and CPS1 deficiency. Neonates with either of these defects are usually normal at birth but present with vomiting, lethargy, hyperventilation, and cerebral edema (due to intracellular accumulation of glutamine) after the first 24–72 hours as a result of introduction of dietary protein. In addition to increased ammonia levels in blood, they have increased glutamine and decreased blood urea nitrogen. OTC deficiency can be differentiated from CPS1 deficiency by the presence of orotic acid in urine.

Explanation Why

N-acetylglutamate increases the activity of carbamoyl phosphate synthetase I (CPS1), a mitochondrial enzyme that converts bicarbonate and ammonia to carbamoyl phosphate using 2 molecules of ATP. This process is the rate-limiting step of the urea cycle. N-acetylglutamate is synthesized primarily in the liver and small intestinal cells when the cellular concentration of

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arginine is increased. In this way, the activity of CPS1 is increased following a protein-rich meal, when ammonia production is expected to be increased.

B - Ornithine translocase

Explanation Why

Ornithine translocase is a mitochondrial protein that is critical for urea cycle activity because it transports ornithine from the cytosol into the mitochondria, where it is converted to citrulline by ornithine transcarbamylase. A defect in ornithine translocase would cause hyperammonemia, but this protein's activity is not affected by N-acetylglutamate levels.

C - Ornithine transcarbamylase

Explanation Why

Ornithine transcarbamylase is a mitochondrial enzyme that is critical for urea cycle activity because it transfers a carbamoyl group onto ornithine to form citrulline. A deficiency of this enzyme would cause hyperammonemia, but this enzyme's activity is not affected by N-acetylglutamate levels.

D - Argininosuccinate synthetase

Explanation Why

Argininosuccinate synthetase is a cytoplasmic enzyme that is critical for urea cycle activity because it synthesizes argininosuccinate from aspartate and citrulline. A deficiency of this enzyme would cause hyperammonemia, but this enzyme's activity is not affected by N-acetylglutamate levels.

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E - Argininosuccinase

Explanation Why

Argininosuccinase is a cytoplasmic enzyme that is critical for urea cycle activity because it converts arginosuccinate to arginine and fumarate. A deficiency of this enzyme would cause hyperammonemia, but this enzyme's activity is not affected by N-acetylglutamate levels.

F - Arginase

Explanation Why

Arginase is a cytoplasmic enzyme that is critical for urea cycle activity because it converts arginine to urea and ornithine. A deficiency of this enzyme would cause hyperammonemia but this enzyme's activity is not affected by N-acetylglutamate levels.

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Question # 22

A 49-year-old woman is admitted to the hospital for the evaluation of postprandial colicky pain in the right upper quadrant of the abdomen. Abdominal ultrasound shows multiple round, hyperechoic structures within the gallbladder lumen. She undergoes a cholecystectomy. A photograph of the content of her gallbladder is shown. This patient is most likely to have which of the following additional conditions?

	Answer	Image
A	Diabetes mellitus	
B	Primary hyperparathyroidism	

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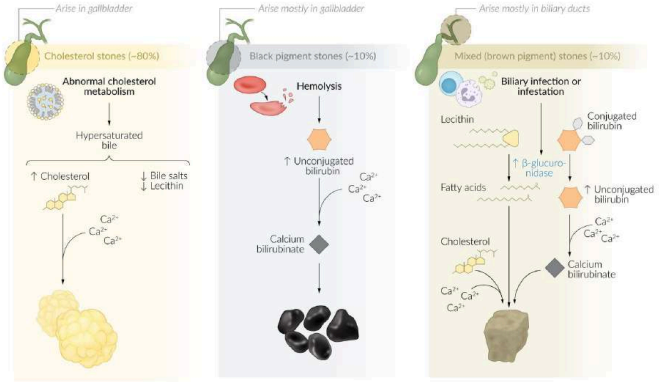
	Answer	Image
C	Chronic hemolytic anemia	
D	Menopausal symptoms	
E	Morbid obesity	

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Hint

The image shows black pigment gallstones.

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Correct Answer

A - Diabetes mellitus

Explanation Why

Patients with diabetes mellitus appear to be at increased risk of gallstone formation. This increased risk is due to hypertriglyceridemia and gallbladder hypomotility with biliary stasis, which is caused by autonomic neuropathy. However, diabetes mellitus typically predisposes to cholesterol stones that are yellowish green in color, not black as seen in this patient.

B - Primary hyperparathyroidism

Explanation Why

Primary hyperparathyroidism leads to hypercalcemia, which predisposes to the formation of renal calcium phosphate stones (nephrolithiasis). This increased risk persists even after parathyroidectomy. However, there is no association between hypercalcemia and the formation of gallstones as seen in this patient.

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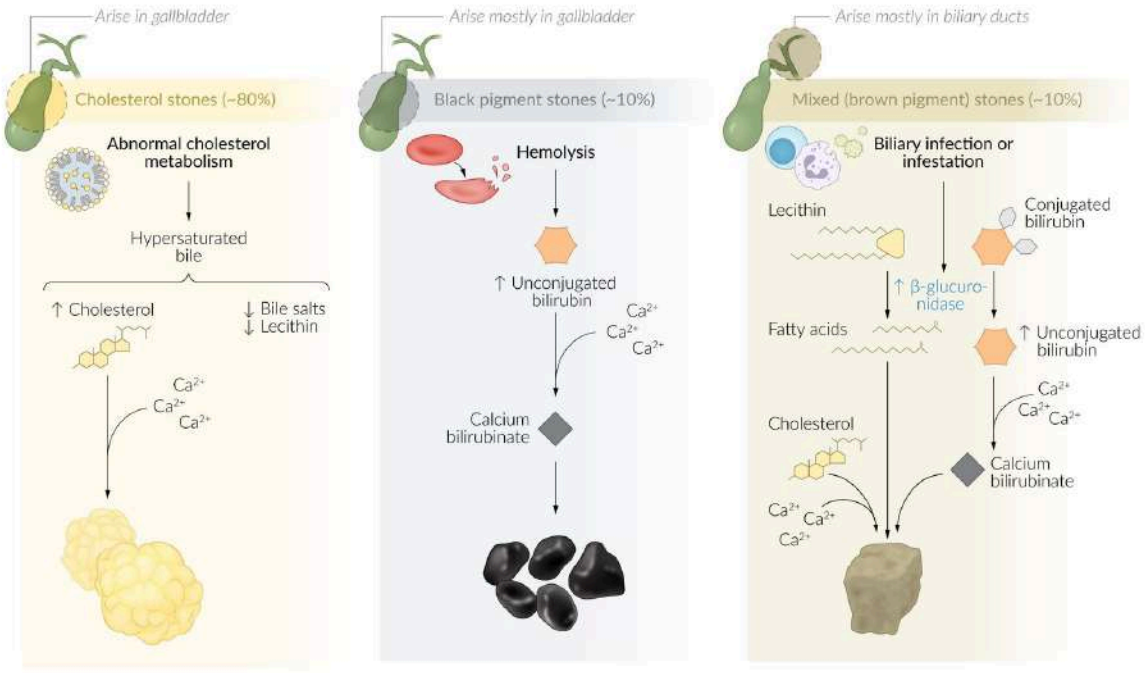
C - Chronic hemolytic anemia

Image



Explanation Why

Black pigment gallstones are associated with chronic hemolytic anemia (e.g., due to hereditary spherocytosis or beta thalassemia major), in which an elevated red blood cell breakdown leads to an increased serum concentration of indirect bilirubin. Excess bilirubin is excreted by the liver into the bile. The excess bilirubin then precipitates within the gallbladder due to supersaturation and reacts with calcium salts to form black calcium bilirubinate stones. Black pigment stones account for approx. 10% of all gallstones.

D - Menopausal symptoms

Explanation Why

Exogenous estrogen therapy used to treat menopausal symptoms can lead to an increased risk of

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cholesterol gallstones because estrogen induces the production and secretion of cholesterol by the liver. Most of this excess cholesterol is excreted into the bile, and this process causes a supersaturation that predisposes to gallstone formation. However, cholesterol gallstones are typically yellowish green in color, not black as seen in this patient.

E - Morbid obesity

Explanation Why

Obesity has been strongly associated with an increased risk of gallbladder disease. This increased risk is most likely due to enhanced cholesterol synthesis and secretion, as well as gallbladder dysmotility. However, these factors typically result in the formation of cholesterol stones that are yellowish green in color, not black as seen in this patient.

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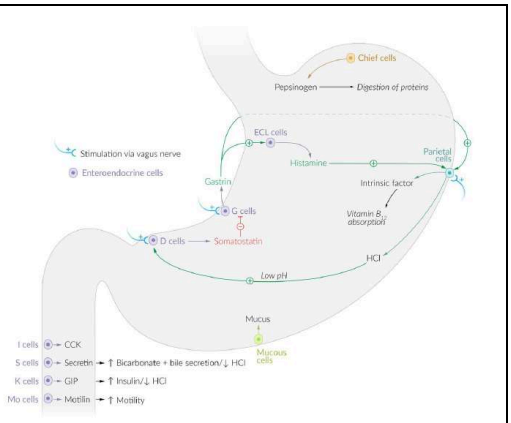
Question # 23

A 43-year-old woman comes to the physician because of worsening heartburn and abdominal pain for the past 4 months. During this period she has also had multiple episodes of greasy diarrhea. Six months ago, she had similar symptoms and was diagnosed with a duodenal ulcer. Her mother died of complications from uncontrolled hypoglycemia and had primary hyperparathyroidism. The patient does not drink alcohol or smoke cigarettes. Her only medications are pantoprazole and ranitidine. Her epigastric region is tender when palpated. An esophagogastroduodenoscopy shows a friable ulcer in the distal duodenum. Further evaluation is most likely to show which of the following?

	Answer	Image
A	Anti-intrinsic factor antibodies in the serum	
B	Anti-tissue transglutaminase antibodies in the serum	
C	Parietal cell hyperplasia in the stomach	
D	Noncaseating granulomas in the jejunum	
E	Dystrophic calcifications in the pancreas	

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Hint

Treatment-resistant peptic ulcer disease and features of malabsorption, combined with a family history suggestive of multiple endocrine neoplasia (primary hyperparathyroidism and pancreatic insulinoma), raises suspicion for Zollinger-Ellison syndrome (ZES).

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Correct Answer

A - Anti-intrinsic factor antibodies in the serum

Explanation Why

Serum anti-intrinsic factor antibodies are seen in pernicious anemia. They bind to intrinsic factor, thus blocking the binding of and absorption of vitamin B12. Although this patient's malabsorption puts her at risk of vitamin deficiencies, vitamin B12 deficiency causes signs of megaloblastic anemia and/or neurologic symptoms, which are not present in this patient. More importantly, pernicious anemia does not explain this patient's gastrointestinal symptoms or history of recurrent PUD.

B - Anti-tissue transglutaminase antibodies in the serum

Explanation Why

Anti-tissue transglutaminase antibodies can be found in the serum of patients with celiac disease. This condition can manifest with symptoms of malabsorption, such as anemia, vitamin deficiencies, and in some individuals, steatorrhea, which this patient has. However, celiac disease would not explain this patient's history of recurrent PUD.

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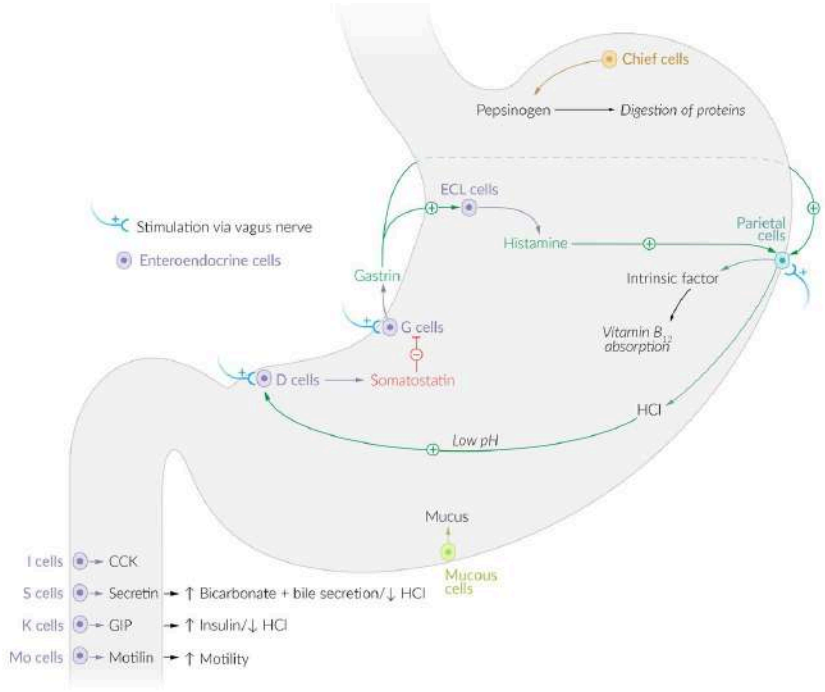
C - Parietal cell hyperplasia in the stomach

Image



Explanation Why

Parietal cell hyperplasia in the stomach can be seen in ZES, which involves a gastrin-secreting neuroendocrine tumor of the gastrointestinal tract. Hypergastrinemia leads to stimulation of parietal cells and excessive gastric acid production. As neuroendocrine tumors carry somatostatin receptors, radiolabelled octreotide can be used diagnostically to locate the tumor.

D - Noncaseating granulomas in the jejunum

Explanation Why

Noncaseating granulomas in the jejunum are the histological correlate of Crohn disease. Crohn disease typically manifests with diarrhea, which this patient reports. However, diarrhea in patients with Crohn disease is typically loose and watery, rather than greasy. Additionally, Crohn disease

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would not explain this patient's history of recurrent PUD.

E - Dystrophic calcifications in the pancreas

Explanation Why

Dystrophic calcification in the pancreas may be found in chronic pancreatitis. Multiple endocrine neoplasia is associated with pancreatic tumors. Both chronic pancreatitis and pancreatic tumors can cause impaired pancreatic enzyme secretion and thus symptoms of malabsorption (e.g., steatorrhea), which are seen in this patient. However, this patient's history of recurrent PUD is inconsistent with chronic pancreatitis.

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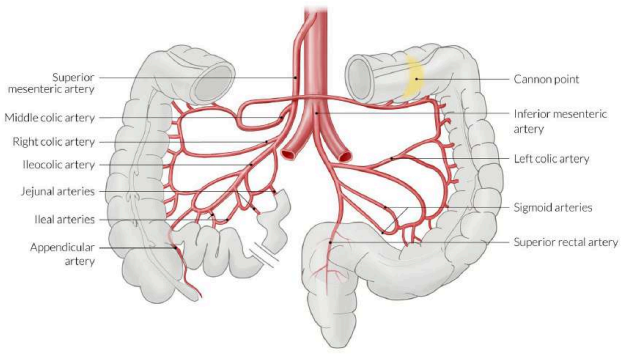
Question # 24

A 65-year-old woman with atrial fibrillation comes to the emergency department because of sudden-onset severe abdominal pain, nausea, and vomiting for the past 2 hours. She has smoked a pack of cigarettes daily for the past 25 years. Her pulse is 110/min and blood pressure is 141/98 mm Hg. Abdominal examination shows diffuse abdominal tenderness without guarding or rebound. A CT angiogram of the abdomen confirms an acute occlusion in the inferior mesenteric artery. Which of the following structures of the gastrointestinal tract is most likely to be affected in this patient?

	Answer	Image
A	Rectosigmoid colon	
B	Terminal ileum	
C	Hepatic flexure	
D	Lower rectum	
E	Ascending colon	
F	Transverse colon	

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Hint

Given this patient's acute presentation, history of atrial fibrillation, and severe abdominal pain, she most likely has colonic ischemia due to an embolism. Ischemia is most likely to occur in the watershed areas of the colon.

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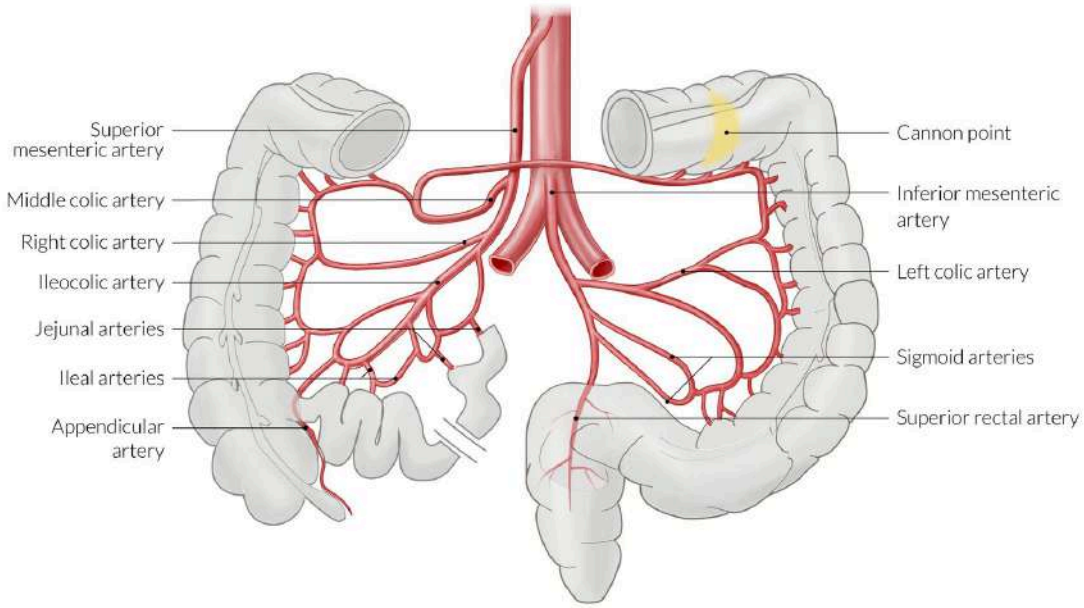
Correct Answer

A - Rectosigmoid colon

Image



Explanation Why

The rectosigmoid colon is supplied by the sigmoid artery and the superior rectal artery, which are branches of the inferior mesenteric artery (IMA). The effects of reduction or cessation of blood flow to the colon are particularly prominent at the watershed areas of the colon (i.e., rectosigmoid colon and splenic flexure), where collateral blood flow is limited. During acute ischemic events, the lack of collateral blood supply renders these regions particularly prone to ischemia.

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B - Terminal ileum

Explanation Why

The terminal ileum is predominantly supplied by the ileocolic artery (a branch of the superior mesenteric artery) and would, therefore, not be affected by occlusion in the inferior mesenteric artery.

C - Hepatic flexure

Explanation Why

The hepatic flexure, which is located between the ascending and the transverse colon, is supplied by branches of the superior mesenteric artery (SMA). It would therefore not be affected by an occlusion in the inferior mesenteric artery (IMA).

D - Lower rectum

Explanation Why

The lower rectum (below the pectinate line) has an extensive blood supply by the middle rectal artery (arises from the internal iliac artery) and inferior rectal artery (arises from the internal pudendal artery). The lower rectum would not be affected by occlusion in the inferior mesenteric artery.

E - Ascending colon

Explanation Why

The ascending colon is predominantly supplied by the right colic artery (a branch of the superior

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mesenteric artery) and would, therefore, not be affected by occlusion in the inferior mesenteric artery.

F - Transverse colon

Explanation Why

The transverse colon is predominantly supplied by the middle colic artery (a branch of the superior mesenteric artery) and would, therefore, not be affected by occlusion in the inferior mesenteric artery.

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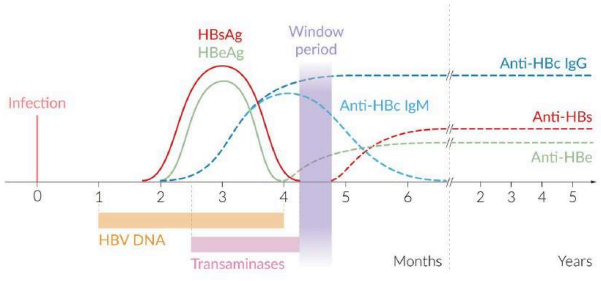
Question # 25

A 51-year-old man comes to the physician for follow-up evaluation. Nine months ago, he was diagnosed with acute viral hepatitis B infection. Physical examination shows no abnormalities. Serum studies show increased hepatic transaminase activity and a hepatitis B viral DNA load of 4286 IU/mL. Which of the following sets of findings is most likely in this patient?

	HBeAg	Anti-HBs	Anti-HBc IgG	Anti-HBc IgM
A	Negative	positive	positive	negative
B	Negative	negative	positive	negative
C	Negative	positive	negative	negative
D	Negative	negative	negative	positive
E	Positive	negative	positive	negative
F	Positive	negative	negative	positive

	Answer	Image
A	A	
B	B	
C	C	

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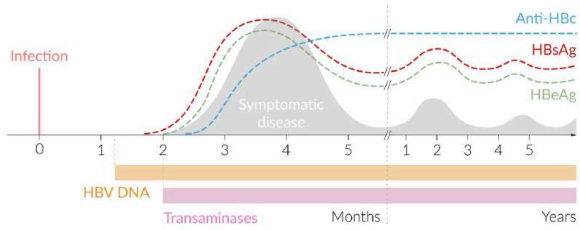
	Answer	Image
D	D	
E	E	
F	F	

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Hint

This patient who previously had acute hepatitis B infection and currently presents with increased hepatic transaminase activity and an HBV DNA load of 4286 U/L most likely has active chronic hepatitis B infection.

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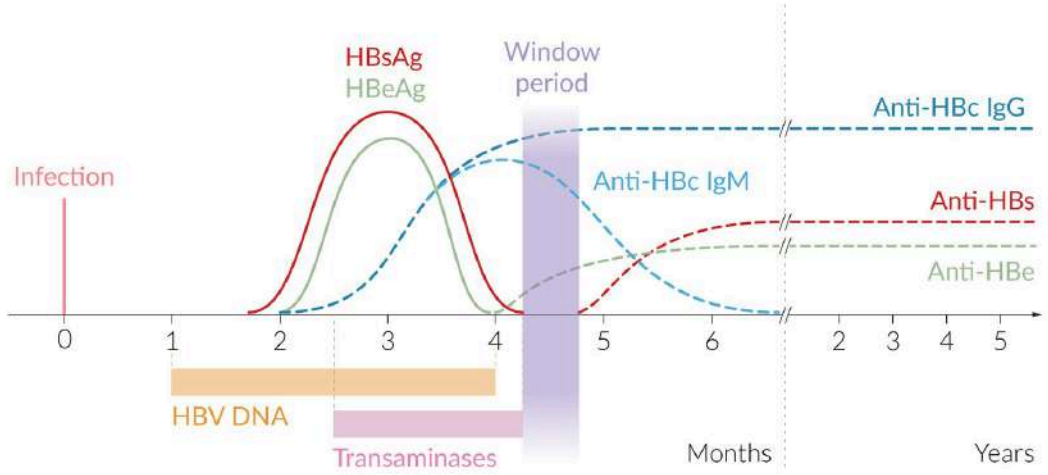
Correct Answer

A - A

Image



Explanation Why

Positive anti-HBs and IgG anti-HBc with negative HBeAg is characteristic of complete recovery from acute hepatitis B infection (immunity due to natural infection). Most adults who develop acute hepatitis B infection would recover completely and be asymptomatic, as seen here. However, hepatic transaminase activity would be normal and HBV DNA would be undetectable in patients who recover completely.

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B - B

Explanation Why

Positive IgG anti-HBc with negative HBeAg and anti-HBs is characteristic of inactive chronic hepatitis B infection. 5–10% of adults who develop acute hepatitis B infection will develop chronic hepatitis B infection. However, patients with inactive chronic hepatitis B infection would typically have normal hepatic transaminase activity and an HBV DNA load < 2000 IU/L.

C - C

Explanation Why

Positive anti-HBs with negative HBeAg and anti-HBc is characteristic of immunity against hepatitis B as a result of vaccination. A different set of findings would be expected in this patient who developed acute viral hepatitis B infection in the past.

D - D

Explanation Why

Positive IgM anti-HBc with negative HBeAg, anti-HBs, and IgG anti-HBc is characteristic of the window period of acute hepatitis B infection. A different set of findings would be expected in an asymptomatic patient who already had acute viral hepatitis B infection.

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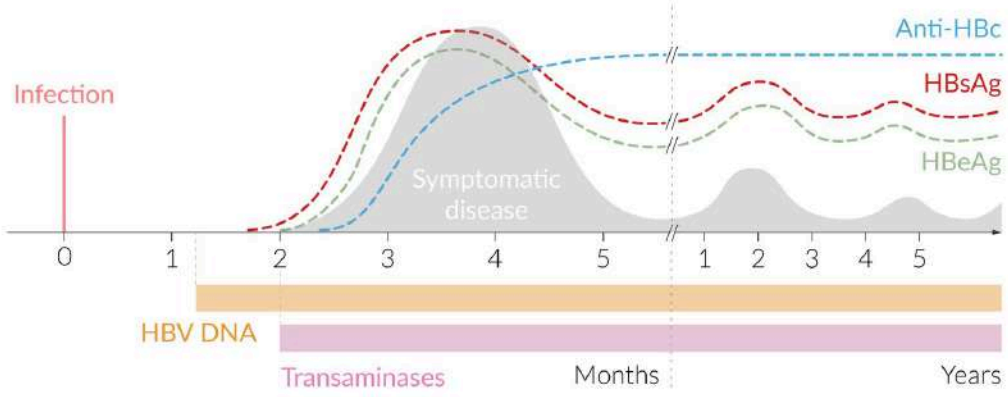
E - E

Image



Explanation Why

Up to 10% of patients who develop acute hepatitis B infection will develop chronic hepatitis B infection, which is characterized by the persistence of HBsAg and HBV DNA for more than 6 months after the initial infection, and the absence of anti-HBs. IgG anti-HBc may be present or absent with chronic hepatitis B infection. Chronic hepatitis B infection can be classified as “active” (marked viral replication characterized by increased HBeAg) or “inactive” (low or no viral replication characterized by an absence of serum HBeAg). Patients with active chronic hepatitis B would have an HBV DNA load > 2000 IU/L and/or increased hepatic transaminase levels.

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F - F

Explanation Why

Positive HBeAg and IgM anti-HBc with negative anti-HBs is characteristic of acute viral hepatitis B infection, which would cause increased hepatic transaminase activity and increased HBV DNA load. A different set of findings would be expected in this asymptomatic patient who presents nine months after the initial episode of acute viral hepatitis B infection.

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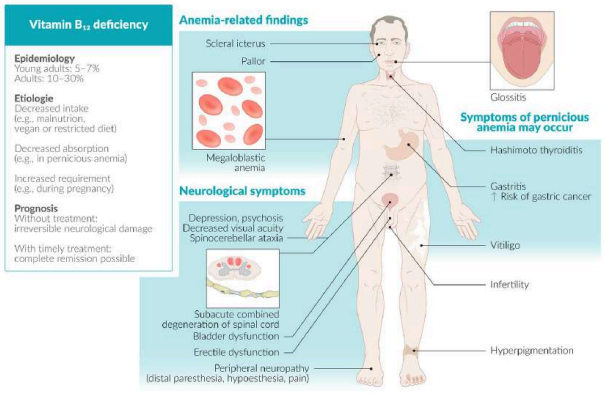
Question # 26

A 37-year-old man with Crohn disease is admitted to the hospital because of acute small bowel obstruction. Endoscopy shows a stricture in the terminal ileum. The ileum is surgically resected after endoscopic balloon dilatation fails to relieve the obstruction. Three years later, he returns for a follow-up examination. He takes no medications. This patient is most likely to have which of the following physical exam findings?

	Answer	Image
A	Weakness and ataxia	
B	Hyperreflexia with tetany	
C	Gingival swelling and bleeding	
D	Pallor with koilonychia	
E	Dry skin and keratomalacia	

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Hint

The distal ileum is the primary site of vitamin B_{12} absorption (in the form of B_{12}-intrinsic factor complex).

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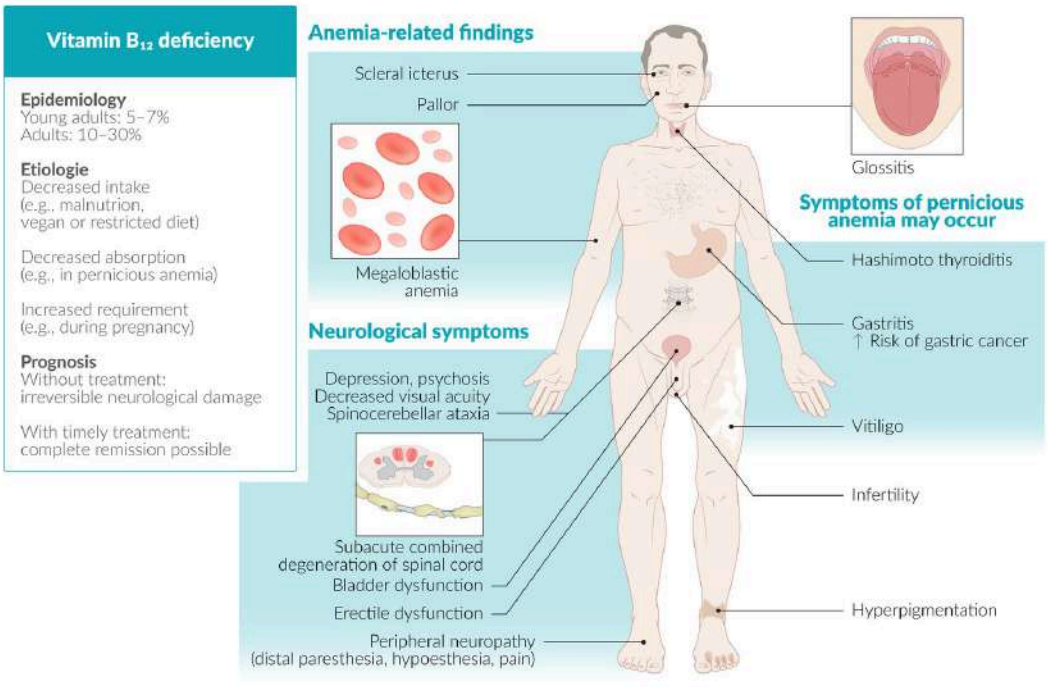
Correct Answer

A - Weakness and ataxia

Image



Explanation Why

Vitamin B_{12} deficiency can present with symmetric neurological deficits, including limb weakness and ataxia. Vitamin B_{12} is a cofactor of methylmalonyl-CoA mutase and methionine synthase, both of which are necessary for proper neuronal function. The terminal ileum is the primary site of vitamin B_{12} absorption and therefore resection of this structure, as seen in this case, can result in symptoms of vitamin B_{12} deficiency unless properly supplemented.

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B - Hyperreflexia with tetany

Explanation Why

Hyperreflexia with tetany would be consistent with hypocalcemia. Although passive calcium uptake occurs throughout the entire small intestine, the majority of calcium absorption occurs through active transcellular transport in the duodenum and proximal jejunum. The resection of this patient's terminal ileum is unlikely to result in significant calcium deficiency.

C - Gingival swelling and bleeding

Explanation Why

Gingival swelling and bleeding would be consistent with vitamin C deficiency (scurvy). Vitamin C is a water-soluble vitamin that functions as an important cofactor in collagen synthesis. This patient is at risk of a malabsorption syndrome but vitamin C absorption is not dependent on the terminal ileum, making significant vitamin C deficiency unlikely in this patient.

D - Pallor with koilonychia

Explanation Why

Pallor with koilonychia is consistent with iron deficiency anemia. Iron is first reduced to its ferrous form (Fe^{2+}) before being absorbed in the duodenum and upper jejunum. This patient is at risk of a malabsorption syndrome but iron absorption is not dependent on the terminal ileum, making these findings unlikely in this patient.

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E - Dry skin and keratomalacia

Explanation Why

Dry skin and keratomalacia are consistent with Vitamin A deficiency. Vitamin A is a fat-soluble vitamin, and therefore its deficiency is associated with fat malabsorption conditions (e.g., celiac disease, cystic fibrosis). The majority of fat-soluble vitamin absorption occurs in the proximal half of the small intestine. This patient is at risk for a malabsorption syndrome but the resection of his terminal ileum would unlikely result in significant vitamin A deficiency.

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Question # 27

A 52-year-old woman comes to the physician because of abdominal discomfort, anorexia, and mild fatigue. She has systemic lupus erythematosus and takes hydroxychloroquine. She does not drink alcohol or use illicit drugs. Physical examination shows no abnormalities. Serum studies show:

Alanine aminotransferase	455 U/L
Aspartate aminotransferase	205 U/L
Hepatitis B surface antigen	positive
Hepatitis B surface antibody	negative
Hepatitis B envelope antigen	positive
Hepatitis B core antigen IgG antibody	positive

Which of the following is the most appropriate pharmacotherapy for this patient?

	Answer	Image
A	Pegylated interferon-gamma	
B	Acyclovir	
C	Tenofovir	
D	Dolutegravir	

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	Answer	Image
E	Sofosbuvir	

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Hint

Positive HBsAg antigens and IgG anti-HBc antibodies indicate chronic hepatitis B infection. The presence of HBeAg antigens in serum indicates active viral replication (chronic HBV infection with high infectivity).

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Correct Answer

A - Pegylated interferon-gamma

Explanation Why

Interferon-gamma has no role in the treatment of HBV but is used as an adjuvant immunomodulatory therapy for chronic granulomatous disease in some centers. It augments superoxide and nitric oxide production in phagocytes that lack NADPH oxidase.

B - Acyclovir

Explanation Why

Acyclovir is a nucleoside analog used to treat varicella-zoster virus and herpes simplex virus infections. It inhibits viral DNA polymerase when incorporated into the DNA and terminates chain elongation. However, it has no role in the treatment of HBV infection.

C - Tenofovir

Explanation Why

Tenofovir is a nucleotide analog that inhibits reverse transcriptase. It is used for the treatment of HIV and HBV infections. Antiviral therapy with tenofovir, entecavir, or pegylated interferon alpha is indicated in patients with an active chronic HBV infection. To avoid exacerbation of disease, immune system upregulators, such as IFN-α, are contraindicated in patients with autoimmune diseases like SLE. The drugs of choice for this patient are therefore either tenofovir or entecavir.

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D - Dolutegravir

Explanation Why

Dolutegravir inhibits integration of HIV genome into host DNA by inhibiting HIV integrase. However, it has no role in the treatment of HBV infection.

E - Sofosbuvir

Explanation Why

Sofosbuvir is a nucleoside analog that inhibits hepatitis C virus RNA-dependent RNA polymerase. It is phosphorylated to nucleoside triphosphate and incorporated into the viral genome during RNA replication resulting in chain termination. However, it is not the preferred treatment option for chronic HBV infection.

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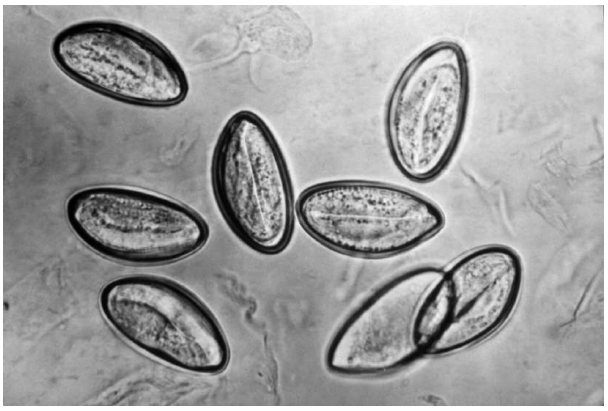
Question # 28

A 10-year-old girl is brought to the physician because of itching of the vulva and anal region for the past 2 weeks. She has difficulty sleeping because of the itching. Physical examination shows excoriation marks around the vulva and perianal region. There is minor perianal erythema, but no edema or fissures. Microscopy of an adhesive tape applied to the perianal region shows multiple ova. Which of the following is the most appropriate treatment for this patient?

	Answer	Image
A	Mebendazole	
B	Melarsoprol	
C	Diethylcarbamazine	
D	Nifurtimox	
E	Ivermectin	
F	Praziquantel	

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Hint

This patient has a positive tape test showing the presence of ova (i.e., the eggs of a worm). Her pruritus is therefore most likely caused by a pinworm infection (i.e., enterobiasis). Gravid female pinworms migrate to the rectum of infected individuals, usually at night, and deposit their ova nocturnally in the anogenital region, causing inflammation and itching.

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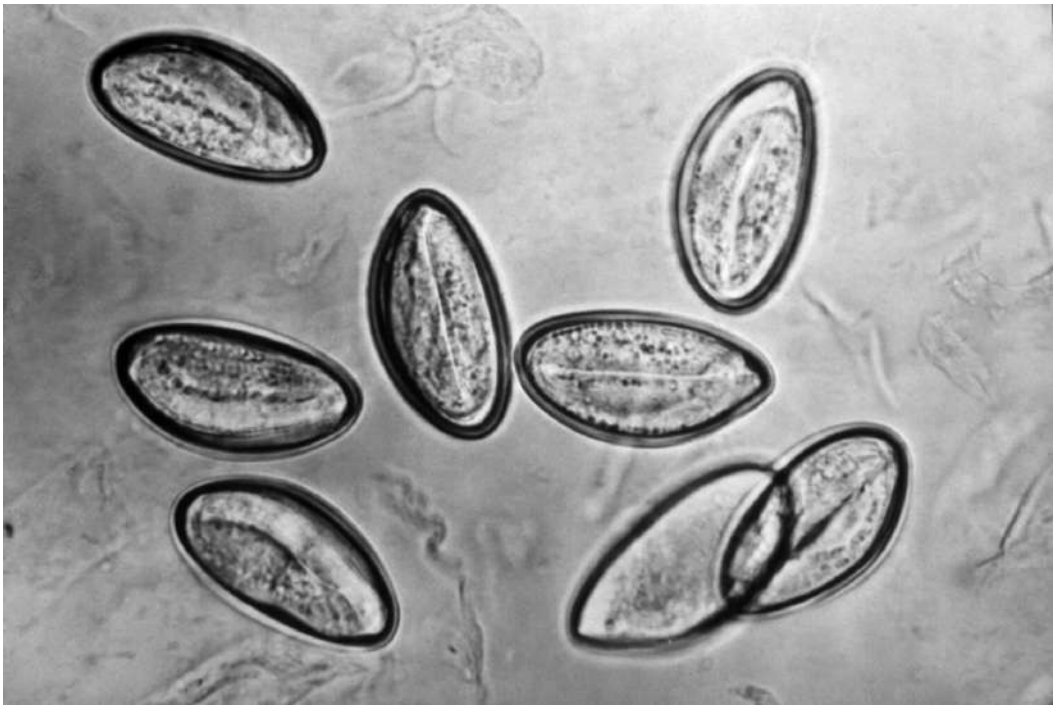
Correct Answer

A - Mebendazole

Image



Explanation Why

Mebendazole or another bendazole (e.g., albendazole) is an appropriate treatment for pinworm infection, which is caused by *Enterobius vermicularis*. Alternatively, pyrantel pamoate can be used. Initial infection with pinworms is fecal-oral, but reinfection occurs via the digital-oral route following nocturnal pruritus due to pinworm eggs.

B - Melarsoprol

Explanation Why

Melarsoprol is used in the treatment of African trypanosomiasis, caused by *Trypanosoma brucei*,

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which manifests with recurrent fever, lymphadenopathy, somnolence, and coma. Perianal pruritus and a positive tape test, as seen here, are not typical for trypanosomiasis, and melarsoprol is generally not used for the treatment of enterobiasis.

C - Diethylcarbamazine

Explanation Why

Diethylcarbamazine is used to treat lymphatic filariasis, which is caused by *Wuchereria bancrofti*, and loiasis, which is caused by *Loa loa.* Lymphatic filariasis presents with fever, painful lymphadenopathy, and progressive swelling of the region drained by the obstructed lymphatics (often the lower extremities), potentially leading to elephantiasis. Loiasis is usually asymptomatic but may present with localized subcutaneous swellings and a visible migrating worm in the conjunctiva. Neither lymphatic filariasis nor loiasis manifests with perianal pruritus and a positive tape test, and diethylcarbamazine is generally not used for the treatment of enterobiasis.

D - Nifurtimox

Explanation Why

Nifurtimox is used to treat Chagas disease, caused by *Trypanosoma cruzi*, which manifests with nonspecific symptoms (e.g., fever, malaise, anorexia) and, rarely, edema or more severe disease of the heart, gastrointestinal, and/or nervous system. However, it does not present with perianal pruritus and a positive tape test, as seen here, and nifurtimox is generally not used for the treatment of enterobiasis.

E - Ivermectin

Explanation Why

Ivermectin is the drug of choice for the treatment of infection with *Strongyloides stercoralis* or *Onchocerca volvulus*. Strongyloidiasis can present with pruritus, typically of the feet, where larvae enter the skin. However, perianal pruritus, as this patient has, is not common. Onchocerciasis can cause skin changes as well as ocular disorders and blindness. Neither condition is known for causing

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perianal pruritus and a positive tape test. Ivermectin is generally not used for the treatment of enterobiasis.

F - Praziquantel

Explanation Why

Praziquantel is effective against *Schistosoma*, *Taeniasis*, *Clonorchis sinensis*, and *Diphyllobothrium latum* (fish tapeworm) infections. Intestinal schistosomiasis, taeniasis, and clonorchiasis, if symptomatic, all manifest with gastrointestinal symptoms such as abdominal pain, nausea, and vomiting. Schistosomiasis may also cause gastrointestinal strictures or bleeding. Chronic infection with fish tapeworm can lead to vitamin B12 deficiency and anemia. However, none of these infections manifest with perianal pruritus and a positive tape test. Praziquantel is not used for the treatment of enterobiasis.

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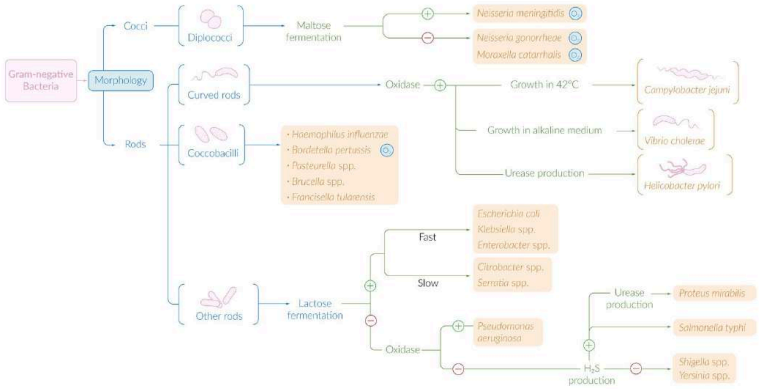
Question # 29

A 24-year-old man comes to the physician with a 2-day history of fever, crampy abdominal pain, and blood-tinged diarrhea. He recently returned from a trip to Mexico. His temperature is 38.2°C (100.8°F). Abdominal examination shows diffuse tenderness to palpation; bowel sounds are hyperactive. Stool cultures grow nonlactose fermenting, oxidase-negative, gram-negative rods that do not produce hydrogen sulfide on triple sugar iron agar. Which of the following processes is most likely involved in the pathogenesis of this patient's condition?

	Answer	Image
A	Invasion of colonic microfold cells	
B	Inhibition of host cytoskeleton organization	
C	Overactivation of adenylate cyclase	
D	Dissemination via bloodstream	
E	Flagella-mediated gut colonization	

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Hint

This patient presents with a fever, abdominal cramps, and bloody diarrhea, which is concerning for bacterial gastroenteritis. The most likely causal organism is *Shigella*, a rod-shaped, gram-negative, oxidase-negative, and nonlactose fermenting rod that does not produce H_2S on triple sugar iron (TSI) agar.

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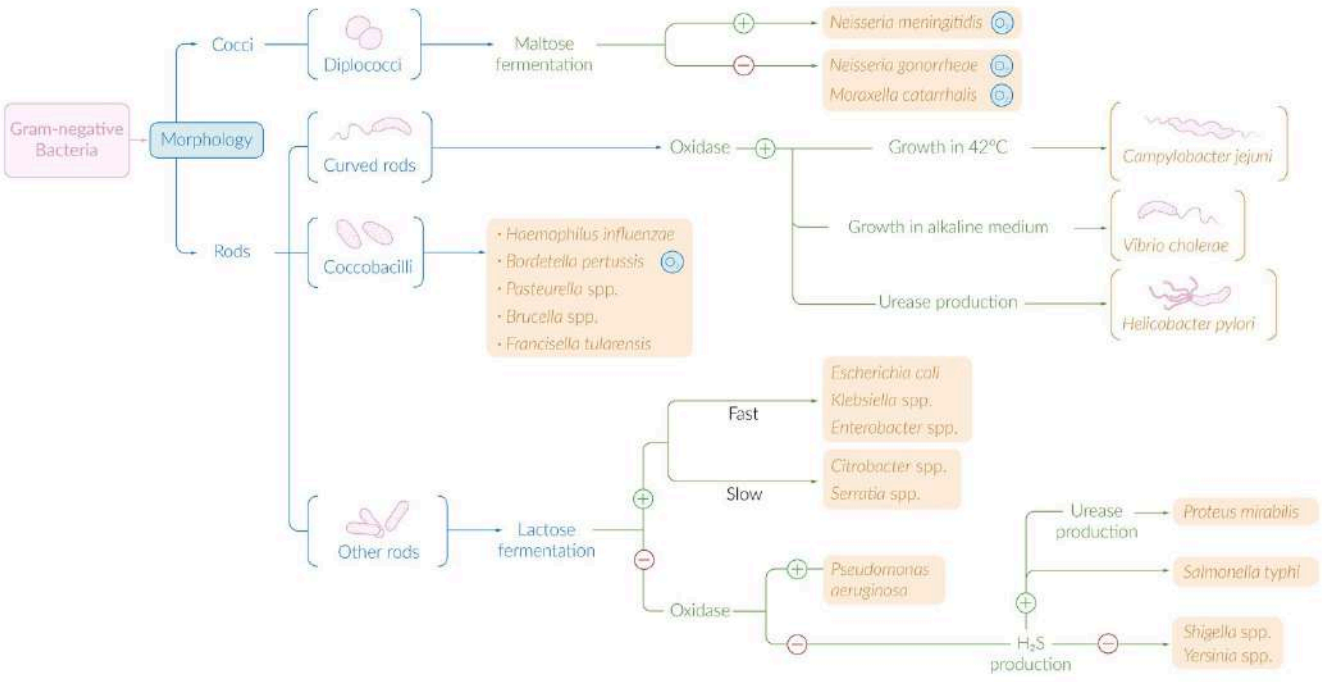
Correct Answer

A - Invasion of colonic microfold cells

Image



Explanation Why

Invasion of colonic microfold cells is the mechanism by which *Shigella* causes host illness. *Shigella* enters cells via pinocytosis before lysing vesicles and entering the cytoplasm. Once inside the cytoplasm, *Shigella* produces Shiga toxin and rapidly poisons the cell. This mechanism is key to *Shigella's* ability to cause disease even in cases of very small exposure to the bacteria (i.e., *Shigella* has a very low infectious dose). Once inside the colonic mucosa, *Shigella* travels from cell to cell via actin polymerization.

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B - Inhibition of host cytoskeleton organization

Explanation Why

Inhibition of host cytoskeleton organization via actin depolymerization is the mechanism of action of toxin B, secreted by *Clostridioides difficile*, the causative organism of pseudomembranous colitis. Pseudomembranous colitis may manifest with blood-tinged diarrhea. However, the main risk factor for the development of clostridium enterocolitis is prior antibiotic use, which this patient does not report. Furthermore, stool culture identified gram-negative rods, while *C. difficile* is a gram-positive rod.

C - Overactivation of adenylate cyclase

Explanation Why

Overactivation of adenylate cyclase is the mechanism of cholera toxin (produced by *Vibrio cholerae*) and of heat-labile toxin (produced by enterotoxigenic *E. coli*; ETEC). Both toxins increase cAMP, leading to higher chloride secretion with resulting water efflux. However, the result of such water efflux is profuse, nonbloody diarrhea, in contrast to this patient's blood-tinged diarrhea. Moreover, *V. cholerae* is oxidase positive and comma-shaped, not a rod; and *E. coli*, though rod-shaped, is a (fast) lactose fermenter.

D - Dissemination via bloodstream

Explanation Why

Dissemination via the bloodstream is an aspect of *Salmonella* virulence. Salmonellosis is usually contracted after eating tainted poultry or eggs and manifests with bloody diarrhea, which is seen here. *Salmonella*, however, is an H_2S producer when grown on TSI agar. *Shigella*, the most likely bacteria in this patient, moves between cells along the host cells' actin filaments rather than via the bloodstream. Usurping the host's cytoskeleton allows *Shigella* to evade circulating leukocytes.

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E - Flagella-mediated gut colonization

Explanation Why

Flagella-mediated gut colonization is an important component of *Campylobacter jejuni* virulence. Enteritis caused by this bacteria typically manifests with bloody diarrhea, which this patient has, but also includes high fever, myalgias, and malaise, which are not mentioned here. *C. jejuni* is oxidase positive, whereas the identified organism in this instance is oxidase negative.

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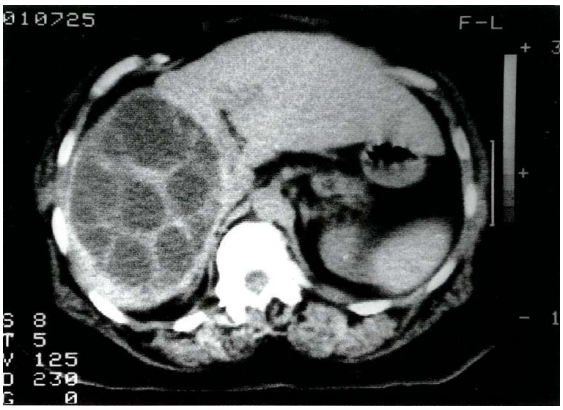
Question # 30

A 42-year-old woman comes to the physician because of episodic abdominal pain and fullness for 1 month. She works as an assistant at an animal shelter and helps to feed and bathe the animals. Physical examination shows hepatomegaly. Abdominal ultrasound shows a 4-cm calcified cyst with several daughter cysts in the liver. She undergoes CT-guided percutaneous aspiration under general anesthesia. Several minutes into the procedure, one liver cyst spills, and the patient's oxygen saturation decreases from 95% to 64%. Her pulse is 136/min, and blood pressure is 86/58 mm Hg. Which of the following is the most likely causal organism of this patient's condition?

	Answer	Image
A	Strongyloides stercoralis	
B	Trichinella spiralis	
C	Taenia solium	
D	Schistosoma mansoni	
E	Clonorchis sinensis	
F	Echinococcus granulosus	

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	Answer	Image
G	Ascaris lumbricoides	

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Hint

This woman with previous exposure to animals has developed anaphylactic shock (tachycardia, tachypnea, hypotension, hypoxia) due to spillage of cyst contents into the bloodstream, which is a complication of the surgical management of a particular tapeworm infection.

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Correct Answer

A - Strongyloides stercoralis

Explanation Why

Strongyloides stercoralis is a threadworm that penetrates the skin of hosts and migrates to the lungs, where it matures. Larvae then travel to the pharynx and are swallowed. Infection can manifest with cutaneous, respiratory, or intestinal symptoms. Hepatic involvement is uncommon; this condition does not cause the calcified, unilocular liver cysts seen in this case.

B - Trichinella spiralis

Explanation Why

Trichinella spiralis is a nematode that causes trichinosis, a condition that manifests with intestinal symptoms, splinter hemorrhages, retinal and conjunctival hemorrhages, periorbital edema, rash, and chemosis. Infection spreads through fecal-oral transmission and consumption of undercooked meat. Hepatic involvement is uncommon; this condition does not cause the calcified, unilocular liver cysts seen in this case.

C - Taenia solium

Explanation Why

Taenia solium (pork tapeworm) infection occurs after ingestion of larvae through undercooked pork or contamination with human feces. It causes intestinal taeniasis, cysticercosis, and neurocysticercosis. Hepatic involvement is uncommon; this condition does not cause the calcified, unilocular liver cysts seen in this case.

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D - Schistosoma mansoni

Explanation Why

Schistosoma mansoni uses freshwater snails as intermediate hosts and infects humans via penetration of the skin. Infection manifests with a pruritic, maculopapular rash at the point of entry and a serum sickness-like disease. Chronic schistosomiasis can manifest with hepatic, splenic, pulmonary, and/or neurologic involvement. However, it does not typically cause calcified, unilocular liver cysts as seen in this case.

E - Clonorchis sinensis

Explanation Why

Clonorchis sinensis (Chinese liver fluke) is a trematode transmitted by ingestion of undercooked fish. It causes infection and obstruction of the biliary tract and is associated with chronic inflammation and increased risk of cholangiocarcinoma. It does not typically cause calcified, unilocular liver cysts as seen in this case.

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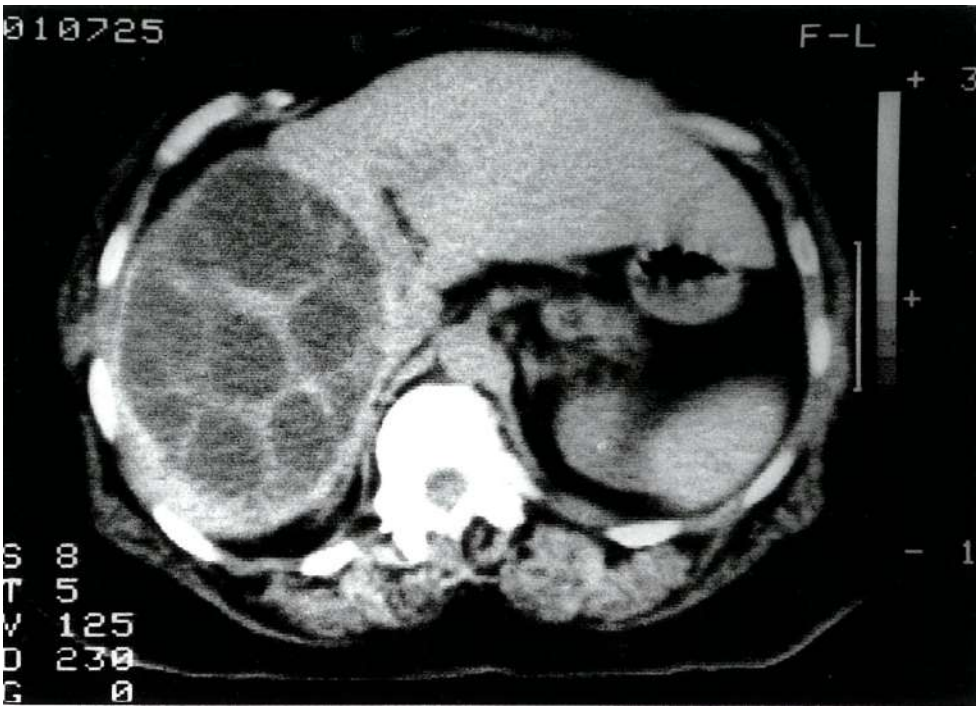
F - Echinococcus granulosus

Image



Explanation But

Echinococcus granulosus, which causes cystic echinococcosis, typically presents with unilocular hydatid cysts, while *Echinococcus multilocularis*, the causal organism of alveolar echinococcosis, is characterized by formation of multiple cysts with infiltrative growth.

Explanation Why

Echinococcus granulosus is a tapeworm of which the definitive hosts are foxes, dogs, and cats. The intermediate hosts are sheep and rodents. Infection occurs through fecal-oral transmission of eggs. Hepatic echinococcosis typically causes malaise, nausea, vomiting, hepatomegaly, and an, anechoic, well-defined, hepatic cyst (hydatid cyst) with or without daughter cysts and eggshell calcification on ultrasonography. Any invasive procedure (drainage or surgery) of hydatid cysts should be performed with the utmost care to prevent spillage of cyst contents, which can cause life-threatening anaphylactic shock and/or secondary seeding of infection, as seen in this patient.

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G - Ascaris lumbricoides

Explanation Why

Ascaris lumbricoides is a nematode that spreads via fecal-oral transmission. Larvae invade the intestines and then migrate from the portal circulation to the lungs, from which they are coughed up and swallowed. Infections manifest with respiratory and intestinal symptoms. Adult worms can migrate to the biliary tract and cause obstruction with cholestasis. However, it does not typically cause calcified, unilocular liver cysts as seen in this case.

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Question # 31

A 53-year-old man comes to the physician for an annual check-up. He has no complaints. He was diagnosed with hepatitis B 13 years ago. Physical examination shows no abnormalities. Laboratory studies show an aspartate aminotransferase of 19 U/L, an alanine aminotransferase of 17 U/L. His hepatitis B DNA is detected, but the load indicates a very low chance of infectivity. Which of the following set of serological findings is most likely to be found in this patient?

	HBsAg	Anti-HBs	HBeAg	Anti-HBe	Anti-HBc IgM	Anti-HBc IgG
(A)	Positive	negative	negative	positive	negative	positive
(B)	Negative	negative	negative	negative	positive	negative
(C)	Positive	negative	positive	negative	positive	negative
(D)	Negative	positive	negative	negative	negative	negative
(E)	Positive	negative	positive	negative	negative	positive
(F)	Negative	positive	negative	positive	negative	positive

	Answer	Image
A	A	
B	B	
C	C	
D	D	

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	Answer	Image
E	E	
F	F	

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Hint

This patient has inactive chronic hepatitis B, as indicated by his low hepatitis B DNA load (indicating very low infectivity), normal ALT level, and lack of symptoms. HBsAg, a surface antigen, is a protein on the surface of hepatitis B virus (typically the first evidence of infection). HBeAg, an envelope antigen, is a protein secreted by the virus that indicates viral replication and infectivity. HBcAg is a viral core antigen that is expressed by infected liver cells.

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Correct Answer

A - A

Explanation Why

The presence of HBcAg antibodies indicate either a recent (anti-HBc IgM) or resolved or chronic (anti-HBc IgG) hepatitis B infection. The combination of positive HbsAg, positive anti-HBe, positive anti-HBc IgG, and negative anti-HBs antibodies indicates a chronic hepatitis B infection and low infectivity of this patient.

B - B

Explanation Why

The presence of HBcAg antibodies indicates either a recent (anti-HBc IgM), or a resolved or chronic (anti-HBc IgG) hepatitis B infection. The presence of isolated positive anti-HBc IgM with negative HBsAg indicates a "window period" of a resolving HBV infection when HBsAg is disappearing and anti-HBs is not yet detectable. However, this patient has an inactive chronic hepatitis B infection.

C - C

Explanation Why

The presence of HBcAg antibodies indicates either a recent (anti-HBc IgM), or a resolved or chronic (anti-HBc IgG) hepatitis B infection. The combination of positive HBsAg, positive HBeAg, and positive anti-HBc IgM indicates an acute hepatitis B infection. However, this patient has an inactive chronic hepatitis B infection.

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D - D

Explanation Why

The presence of anti-HBs indicates immunity to HBV due to vaccination or resolved infection. Anti-HBs usually appear 1–3 months after infection. Positive anti-HBs only indicates status post-vaccination. However, this patient has an inactive chronic hepatitis B infection.

E - E

Explanation Why

The presence of HBcAg antibodies indicate either a recent (anti-HBc IgM) or resolved or chronic (anti-HBc IgG) hepatitis B infection. The combination of positive HBsAg, positive HBeAg, and positive anti-HBc IgG indicates an active chronic hepatitis B infection, which is a very contagious type of infection with high viral loads (> 2000 IU/mL). This patient's viral load indicates low infectivity, which is consistent with inactive chronic hepatitis B infection.

F - F

Explanation Why

The presence of anti-HBs indicates immunity to HBV due to vaccination or resolved infection and usually appears 1–3 months after infection. The presence of HBeAg antibodies (anti-HBe) indicates clearance of hepatitis B virus. The presence of anti-HBcAg antibodies indicates either a recent (anti-HBc IgM) or a resolved or chronic (anti-HBc IgG) hepatitis B infection. The combination of anti-HBs, anti-HBe, and anti-HBc IgG indicates a prior infection that has resolved, in which HBV DNA is no longer detectable. However, this patient has an inactive chronic hepatitis B infection.

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Question # 32

A 55-year-old man with chronic hepatitis B virus infection comes to the physician because of generalized fatigue and a 5.4 kg (12 lb) weight loss over the past 4 months. Physical examination shows hepatomegaly. Laboratory studies show an α-fetoprotein concentration of 380 ng/ml (N < 10 ng/mL). A CT scan of the abdomen with contrast shows a solitary mass in the left lobe of the liver that enhances in the arterial phase. Which of the following is the most likely underlying pathogenesis of this patient's current condition?

	Answer	Image
A	Overexpression of secretory hepatitis antigen	
B	Intracellular accumulation of misfolded protein	
C	Gain of function mutation of a proto-oncogene	
D	Viral cytotoxin-induced cellular dysplasia	
E	Integration of foreign DNA into host genome	

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Hint

A solitary hepatic mass in an individual with elevated α-fetoprotein levels is strongly suggestive of hepatocellular carcinoma (HCC). Chronic hepatitis B virus infection is an important risk factor for HCC.

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Correct Answer

A - Overexpression of secretory hepatitis antigen

Explanation Why

Overexpression of secretory hepatitis B virus (HBV) antigen (i.e., HBeAg) indicates a state of active replication and high infectivity. Though mechanisms contributing to the development of hepatocellular carcinoma may already be active in early stages of acute HBV infections, viral replication alone does not induce hepatocarcinogenesis.

B - Intracellular accumulation of misfolded protein

Explanation Why

Intracellular accumulation of misfolded proteins has been observed in patients with α1-antitrypsin deficiency (AATD). In this condition, impaired secretion of a variant AAT protein leads to pathologic polymerization and accumulation of AAT within hepatocytes. AAT protein deposits appear as intracellular inclusions that stain positive with periodic acid-Schiff reagent. Subsequent liver damage may lead to hepatitis, cirrhosis, and hepatocellular carcinoma. However, this patient has chronic hepatitis B virus infection, not AATD.

C - Gain of function mutation of a proto-oncogene

Explanation Why

A gain of function mutation converts a proto-oncogene into an oncogene, causing uncontrolled cell proliferation with an increased risk for cancer development. For instance, activating mutation of proto-oncogenes cMYC, JAK2, and c-KIT have been associated with Burkitt lymphoma, chronic myeloproliferative disorders, and gastrointestinal stromal tumor, respectively. Although altered expression of regulatory genes contributes to liver carcinogenesis, there is no specific proto-oncogene associated with hepatocellular carcinoma.

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D - Viral cytotoxin-induced cellular dysplasia

Explanation Why

Hepatitis B virus (HBV) does not have a direct cytotoxic effect. However, infected hepatocytes are destroyed by $CD8^+$ cytotoxic T cells as part of the host immune response. Chronic intrahepatic inflammation maintains a cycle of liver cell necrosis, mitosis, and regenerative hyperplasia that can induce cellular dysplasia and, eventually, hepatocellular carcinoma.

E - Integration of foreign DNA into host genome

Explanation Why

Integration of hepatitis B virus DNA into the host genome alters the expression of endogenous host genes important for cell growth, proliferation, and differentiation. It also induces chromosomal instability. Although viral DNA integration occurs randomly, it often involves segments of genes encoding for key factors in carcinogenesis, such as p53, pRb, cyclins A and D1, and TGF beta. Therefore, accumulation of genetic damage and altered expression of these regulatory proteins contribute to the development of HCC. Furthermore, continuous expression of certain viral proteins (e.g., HBx protein) that modulate the expression of host genes has also been implicated in the development of HCC.

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Question # 33

A 46-year-old man comes to the emergency department because of a 10-day history of right upper quadrant abdominal pain. He has also been feeling tired and nauseous for the past 6 weeks. On examination, scleral icterus is present. Abdominal examination shows tenderness to palpation in the right upper quadrant. The liver edge is palpated 2 cm below the right costal margin. Laboratory studies show:

Aspartate aminotransferase	1780 U/L
Alanine aminotransferase	2520 U/L
Hepatitis A IgM antibody	negative
Hepatitis B surface antigen	negative
Hepatitis B surface antibody	negative
Hepatitis B core IgM antibody	positive
Hepatitis C antibody	positive
Hepatitis C RNA	negative

Which of the following is the most appropriate treatment for this patient?

	Answer	Image
A	Ribavirin and interferon	
B	Supportive therapy	
C	Ledipasvir and sofosbuvir	

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	Answer	Image
D	Tenofovir	
E	Emergency liver transplantation	
F	Pegylated interferon-alpha	

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Hint

Sudden onset of nausea, jaundice, fever, and right upper quadrant pain with massively elevated serum transaminase levels (> 1000 U/L) suggests a diagnosis of acute viral hepatitis. The presence of anti-HBc IgM antibodies without concurrent HBsAg or anti-HBs antibodies indicates that this patient is in the window period of acute hepatitis B infection.

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Correct Answer

A - Ribavirin and interferon

Explanation Why

A combination of ribavirin and interferon can be used to treat chronic hepatitis C caused by genotypes 2 and 3. A patient with a chronic hepatitis C infection will have increased levels of antibodies against HCV and possibly elevated serum transaminase levels. However, the serum transaminase levels would only be mildly to moderately increased (< 500 U/L) and HCV RNA would be detectable. The absence of HCV RNA most likely indicates a past hepatitis C infection that has resolved.

B - Supportive therapy

Explanation But

The presence of HBsAg on serology denotes an acute hepatitis B infection. While anti-HBc is the first antibody to be made, it does not proffer immune clearance of hepatitis B. However, anti-HBc may be the only marker of infection during the seroconversion of HBsAg to anti-HBs (i.e., during the window period). During this time, all HBsAgs and anti-HBs are in antigen-antibody complexes, so they cannot be detected in the serum. Immune clearance is established when additional unbound anti-HBs becomes detectable on serology.

Explanation Why

Supportive therapy is all that is required for a patient with acute hepatitis B infection. A negative HBsAg with positive anti-HBc IgM antibodies indicate that the infection is resolving. Anti-HBs antibody titers may not increase for up to 1–2 weeks following the disappearance of HbsAg from serum (window period), which is why measuring anti-HBc antibody titers in patients with suspected acute hepatitis B infection is important.

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C - Ledipasvir and sofosbuvir

Explanation Why

A combination of ledipasvir and sofosbuvir can be used to treat chronic hepatitis C infection caused by genotypes 1, 4, 5, and 6 of HCV. A patient with chronic hepatitis C infection will have increased levels of antibodies against HCV and may have elevated serum transaminase levels. However, the serum transaminase levels would only be mildly or moderately increased (< 500 U/L), and HCV RNA would be detectable. The absence of HCV RNA most likely indicates a past hepatitis C infection that has resolved.

D - Tenofovir

Explanation Why

Tenofovir is used to treat immune-active chronic hepatitis B (CHB). A patient with immune-active CHB would have elevated serum transaminase levels and negative anti-HBs antibodies. However, in CHB, anti-HBc IgG antibodies would be expected instead of anti-HBc IgM antibodies, HbsAg would be present, and the serum transaminase levels would only be mildly or moderately increased (< 500 U/L).

E - Emergency liver transplantation

Explanation Why

In a patient with acute viral hepatitis, emergency liver transplantation is indicated if fulminant liver failure occurs. However, fulminant hepatic failure following hepatitis B infection is seen in only 0.5% of cases, and it would manifest with features of hepatic encephalopathy (e.g., altered mental status, asterixis), increased PT/INR, and an AST:ALT ratio > 1. None of these features are present in this patient.

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F - Pegylated interferon-alpha

Explanation Why

Pegylated interferon alpha is used to treat immune-active chronic hepatitis B (CHB) and acute hepatitis C infection. A patient with immune-active CHB would have elevated serum transaminase levels and negative anti-HBs antibodies. However, in CHB anti-HBc IgG antibodies would be expected instead of anti-HBc IgM antibodies, HbsAg would be present, and the serum transaminase levels would only be mildly or moderately increased (< 500 U/L). A patient with acute hepatitis C infection will have massively increased serum transaminase levels and increased titers of antibodies against HCV, as seen here, but HCV RNA would also be detectable. The absence of HCV RNA most likely indicates a past hepatitis C infection that has resolved.

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Question # 34

A 75-year-old man comes to the physician because of a 2-month history of intermittent bright red blood in his stool, progressive fatigue, and a 5-kg (11-lb) weight loss. He appears thin and fatigued. Physical examination shows conjunctival pallor. Hemoglobin concentration is 7.5 g/dL and MCV is 77 μm^3. Results of fecal occult blood testing are positive. A colonoscopy shows a large, friable mass in the anal canal proximal to the pectinate line. Primary metastasis to which of the following lymph nodes is most likely in this patient?

	Answer	Image
A	Inferior mesenteric	
B	Internal iliac	
C	Superior mesenteric	
D	External iliac	
E	Para-aortic	
F	Superficial inguinal	
G	Deep inguinal	

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Hint

These lymph nodes also receive lymphatics from the gluteal region, inferior pelvic viscera (including rectum, prostate, and part of the cervix), and the perineum (including membranous urethra and spongy urethra).

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Correct Answer

A - Inferior mesenteric

Explanation Why

The inferior mesenteric lymph nodes receive lymphatic drainage from the splenic flexure of the colon to the upper rectum. This patient's mass is located in the proximal anal canal, which lies distal in the GI tract to the rectum.

B - Internal iliac

Explanation Why

The internal iliac lymph nodes receive lymphatic drainage from the upper part of the anal canal, proximal to the pectinate line. The internal iliac lymph nodes would therefore be the most likely site of lymphatic metastasis in this patient with a mass in the proximal anal canal.

C - Superior mesenteric

Explanation Why

The superior mesenteric lymph nodes receive lymphatic drainage from the distal duodenum to the colon proximal to the splenic flexure. They also receive lymphatic drainage from the inferior mesenteric lymph nodes. This patient's mass is located distal to the regions of drainage for these lymph nodes.

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D - External iliac

Explanation Why

The external iliac lymph nodes drain the uterus and superior portion of the bladder. This patient's mass is located in the colon so involvement of these nodes would be unexpected.

E - Para-aortic

Explanation Why

The para-aortic lymph nodes receive lymphatic drainage from the testes, ovaries, uterus, kidneys, and adrenals. This patient's mass is located in the proximal anal canal, outside of the regions of drainage for these lymph nodes.

F - Superficial inguinal

Explanation Why

The superficial inguinal lymph nodes receive lymphatic drainage from the lower part of the anal canal, distal to the pectinate line. They also receive drainage from the skin below the umbilicus and parts of the GU system. Although this patient's mass is located in the anal canal, it is proximal to the pectinate line.

G - Deep inguinal

Explanation Why

The deep inguinal lymph nodes typically drain the tissues of the glans penis, vulva, and, in some

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cases, the anus distal to the pectinate line. This patient's mass is proximal to the pectinate line, so tumor spread is possible in cases of distant metastatic disease but primary involvement would not be expected.

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Question # 35

A 14-year-old girl is brought to the physician by her father because of fever, chills, abdominal pain, and profuse non-bloody diarrhea. Her symptoms began one week ago, when she had several days of low-grade fever and constipation. She returned from Indonesia 2 weeks ago, where she spent the summer with her grandparents. Her temperature is 39.3°C (102.8°F). Examination shows diffuse abdominal tenderness and mild hepatosplenomegaly. There is a faint salmon-colored maculopapular rash on her trunk and abdomen. Which of the following is the most likely causal organism?

	Answer	Image
A	Giardia lamblia	
B	Yersinia enterocolitica	
C	Schistosoma mansoni	
D	Entamoeba histolytica	
E	Escherichia coli	
F	Clostridioides difficile	
G	Cryptosporidium parvum	
H	Campylobacter jejuni	

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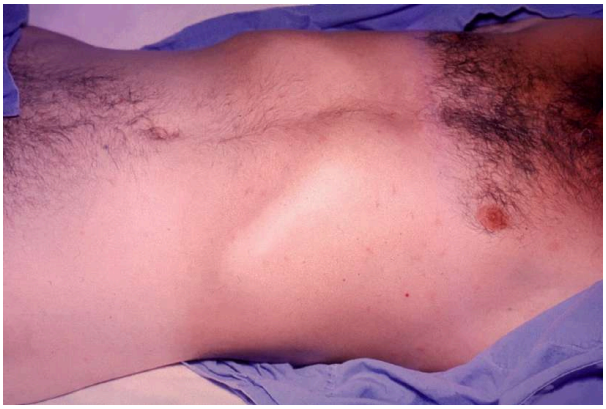
	Answer	Image
I	Shigella dysenteriae	
J	Salmonella typhi	
K	Clostridium perfringens	
L	Vibrio cholerae	

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Hint

This patient's illness may have been prevented with an intramuscular Vi capsular polysaccharide vaccine.

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Correct Answer

A - Giardia lamblia

Explanation Why

Giardia lamblia causes giardiasis, which is characterized by bloating, flatulence, and foul-smelling, fatty, frothy diarrhea. The causal organism is usually transmitted through contaminated water, and affected patients usually have a recent history of camping or exposure to fresh water. Fever, rash, and constitutional symptoms are not common features.

B - Yersinia enterocolitica

Explanation Why

Yersinia enterocolitica causes diarrhea and usually appears after ingestion of spoiled meat. Patients typically present with low-grade fever, abdominal pain, and diarrhea; the diarrhea may be bloody in some cases, and the duration of symptoms is variable. Patients may also develop symptoms that mimic appendicitis (pseudoappendicitis). While this patient does have fever, abdominal pain, and diarrhea, hepatosplenomegaly and a salmon-colored rash are not features of *Yersinia* infection, making this diagnosis unlikely.

C - Schistosoma mansoni

Explanation Why

Schistosoma mansoni causes schistosomiasis. In the acute period, infection may cause pruritus, but it is most commonly asymptomatic. Chronically infected patients sometimes develop episodic fever and malaise that may be accompanied by abdominal pain, hepatosplenomegaly, dysuria, hematochezia, and/or hematuria. This patient's relatively acute onset of symptoms and the presence of a faint salmon-colored maculopapular rash are not consistent with this diagnosis. Furthermore, *Schistosoma mansoni* is usually found in Africa and South America, not in Indonesia.

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D - Entamoeba histolytica

Explanation Why

Entamoeba histolytica causes amebiasis, which can manifest in a variety of symptoms depending on the severity of illness. Mild infections may take the form of loose stools and vague abdominal pain, whereas severe infections involve a dysentery-like syndrome characterized by fever, abdominal pain, and bloody diarrhea. In the setting of amebic liver abscess, hepatosplenomegaly may be present, along with significant right upper quadrant pain. However, a rash would not be expected in amebiasis, making this diagnosis much less likely.

E - Escherichia coli

Explanation Why

Escherichia coli causes a spectrum of clinical entities that depend on the causative strain. Enteroinvasive *E. coli* causes a dysentery-like illness, with fever, abdominal pain, and bloody diarrhea. Enterotoxigenic *E. coli* causes traveler's diarrhea, which is characterized by watery diarrhea, with minimal constitutional symptoms. *E. coli* infections would not typically cause a rash or fluctuating fever.

F - Clostridioides difficile

Explanation Why

Clostridioides difficile causes pseudomembranous colitis, which is often considered a nosocomial infection, as it is strongly associated with recent broad-spectrum antibiotic exposure. Mild infections can manifest with bloody diarrhea alone, while more severe infections manifest with dysentery, crampy abdominal pain, and fever. However, this patient has no history of recent antibiotic use, and a rash and hepatosplenomegaly would not be expected in *C. difficile* infection, making this diagnosis unlikely.

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G - Cryptosporidium parvum

Explanation Why

Cryptosporidium parvum causes a form of self-limiting traveler's diarrhea in immunocompetent patients, with loose, profound watery stools and minimal constitutional symptoms. In immunosuppressed patients (classically patients with AIDS), it can cause potentially life-threatening diarrhea. The high fever, hepatosplenomegaly, and rash seen in this patient would not be consistent with this diagnosis.

H - Campylobacter jejuni

Explanation Why

Campylobacter jejuni is associated with a dysentery-like illness, with fever, abdominal pain, and bloody diarrhea. It is a common cause of bloody diarrhea in children and is transmitted via the fecal-oral route, contaminated food products (such as poultry or unpasteurized milk), and infected animals. Rash, hepatosplenomegaly, and profuse, watery diarrhea are not associated features.

I - Shigella dysenteriae

Explanation Why

Shigella dysenteriae causes shigellosis, which is characterized by high fever, cramping abdominal pain, and bloody mucoid diarrhea. The progression of illness is more rapid, and the diarrhea is rarely profuse. There would be no associated rash, as seen in this patient.

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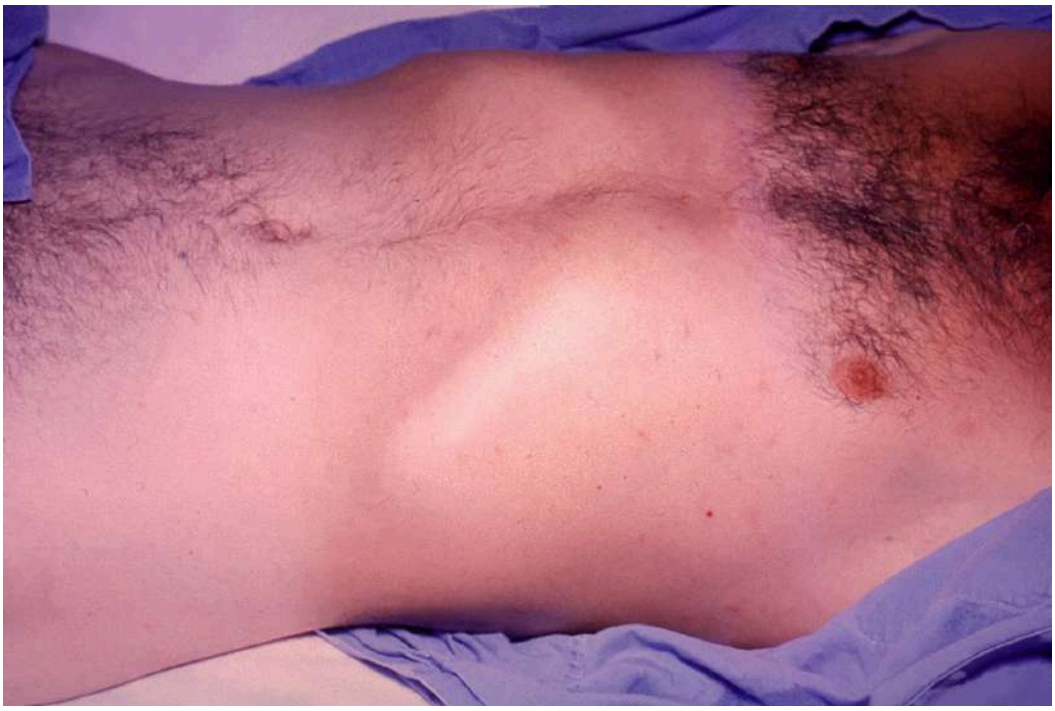
J - Salmonella typhi

Image



Explanation But

Treatment with a third-generation cephalosporin (e.g., ceftriaxone) or a fluoroquinolone is indicated. The WHO recommends typhoid fever vaccination, which contains the Vi capsular polysaccharide antigen, to those traveling to high-risk areas (East and Southeast Asia, Latin America, Africa).

Explanation Why

Salmonella typhi is most likely to have caused this patient's symptoms, who has recently traveled to an endemic region. Typhoid infection is characterized by a fluctuating fever and malaise followed by profound fatigue, high fever, and relative bradycardia. Initial constipation can be followed by profuse diarrhea (pea-soup diarrhea), a salmon-colored maculopapular rash (rose spots), and hepatosplenomegaly, usually in the second week after onset. *Salmonella typhi* is transmitted via the fecal-oral route, with the bacteria initially entering the host through intestinal Peyer patches. After a period of replication, the organism enters the bloodstream and can seed several organs (e.g., the liver and spleen).

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K - Clostridium perfringens

Explanation Why

Clostridium perfringens is a common cause of food poisoning and manifests with self-limiting abdominal cramping, diarrhea, vomiting, and fever several hours after ingesting tainted food. Infection usually resolves within 24 hours and does not present with a rash or hepatosplenomegaly, making the diagnosis extremely unlikely in this patient.

L - Vibrio cholerae

Explanation Why

Vibrio cholerae, which causes cholera, is associated with profuse, watery diarrhea (rice-water stools), which can lead to severe dehydration and death. Affected patients usually have a history of consuming raw or undercooked seafood. The onset is rapid, with no prodrome of constipation, rash, or hepatosplenomegaly.

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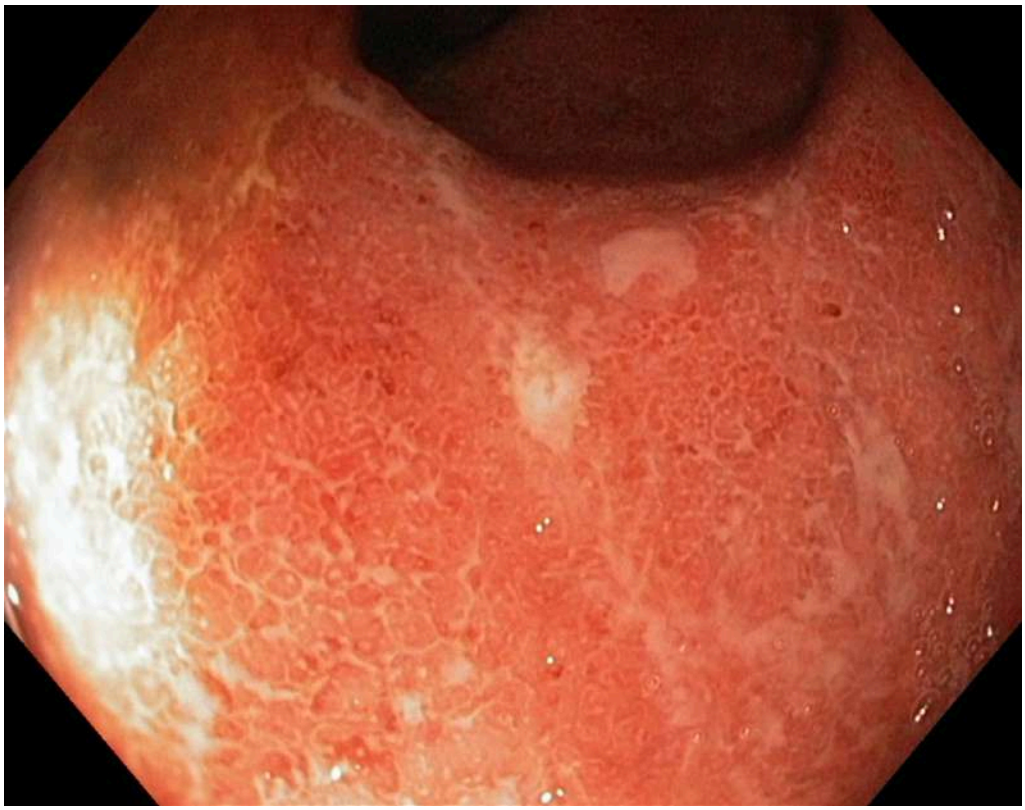
Question # 36

A 28-year-old man comes to the physician because of a 6-month history of progressive fatigue and intermittent diarrhea. During this time, he has had a 6-kg (13-lb) weight loss. Physical examination shows pale conjunctivae. Abdominal examination shows tenderness to palpation in the lower quadrants. An image from a colonoscopy of the descending colon is shown. Further evaluation is most likely to show which of the following findings?



	Answer	Image
A	Positive lactose hydrogen breath test	
B	Anti-Saccharomyces cerevisiae antibodies	
C	Perinuclear antineutrophil cytoplasmic antibodies	

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	Answer	Image
D	PAS-positive cytoplasmic granules	
E	Anti-tissue transglutaminase antibodies	

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Hint

This patient has chronic intermittent diarrhea, weight loss, fatigue, and lower abdominal pain, which are typical for an inflammatory bowel disease (IBD). The conjunctival pallor suggests anemia, possibly due to chronic gastrointestinal bleeding. The colonoscopy shows an erythematous and inflamed mucosa with fibrin-covered ulcerations, which are highly suggestive of ulcerative colitis.

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Correct Answer

A - Positive lactose hydrogen breath test

Explanation Why

A lactose hydrogen breath test measures hydrogen levels following the ingestion of a carbohydrate-loaded drink. It is positive in lactose intolerance, which is characterized by an inability to digest lactose due to lactase deficiency. It also causes diarrhea and abdominal cramps, which are seen in this patient. However, symptoms usually also include bloating and occur after consuming dairy products. Additionally, patients with lactose intolerance have a macroscopically normal colonic mucosa.

B - Anti-Saccharomyces cerevisiae antibodies

Explanation But

ASCA is found in up to 20% of patients with ulcerative colitis; however, another antibody is much more common.

Explanation Why

Anti-Saccharomyces cerevisiae antibodies (ASCA) are a group of antibodies directed at components of the cell wall of the yeast *Saccharomyces cerevisiae*. ASCA is associated with chronic inflammatory bowel disease, particularly with Crohn disease (up to 70%). Crohn disease would manifest with nonbloody chronic diarrhea, abdominal pain, fatigue, and weight loss, which are seen in this patient. However, endoscopy would show linear ulcers, the cobblestone sign, fissures, fistulas, erythema, and transmural inflammation.

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C - Perinuclear antineutrophil cytoplasmic antibodies

Explanation Why

Perinuclear antineutrophil cytoplasmic antibodies (pANCA) are autoantibodies against myeloperoxidase granules in the perinuclear region of the cytoplasm. They are positive in up to 80% of patients with ulcerative colitis, with no correlation between the titer and disease activity. pANCA can also be increased in patients with other inflammatory disorders, including autoimmune systemic vasculitis (especially Churg-Strauss syndrome and microscopic polyangiitis) and primary sclerosing cholangitis.

D - PAS-positive cytoplasmic granules

Explanation Why

PAS-positive cytoplasmic granules in the intestinal mucosa are seen in patients with Whipple disease, an infection caused by *Tropheryma whipplei*. Symptoms include diarrhea, fatigue, and weight loss due to malabsorption. However, this condition occurs more commonly in elderly men, and an endoscopy would show pale yellow, eroded patches rather than the ulcerations seen in this patient.

E - Anti-tissue transglutaminase antibodies

Explanation Why

Anti-tissue transglutaminase antibodies are antibodies (mainly IgG and IgA) against tissue transglutaminase in the small intestine. They are present in over 90% of patients with celiac disease. Symptoms of celiac disease can include diarrhea, weight loss, and fatigue (due to malabsorption and vitamin deficiencies), all of which this patient has. However, endoscopy would demonstrate villous atrophy and crypt hyperplasia (a smooth or atrophic mucous membrane), not the ulcerations seen in this patient.

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Question # 37

Two months after giving birth to a boy, a 27-year-old woman comes to the physician with her infant for a well-child examination. She was not seen by a physician during her pregnancy. Physical examination of the mother and the boy shows no abnormalities. Laboratory studies show elevated titers of hepatitis B surface antigen in both the mother and the boy. Which of the following statements regarding the infant's condition is most accurate?

	Answer	Image
A	Hepatitis B e antigen titer is likely undetectable	
B	Chronic infection is unlikely	
C	Lifetime risk of hepatocellular carcinoma is low	
D	The viral replication rate is low	
E	Significant elevation of transaminases is not expected	
F	Breastfeeding should be avoided	

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Hint

Elevated titers of HbsAg in both the mother and the infant suggest vertical transmission of the hepatitis B virus (HBV).

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Correct Answer

A - Hepatitis B e antigen titer is likely undetectable

Explanation Why

Hepatitis B e antigen (HBeAg) titer is readily detectable in neonates with HBV. This is consistent with the high transmission rates seen in the perinatal period. The risk of transmission is 80% to 90% from women seropositive for hepatitis B surface antigen (HBsAg) and HBeAg. Mothers without the e antigen or with anti-HBe transmit the infection only in 5% to 20 % of cases.

B - Chronic infection is unlikely

Explanation Why

Without treatment, chronic course of infection is very common in neonatal hepatitis from vertical transmission. Up to 90% of infants infected perinatally will develop chronic infection.

C - Lifetime risk of hepatocellular carcinoma is low

Explanation Why

The risk of hepatocellular carcinoma is significant in neonatal hepatitis. Perinatal infection with HBV, carries an approximately 90 % chance of the infant becoming a chronic carrier, with an estimated 15 % to 25 % risk of dying in adulthood from cirrhosis or liver cancer.

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D - The viral replication rate is low

Explanation Why

HBV replicates rapidly upon entering the newborn because of the inability of the infantile immune system to mount a HBV-specific immune response. Therefore, the viral replication rate would be expected to be high, not low.

E - Significant elevation of transaminases is not expected

Explanation But

Newborns of mothers with unknown HBV status should receive vaccine within 12 hours of birth. If the mother tests positive for HBsAg, hepatitis B immune globulin should be administered as soon as possible. Newborns of HBsAg negative mothers should be given the hepatitis B vaccine series before hospital discharge.

Explanation Why

Transaminases are usually normal or only mildly elevated in cases of vertical transmission of HBV. Because HBV is not cytopathic itself and newborns lack mature cytotoxic T-cells that mediate damage infected hepatocytes, the degree of hepatic tissue damage will be very limited. Rarely, infected neonates may develop acute hepatitis B, which is usually mild and self-limited.

F - Breastfeeding should be avoided

Explanation Why

Breastfeeding should be recommended to all patients with maternal HBV, as HBV infection is not a contraindication to breastfeeding. Women with HBV infection should be counseled that breastfeeding does not increase the likelihood of infection in their children. However, breastfeeding should be delayed until passive-active postexposure prophylaxis has been given. Since, in this patient, vertical transmission of HBV has already occurred, there is no reason to delay breastfeeding.

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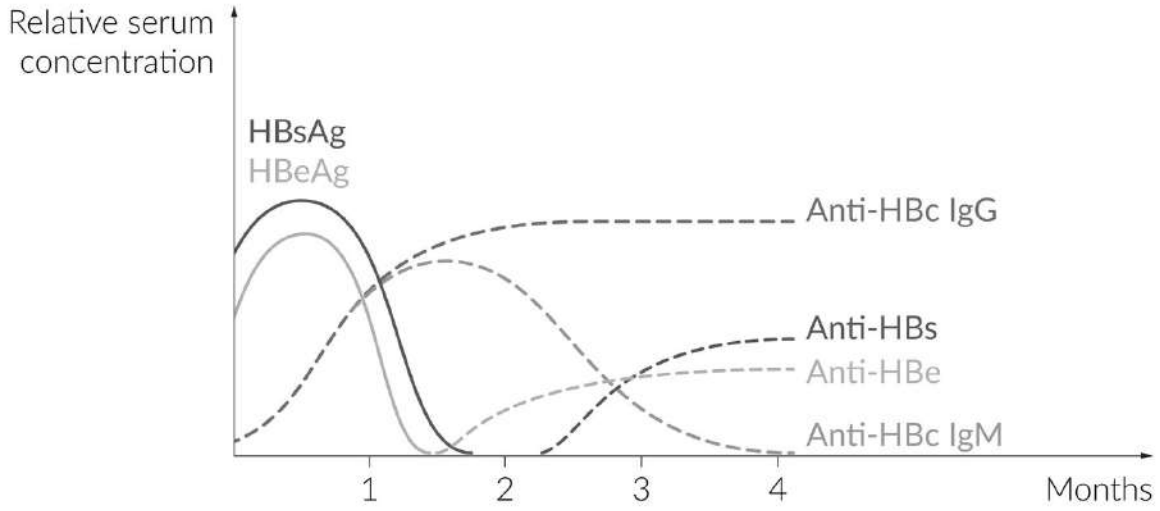
Question # 38

A 37-year-old man comes to the physician because of a 3-day history of fatigue and yellowish discoloration of his eyes and skin. Physical examination shows mild right upper quadrant abdominal tenderness. The course of different serum parameters over the following 4 months is shown. Which of the following is the most likely explanation for the course of this patient's laboratory findings?



	Answer	Image
A	Chronic hepatitis B infection with low infectivity	

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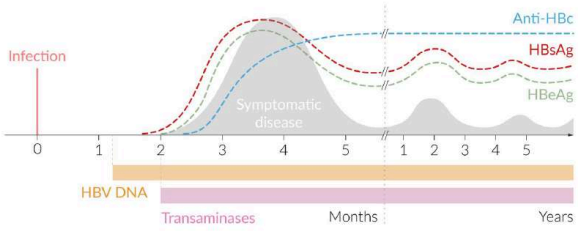
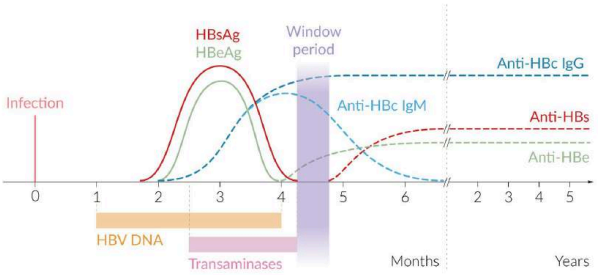
	Answer	Image
B	Chronic hepatitis B infection with high infectivity	
C	Adverse reaction to hepatitis B vaccination	
D	Acute exacerbation of previous hepatitis B infection	
E	Resolved acute hepatitis B infection	

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Hint

The depicted natural history of hepatitis B virus infection is observed in 95% of infected adults.

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Correct Answer

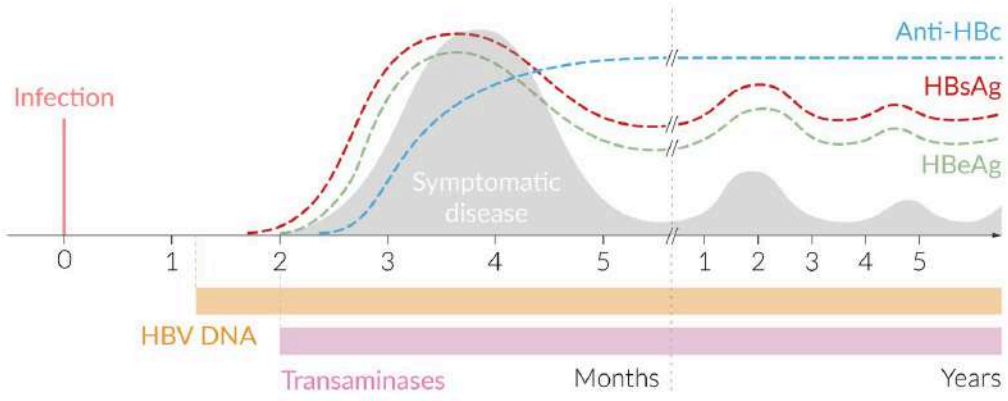
A - Chronic hepatitis B infection with low infectivity

Explanation Why

The serologic findings of chronic hepatitis B infection with low infectivity include positive HBsAg, anti-HBe antibodies, and anti-HBc IgG. In this patient, the presence of anti-HBs antibodies and the clearance of HBsAg over the course of time do not support chronic hepatitis B infection.

B - Chronic hepatitis B infection with high infectivity

Image



Explanation Why

The serologic findings of chronic hepatitis B infection with high infectivity include positive HBsAg, HBeAg (indicates high infectivity together with HBV DNA), and anti-HBc IgG. In this patient, the

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presence of anti-HBs and anti-HBe antibodies and the clearance of HBsAg and HBeAg over the course of time do not support chronic hepatitis B infection with high infectivity.

C - Adverse reaction to hepatitis B vaccination

Explanation Why

Hepatitis B vaccination is composed of HBsAg, which induces seroconversion. Therefore, vaccinated individuals will only have anti-HBs antibodies and not the other serologic findings observed in this patient. Moreover, the presenting features of an adverse reaction to hepatitis B vaccination include injection site redness and swelling, myalgia, nausea, fatigue, runny nose, headache, and dizziness, but not jaundice.

D - Acute exacerbation of previous hepatitis B infection

Explanation Why

Acute exacerbation of previous hepatitis B infection can present with jaundice, abdominal tenderness, and positive HBsAg, HBeAg and anti-HBc IgM antibodies, as seen here. However, patients with an acute exacerbation of previous hepatitis B infection would likely have positive anti-HBe antibodies and higher serum concentration of anti-HBc IgG antibodies at the time of presentation.

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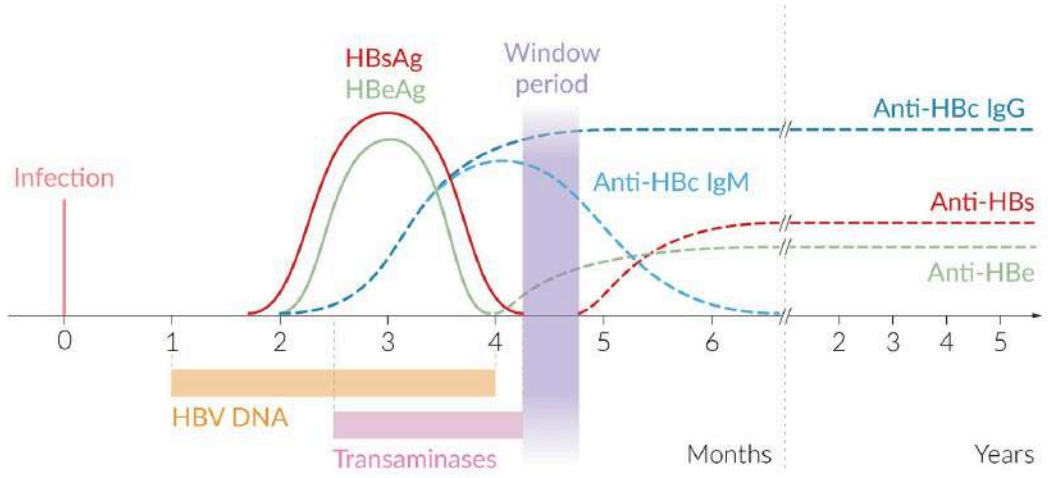
E - Resolved acute hepatitis B infection

Image



Explanation Why

The serologic findings represent the natural history of a resolving acute hepatitis B virus infection. After the infection and incubation period, serum findings show HBsAg and HBeAg, followed shortly by the appearance of antibodies against the hepatitis B core antigen (predominantly IgM isotype in the window phase). With resolution of the acute infection, patients remain negative for HBeAg and HBsAg and positive for anti-HBe and anti-HBs antibodies.

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Question # 39

A 27-year-old man with a history of intravenous drug use comes to the physician because of anorexia, nausea, dark urine, and abdominal pain for 2 weeks. Physical examination shows scleral icterus and right upper quadrant tenderness. Serum studies show:

Alanine aminotransferase	1248 U/L
Aspartate aminotransferase	980 U/L
Hepatitis B surface antigen	negative
Anti-hepatitis B surface antibody	positive
Anti-hepatitis C antibody	negative

Further evaluation shows hepatitis C virus RNA detected by PCR. Without appropriate treatment, which of the following is the most likely outcome of this patient's current condition?

	Answer	Image
A	Hepatocellular carcinoma	
B	Slowly progressive hepatitis	
C	Liver cirrhosis	
D	Transient infection	
E	Fulminant hepatitis	

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Hint

This known IV drug user has symptoms of acute hepatitis. The presence of HCV RNA in combination with elevated transaminases and negative anti-hepatitis C antibodies is indicative of acute hepatitis C (HCV) infection.

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Correct Answer

A - Hepatocellular carcinoma

Explanation Why

Hepatocellular carcinoma (HCC) is a long-term complication of HCV infection that mainly occurs in patients that already developed virus-related liver cirrhosis. Although about one-third of all HCC cases can be attributed to HCV, the estimated risk of those with liver cirrhosis progressing to HCC remains low (< 5% per year).

B - Slowly progressive hepatitis

Explanation Why

Slowly progressive hepatitis is the most likely natural disease course of acute HCV infection. Between 50 and 85% of patients develop chronic hepatitis. Both viral and individual host factors (e.g., genetic polymorphisms) contribute to the overall risk of viral persistence. Up to one-third of chronically infected individuals develop liver cirrhosis within 20 years. As chronic HCV infection and even liver cirrhosis are frequently asymptomatic or present with nonspecific symptoms until late stages, diagnosis and treatment are often delayed.

C - Liver cirrhosis

Explanation Why

Liver cirrhosis is a frequent long-term complication of HCV infection that develops up to 30 years after chronification of an untreated acute infection. The estimated risk is about one-third, but the actual risk remains controversial as it is difficult to assess the actual impact of viral persistence on disease progression independent of potential cofactors contributing to development of cirrhosis. However, a different outcome for this patient's acute HCV is still more likely.

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D - Transient infection

Explanation Why

Transient infection is considered the most favorable disease course of acute HCV infection, but only 20%–50% of affected individuals achieve effective and permanent viral clearance. Although this patient with symptomatic acute hepatitis C is more likely to have spontaneous clearance than asymptomatic patients, a different outcome is still more probable.

E - Fulminant hepatitis

Explanation Why

Fulminant hepatitis, presenting with rapidly developing ascites, jaundice, and encephalopathy, is a rare complication of acute hepatitis C (< 10% of cases). It is most common in patients with underlying chronic hepatitis B virus (HBV) infection. However, this patient's laboratory tests confirm immunity against HBV (negative HBsAg, positive anti-HBs antibody).

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Question # 40

A 46-year-old woman comes to the physician because of a 3-day history of diarrhea and abdominal pain. She returned from a trip to Egypt 4 weeks ago. Her vital signs are within normal limits. There is mild tenderness in the right lower quadrant. Stool studies show occult blood and unicellular organisms with engulfed erythrocytes. Which of the following is the most appropriate initial pharmacotherapy for this patient?

	Answer	Image
A	Doxycycline	
B	Metronidazole	
C	Albendazole	
D	Paromomycin	
E	Praziquantel	
F	Ciprofloxacin	

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Hint

The patient's clinical presentation (bloody diarrhea, abdominal cramps, RLQ tenderness), the history of recent travel to a subtropical region, and the finding of hematophagous trophozoites in stool confirm the diagnosis of intestinal amebiasis, which is caused by *Entameba histolytica*.

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Correct Answer

A - Doxycycline

Explanation Why

Doxycycline is the treatment of choice for diarrhea due to cholera. However, patients with cholera have frequent, voluminous “rice water” stools, are often severely dehydrated, and are usually febrile. The clinical presentation and the presence of hematophagous trophozoites in stool indicate that this patient does not have cholera.

B - Metronidazole

Explanation Why

Metronidazole is a nitroimidazole antibiotic that is used to treat infections with anaerobic bacteria and certain protozoal infections. It is the drug of choice for the treatment of both symptomatic intestinal amebiasis (amebic dysentery) and extraintestinal amebiasis (e.g., amebic liver abscess). Tinidazole is an effective alternative to metronidazole. Following treatment with metronidazole or tinidazole, all patients with amebiasis should also receive an intraluminal amebicide such as paromomycin or iodoquinol in order to eliminate intestinal carriage of *E. histolytica*.

C - Albendazole

Explanation Why

Albendazole is an antihelminthic drug that is used to treat nematode infections and certain cestode infections (e.g., cysticercosis, echinococcosis). Infections by intestinal nematodes such as hookworms and *Trichuris trichiura* can cause occult blood in stools. Severe trichuriasis has also been known to cause abdominal pain and diarrhea (trichuris dysentery syndrome). However, both these infections have a chronic course unlike the acute symptoms in this patient. Moreover, the absence of eggs and larvae in stools indicates that the patient does not have an intestinal helminthic infection. Albendazole is not effective against this patient's protozoal infection.

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D - Paromomycin

Explanation Why

Oral paromomycin is used as a luminal antibiotic in conjunction with an extraluminal amebicide to eradicate intestinal cysts and eliminate the carrier state. In the US, paromomycin monotherapy is only indicated for patients with asymptomatic intestinal amebiasis. This patient, however, has symptomatic intestinal amebiasis.

E - Praziquantel

Explanation Why

Praziquantel is used to treat most trematode infections (e.g., schistosomiasis, clonorchiasis) and certain cestode infections (e.g., taeniasis). Intestinal taeniasis, clonorchiasis, and certain forms of schistosomiasis (*S. japonicum*, *S. mansoni*) are diagnosed by the presence of eggs in feces. However, the finding of hematophagous trophozoites in stool indicates that the patient has amebiasis, a protozoal disease against which praziquantel is ineffective.

F - Ciprofloxacin

Explanation Why

Ciprofloxacin can be used to treat severe dysentery caused by *Campylobacter jejuni* or *Yersinia enterocolitica*, which can present similarly with abdominal pain and bloody diarrhea. However, both *C. jejuni* and *Y. enterocolitica* are gram-negative organisms that do not ingest erythrocytes. A different drug is required in this patient with hematophagous trophozoites in stool.

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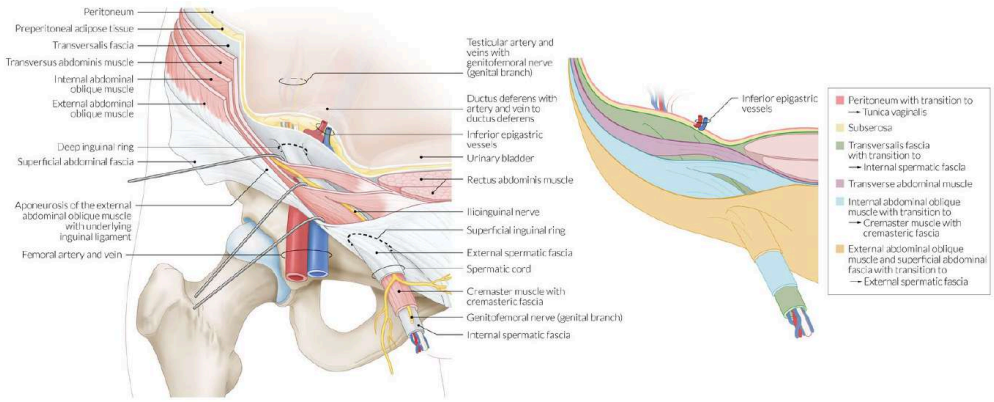
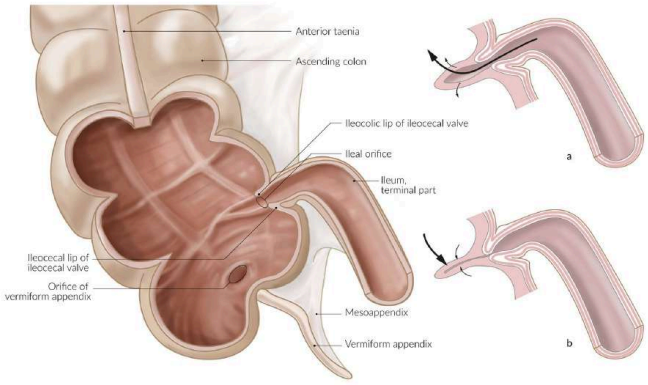
Question # 1

A 24-year-old woman comes to the emergency department because of abdominal pain, fever, nausea, and vomiting for 12 hours. Her abdominal pain was initially dull and diffuse but has progressed to a sharp pain on the lower right side. Two years ago she had to undergo right salpingo-oophorectomy after an ectopic pregnancy. Her temperature is 38.7°C (101.7°F). Physical examination shows severe right lower quadrant tenderness with rebound tenderness; bowel sounds are decreased. Laboratory studies show leukocytosis with left shift. An abdominal CT scan shows a distended, edematous appendix. The patient is taken to the operating room for an appendectomy. During the surgery, the adhesions from the patient's previous surgery make it difficult for the resident physician to identify the appendix. Her attending mentions that she should use a certain structure for guidance to locate the appendix. The attending is most likely referring to which of the following structures?

	Answer	Image
A	Deep inguinal ring	
B	Teniae coli	

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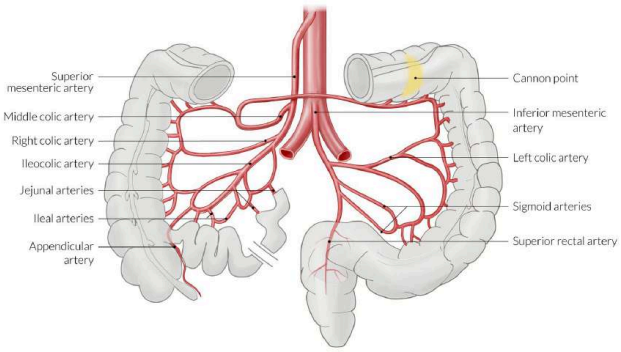
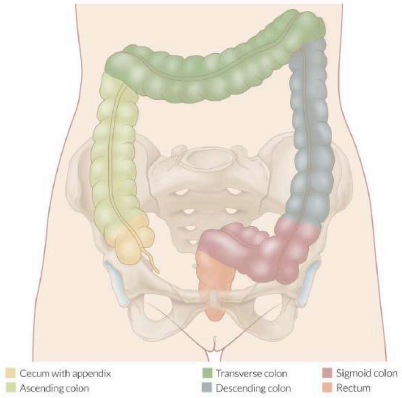
	Answer	Image
C	Ileocolic artery	
D	Right ureter	
E	Epiploic appendages	
F	Colonic haustra	

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Hint

The appendix is an intraperitoneal structure that arises from a point of convergence at the base of the cecum.

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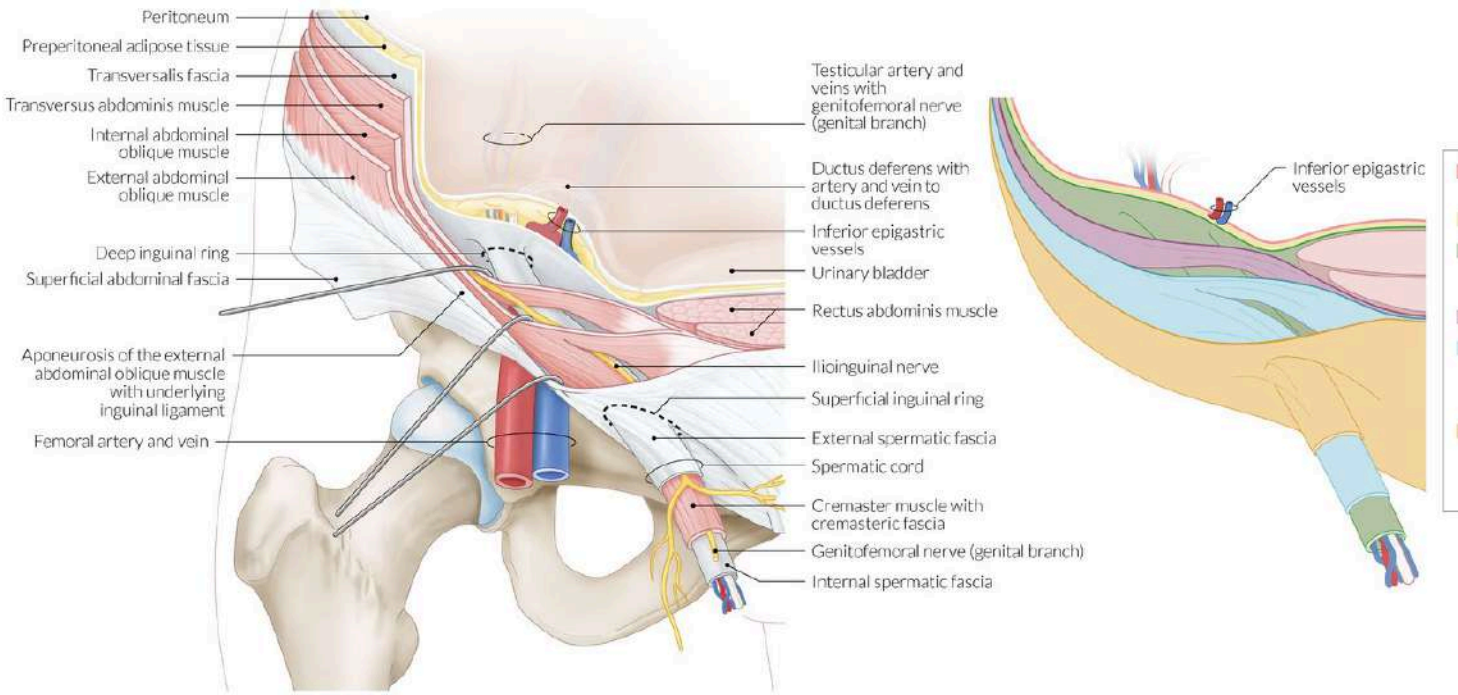
Correct Answer

A - Deep inguinal ring

Image



Explanation Why

The deep inguinal ring is an opening in the transversalis fascia lateral to the epigastric vessels. The right deep inguinal ring is located in the right lower quadrant. However, this structure is part of the abdominal wall and too superficial to be used as guidance for locating the appendix during surgery.

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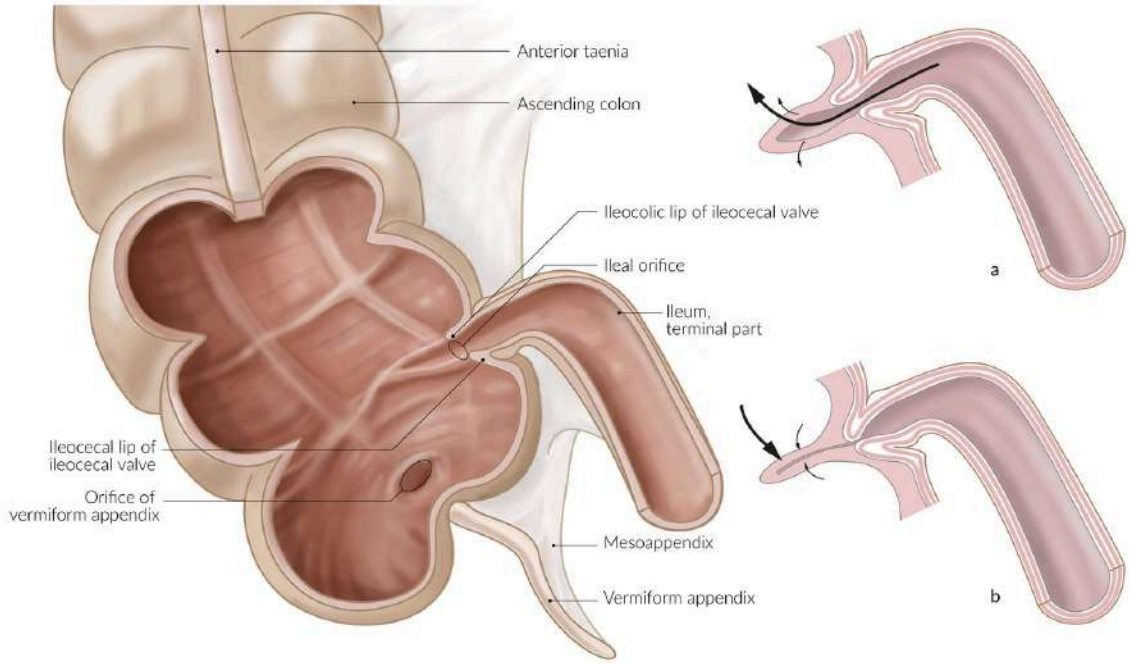
B - Teniae coli

Image



Explanation Why

The teniae coli, three longitudinal smooth muscle bands on the surface of the cecum and colon, converge where the appendix arises from the cecum. Therefore, the teniae coli can be used as guidance to locate the appendix during surgery.

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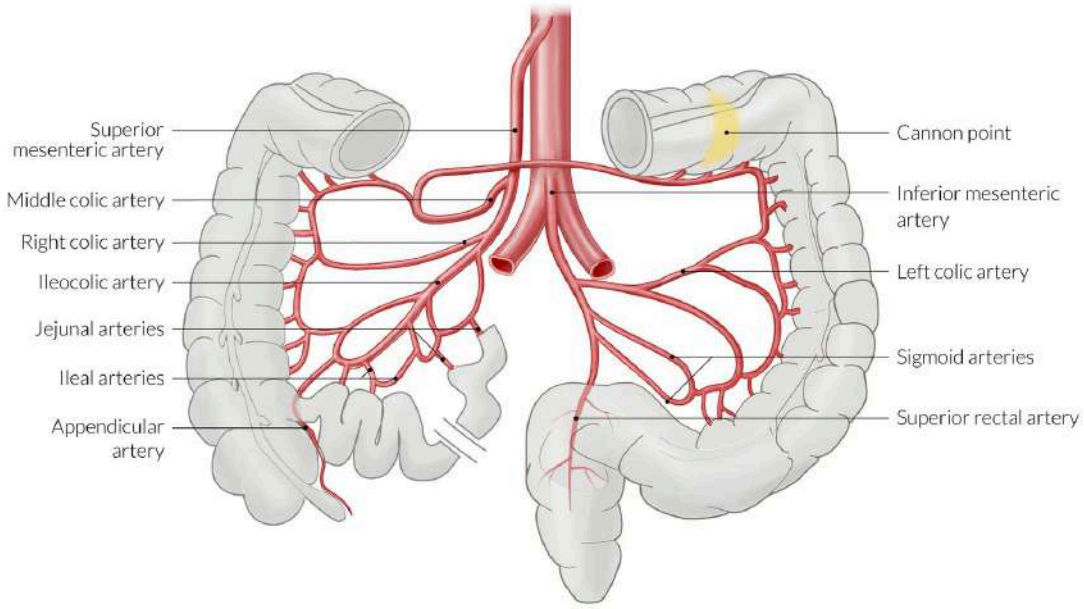
C - Ileocolic artery

Image



Explanation Why

The ileocolic artery arises from the superior mesenteric artery and supplies the distal ileum, cecum, appendix, and proximal ascending colon. This artery or its branches (e.g., appendicular artery) must be ligated during an appendectomy. However, the ileocolic artery is not specific enough to locate the appendix during surgery.

D - Right ureter

Explanation Why

The right ureter is a retroperitoneal organ that lies in proximity to the appendix in the right lower quadrant and, therefore, needs to be identified during appendectomy to prevent iatrogenic injury. However, because the appendix is located intraperitoneally, the right ureter cannot be used for

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guidance during appendectomy.

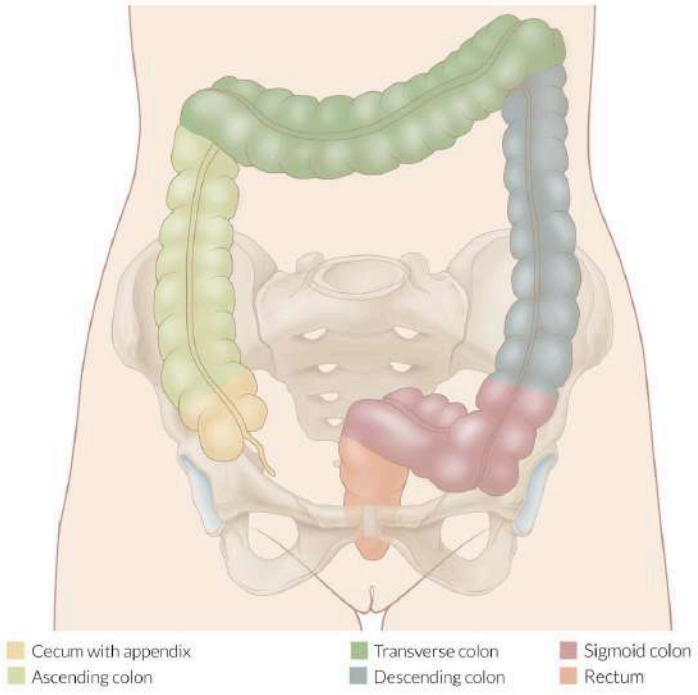
E - Epiploic appendages

Explanation Why

Epiploic appendages appear along the colon as small peritoneal sacs filled with fat. Epiploic appendagitis is a rare differential diagnosis of acute appendicitis. These structures cannot, however, be used as guidance to locate the appendix during surgery.

F - Colonic haustra

Image



Explanation Why

Haustra are outpouchings of the colonic wall that give the colon its segmental appearance. They can be used as guidance to locate the large intestine during surgery. However, haustra are not specific

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enough to locate the appendix.

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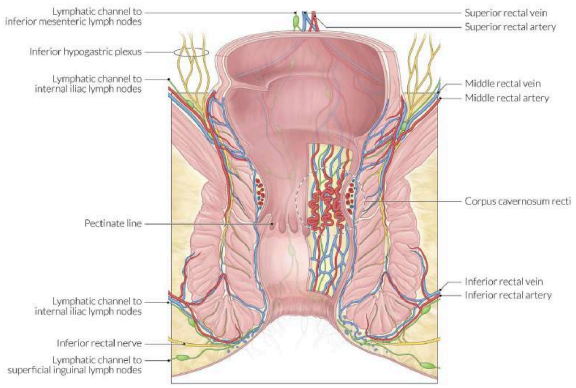
Question # 2

A 45-year-old man comes to the physician because of bright red blood in his stool for 5 days. He has had no pain during defecation and no abdominal pain. One year ago, he was diagnosed with cirrhosis after being admitted to the emergency department for upper gastrointestinal bleeding. He has since cut down on his drinking and consumes around 5 bottles of beer daily. Examination shows scleral icterus and mild ankle swelling. Palpation of the abdomen shows a fluid wave and shifting dullness. Anoscopy shows enlarged bluish vessels above the dentate line. Which of the following is the most likely source of bleeding in this patient?

	Answer	Image
A	Superior rectal vein	
B	Internal pudendal vein	
C	Inferior mesenteric artery	
D	Inferior rectal vein	
E	Internal iliac vein	
F	Middle rectal artery	

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Hint

The patient's anoscopy findings of anorectal varices in addition to his past medical history of liver cirrhosis and upper gastrointestinal bleeding suggest portal hypertension.

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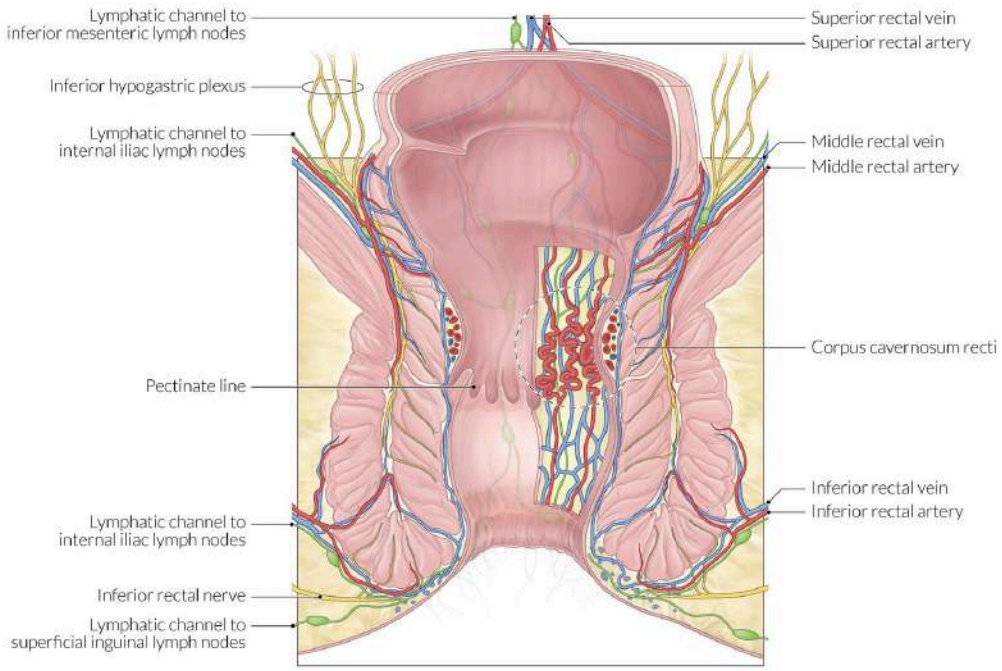
Correct Answer

A - Superior rectal vein

Image



Explanation Why

Anorectal varices occur in patients with portal hypertension as a result of increased blood flow in the portosystemic anastomoses that connect the superior rectal vein with the inferior and middle rectal veins. The superior rectal vein receives blood from the region of the anal canal above the dentate line and drains into the inferior mesenteric vein (portal venous circulation). The superior rectal vein would be the source of bleeding in the case of lesions located above the dentate line, such as the anorectal varices seen in this patient. The inferior rectal veins, which receive blood from the region below the dentate line and drain into the internal pudendal veins (systemic venous circulation), would be the source of bleeding in the case of lesions located below the dentate line, such as external hemorrhoids.

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B - Internal pudendal vein

Explanation Why

Blood from the region of the anal canal below the pectinate line drains into the internal pudendal veins via its tributary. The anorectal varices in this patient are located above the dentate line, which is why a different vessel is the more likely source of bleeding. External hemorrhoids, which manifest with painful rectal bleeding, drain into the internal pudendal veins.

C - Inferior mesenteric artery

Explanation Why

The inferior mesenteric artery does supply blood to the region of the anal canal above the dentate line via its branch, the superior rectal artery. However, the source of bleeding in this patient is an enlarged tortuous vein (varix), not an artery.

D - Inferior rectal vein

Explanation Why

The inferior rectal veins receive blood from the region of the anal canal below the dentate line. The anorectal varices in this patient are located above the dentate line, which is why a different vessel is the more likely source of bleeding. The inferior rectal veins are the source of bleeding in external hemorrhoids, which manifest with painful rectal bleeding.

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E - Internal iliac vein

Explanation Why

Blood from the region of the anal canal below the dentate line ultimately drains into the internal iliac veins. The anorectal varices in this patient are located above the dentate line, which is why a different vessel is the more likely source of bleeding. External hemorrhoids, which manifest with painful rectal bleeding, drain into the internal iliac veins.

F - Middle rectal artery

Explanation Why

The middle rectal artery does supply blood to the region of the anal canal above the dentate line. However, the source of bleeding in this patient is an enlarged tortuous vein (varix), not an artery.

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Question # 3

A 45-year-old woman comes to the emergency department because of abdominal cramping, vomiting, and watery diarrhea for the past 4 hours. One day ago, she went to a seafood restaurant with her family to celebrate her birthday. Three of the attendees have developed similar symptoms. The patient appears lethargic. Her temperature is 38.8°C (101.8°F). Which of the following organisms is most likely responsible for this patient's current symptoms?

	Answer	Image
A	Campylobacter jejuni	
B	Staphylococcus aureus	
C	Vibrio parahaemolyticus	
D	Listeria monocytogenes	
E	Enterohemorrhagic Escherichia coli	
F	Salmonella enterica	
G	Bacillus cereus	

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Hint

The most likely cause of this patient's symptoms is a gram-negative, oxidase-positive rod.

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Correct Answer

A - Campylobacter jejuni

Explanation Why

Campylobacter jejuni causes a foodborne illness that manifests with fever, abdominal cramps, diarrhea and, occasionally, vomiting, as seen here. Although *C. jejuni* is typically transmitted via undercooked poultry or unpasteurized milk, shellfish has also been implicated in some cases of Campylobacter enteritis. Patients with Campylobacter enteritis usually have bloody diarrhea, with symptoms typically beginning 2–4 days after the ingestion of contaminated food. This woman, however, presents with watery diarrhea 1 day after visiting a seafood restaurant.

B - Staphylococcus aureus

Explanation Why

Staphylococcus aureus enterotoxins cause a foodborne illness that manifests with fever, abdominal cramps, vomiting, and watery diarrhea, as seen here. However, the toxins are most commonly transmitted via processed meats, mayonnaise, custard, or nondairy creamers, not seafood. Moreover, symptoms typically begin within 1–4 hours of ingesting the contaminated food, unlike this patient's presentation 1 day after a restaurant visit.

C - Vibrio parahaemolyticus

Explanation Why

Vibrio parahaemolyticus gastroenteritis is typically caused by eating raw or undercooked shellfish (especially oysters). Patients present with fever, abdominal cramps, vomiting, and watery/bloody diarrhea 12–52 hours after ingesting the contaminated shellfish, as seen here. The infection is generally self-limiting. Other pathogens that can be transmitted through shellfish include *Vibrio cholerae*, *Vibrio vulnificus*, hepatitis A virus, hepatitis E virus, norovirus, and *Paragonimus* species.

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D - Listeria monocytogenes

Explanation Why

Listeria monocytogenes causes a foodborne illness that manifests with fever, abdominal cramps, vomiting, and watery diarrhea within 6 hours to 10 days of ingesting the contaminated food, as seen here. However, *L. monocytogenes* is typically transmitted via unpasteurized dairy products or ready-to-eat deli meats, not seafood.

E - Enterohemorrhagic Escherichia coli

Explanation Why

Enterohemorrhagic *Escherichia coli* (EHEC) causes a foodborne illness that can manifest with fever, abdominal cramps, vomiting, and diarrhea, as seen here. However, EHEC is typically transmitted via undercooked meat, unpasteurized dairy products or fruit juices, not seafood. Moreover, patients usually have bloody diarrhea with symptoms beginning 2–10 days after ingesting contaminated food, unlike this patient who presents with watery diarrhea 1 day after eating at a seafood restaurant.

F - Salmonella enterica

Explanation Why

Nontyphoidal serotypes of *Salmonella enterica* cause foodborne illnesses that manifest with fever, abdominal cramps, vomiting, and watery diarrhea within 6–72 hours of ingesting the contaminated food, as seen here. However, *Salmonella enterica* is typically transmitted via undercooked eggs, poultry, or unpasteurized milk products, not seafood. Infection with typhoidal serotypes of *Salmonella enterica* (e.g., *S. Typhi*, *S. Paratyphi*) causes enteric fever, which commonly begins 5–30 days after ingesting the contaminated food.

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G - Bacillus cereus

Explanation Why

Bacillus cereus enterotoxins can cause two forms of foodborne illness. The emetic form manifests with abdominal cramps, vomiting, and, occasionally, watery diarrhea, as seen here. However, the emetic toxins are typically transmitted via improperly refrigerated starch products (e.g., rice) rather than seafood, and the symptoms occur within 30 minutes to 6 hours of ingesting the contaminated food source. The diarrheal form has an incubation period of 6–15 hours and manifests with abdominal cramps and watery diarrhea, as seen here. However, vomiting would not be expected. Foods associated with diarrheal toxin-mediated disease include improperly refrigerated milk, meat, and vegetables. Fever would not be expected in either the emetic or diarrheal form of *B. cereus* infection.

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Question # 4

A 63-year-old man with diverticular disease comes to the emergency department because of painless rectal bleeding, dizziness, and lightheadedness for 2 hours. His temperature is 37.6°C (99.6°F), pulse is 115/min, respirations are 24/min, and blood pressure is 86/60 mm Hg. He appears pale. Physical examination shows bright red rectal bleeding. Colonoscopy shows profuse diverticular bleeding; endoscopic hemostasis is performed. After initiating fluid resuscitation, the patient becomes hemodynamically stable. The following day, laboratory studies show:

Hemoglobin	8 g/dL
Leukocyte count	15,500/mm^3
Platelet count	170,000/mm^3
Serum	
Urea nitrogen	60 mg/dL
Creatinine	2.1 mg/dL
Bilirubin	
Total	1.2 mg/dL
Indirect	0.3 mg/dL
Alkaline phosphatase	96 U/L
Alanine aminotransferase (ALT, GPT)	2,674 U/L
Aspartate aminotransferase (AST, GOT)	2,254 U/L

Which of the following cells in the patient's liver were most likely damaged first?

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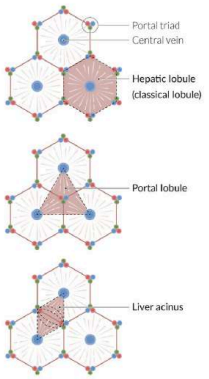
	Answer	Image
A	Hepatic stellate (Ito) cells	
B	Periportal hepatocytes	
C	Hepatic sinusoidal endothelial cells	
D	Hepatic Kupffer cells	
E	Midzonal hepatocytes	
F	Centrilobular hepatocytes	

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Hint

This patient's extremely high serum transaminases with relatively normal cholestatic parameters (normal alkaline phosphatase, mildly elevated direct bilirubin), previous hemodynamic instability, and evidence of prerenal acute kidney injury (BUN:Cr > 20:1) raise suspicion for ischemic hepatitis.

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Correct Answer

A - Hepatic stellate (Ito) cells

Explanation Why

Hepatic stellate cells are located within the space of Disse. These cells secrete extracellular matrix to protect and facilitate healing of the liver in response to transient hepatic injury (e.g., ischemic hepatitis). However, because of their lower metabolic rate, hepatic stellate cells are more resistant to ischemic injury and less likely to be damaged compared to hepatocytes.

B - Periportal hepatocytes

Explanation Why

The liver is organized microscopically into hepatic acini (microvascular unit), which are further divided into three zones based on the degree of oxygenation. Zone 1 (periportal hepatocytes) surrounds the portal triad, and these cells are the most susceptible to viral hepatitis and toxic substance ingestion. However, zone 1 receives oxygen-rich blood and is the least sensitive to ischemic injury. Therefore, periportal hepatocytes are most likely to be damaged last in ischemic hepatitis.

C - Hepatic sinusoidal endothelial cells

Explanation Why

The hepatic sinusoids drain blood from the portal triad (75% deoxygenated blood from the hepatic portal vein; 25% oxygenated blood from the hepatic artery) into the central vein. Sinusoidal endothelial cells are extremely sensitive to reperfusion injury, which may lead to their destruction, induce portal hypertension, and worsen hepatic fibrosis. However, because of their lower metabolic rate, sinusoidal endothelial cells are more resistant to ischemic injury and less likely to be damaged compared to hepatocytes.

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D - Hepatic Kupffer cells

Explanation Why

Hepatic Kupffer cells are located within hepatic sinusoids, and their function is to clear aged erythrocytes, infectious particles, and extracellular debris. Because of their lower metabolic rate, hepatic Kupffer cells are more resistant to ischemic injury and less likely to be damaged compared to hepatocytes.

E - Midzonal hepatocytes

Explanation Why

The liver is organized microscopically into hepatic acini (microvascular unit), which are further divided into three zones based on the degree of oxygenation. Zone 2 (midzonal hepatocytes) is the most susceptible to hepatocellular necroptosis (with councilman bodies) due to yellow fever. However, zone 2 is located between the portal triad and central vein and receives oxygen-intermediate blood, meaning that midzonal hepatocytes are neither the first nor last cells to be damaged by ischemia.

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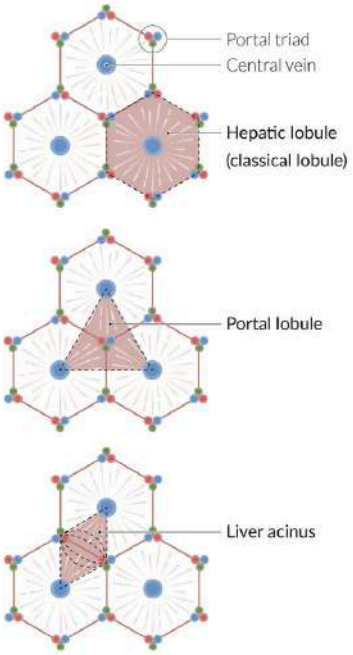
F - Centrilobular hepatocytes

Image



Explanation But

Because zone 3 contains the highest density of cytochrome P450 enzymes, it is also the zone most susceptible to injury from metabolic toxins, such as ethanol, paracetamol, and halothane, which are all transformed by CYP450 into toxic intermediates.

Explanation Why

The liver is organized microscopically into hepatic lobules (anatomic unit), portal lobules (bile-synthetic functional unit), and hepatic acini (microvascular unit). The hepatic acinus is a diamond-shaped zone between two neighboring central veins (long axis) and two opposing portal triads (short axis). Within the acinus, blood enters through the portal triad (75% deoxygenated blood from the hepatic portal vein; 25% oxygenated blood from the hepatic artery) and drains through the sinusoidal capillaries into the central vein. Hepatic acini can be divided into three zones, which are distinguished based on the degree of oxygenation. Zone 3 contains centrilobular hepatocytes and surrounds the central vein. Because zone 3 receives oxygen-poor blood, it is the zone most sensitive to ischemic injury, making centrilobular hepatocytes most likely to be damaged first.

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Question # 5

A 42-year-old woman comes to the emergency department because of a 2-day history of right upper abdominal pain and nausea. She is 163 cm (5 ft 4 in) tall and weighs 91 kg (200 lb); her BMI is 34 kg/m^2. Her temperature is 38.5°C (101.3°F). Physical examination shows a distended abdomen and right upper quadrant tenderness with normal bowel sounds. Laboratory studies show:

Leukocyte count	14,000/mm^3
Serum	
Total bilirubin	1.1 mg/dL
AST	42 U/L
ALT	50 U/L
Alkaline phosphatase	68 U/L

Abdominal ultrasonography is performed, but the results are inconclusive. Cholescintigraphy shows the intrahepatic bile ducts, hepatic ducts, common bile duct, and proximal small bowel. Which of the following is the most likely cause of this patient's symptoms?

	Answer	Image
A	Autodigestion of pancreatic parenchyma	
B	Hypomotility of the gallbadder	
C	Fistula between the gallbladder and small intestine	
D	Infection with a hepatotropic virus	

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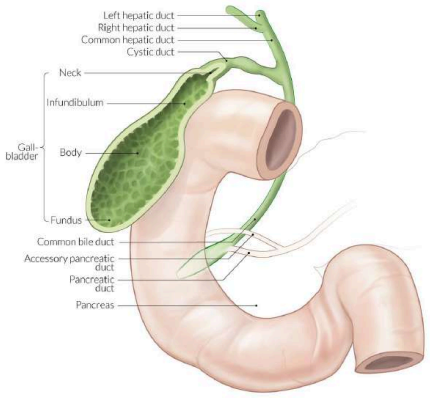
	Answer	Image
E	Obstruction of the cystic duct	
F	Fibrosis of the common bile duct	

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Hint

This patient has risk factors for gallstone disease (e.g., obesity, age > 40, female). Right upper quadrant pain, nausea, fever, and leukocytosis suggest acute cholecystitis.

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Correct Answer

A - Autodigestion of pancreatic parenchyma

Explanation Why

Autodigestion of pancreatic parenchyma due to a local release of digestive proteolytic enzymes is seen in pancreatitis. While pancreatitis can manifest with abdominal pain, nausea, and fever, the abdominal pain in pancreatitis is typically epigastric (not right upper abdominal pain) and radiates towards the back. Moreover, cholescintigraphy showing absent uptake of radioactive tracer in the gallbladder, as seen in this patient, suggests another etiology.

B - Hypomotility of the gallbadder

Explanation Why

Hypomotility of the gallbladder can result in biliary stasis, which predisposes to gallstone development and cholecystitis. This patient's acute symptoms, however, are likely caused by contraction of the gallbladder against an impacted stone rather than by decreased motility of the gallbladder.

C - Fistula between the gallbladder and small intestine

Explanation Why

A cholecystoenteric fistula (fistula between the gallbladder and small intestine) is often due to inflammation of the gallbladder wall. Fistulization provides a conduit for passage of gallstones, which may cause gallstone ileus. Patients with gallstone ileus can present with abdominal pain, nausea, and fever, as seen here. However, physical examination would classically show high-pitched (tympanic) bowel sounds. In addition, even though cholescintigraphy is not a sensitive test for gallstone ileus, it would be expected to show communication between the gallbladder and intestinal tract rather than absent uptake of radioactive tracer in the gallbladder. CT is the preferred imaging modality to confirm gallstone ileus and classically shows bowel obstruction with pneumobilia.

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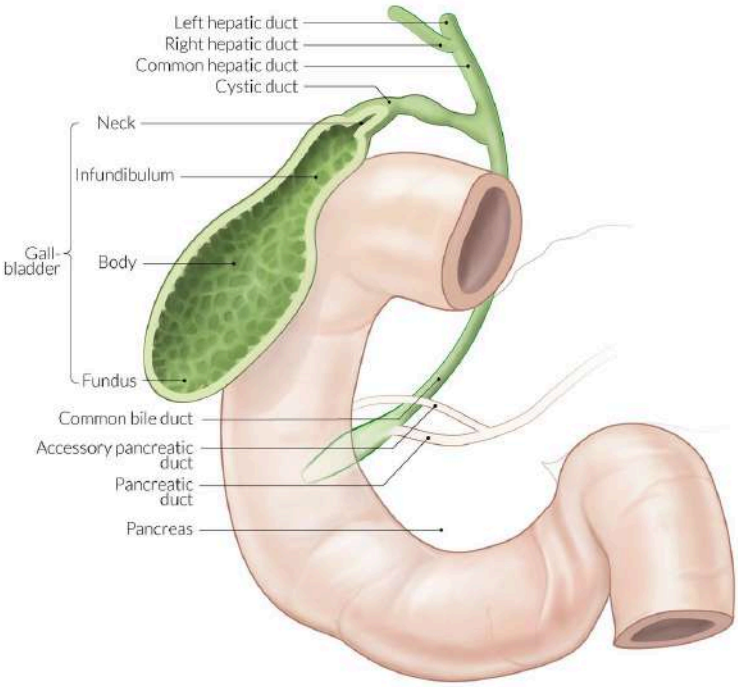
D - Infection with a hepatotropic virus

Explanation Why

Infection with a hepatotropic virus (e.g., hepatitis A) can cause acute hepatitis. While acute hepatitis can manifest with right upper quadrant pain, nausea, and fever, it usually also manifests with markedly elevated liver function tests (e.g., AST, ALT), which are only mildly elevated in this patient. Moreover, a cholescintigraphy showing absent uptake of radioactive tracer in the gallbladder, as seen in this patient, suggests another etiology.

E - Obstruction of the cystic duct

Image



Explanation But

Risk factors for the development of cholelithiasis can be remembered with the 6 Fs: Fat (obesity),

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Female, Fertile (multiparity or pregnancy), Forty (> 40 years of age), Fair-skinned (European, Native American, or Hispanic ancestry), Family history.

Explanation Why

Cholecystitis is usually caused by the passage of a gallstone into the cystic duct. The subsequent obstruction leads to inflammation and symptoms of right upper quadrant abdominal pain, nausea, and fever, as seen in this patient. Cholescintigraphy (HIDA scan) would show decreased or absent uptake of radioactive tracer in the gallbladder due to obstruction of the cystic duct; a HIDA scan is primarily used to diagnose cystic duct obstruction if RUQ ultrasound fails to show gallstones. In uncomplicated cholecystitis, cholestasis parameters (i.e., ALP, GGT, and bilirubin) are typically normal or only mildly elevated because there is usually no obstruction of the hepatic ducts or common bile duct.

F - Fibrosis of the common bile duct

Explanation Why

Fibrosis of the common bile duct is seen in primary sclerosing cholangitis (PSC), which is a chronic inflammatory condition that can manifest with right upper quadrant pain and fever during acute episodes. However, patients with fibrosis of the common bile duct would be expected to have markedly elevated cholestasis parameters (i.e., ALP, GGT, and bilirubin). Moreover, cholescintigraphy would show impaired uptake of the radioactive tracer in the proximal bowel rather than absent uptake of radioactive tracer in the gallbladder.

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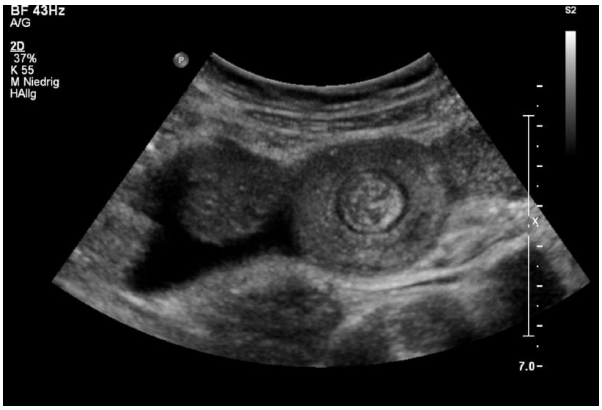
Question # 6

A 6-year-old boy is brought to the emergency department for acute intermittent umbilical abdominal pain and several episodes of nonbilious vomiting for 4 hours. The pain radiates to his right lower abdomen and occurs every 15–30 minutes. During these episodes of pain, the boy draws up his knees to the chest. He had two similar episodes within the past 6 months. Abdominal examination shows periumbilical tenderness with no masses palpated. Transverse abdominal ultrasound shows concentric rings of bowel. His hemoglobin concentration is 10.2 g/dL. Which of the following is the most common underlying cause of this patient's condition?

	Answer	Image
A	Meckel diverticulum	
B	Malrotation with volvulus	
C	Intestinal polyps	
D	Intestinal adhesions	
E	Acute appendicitis	

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Hint

This 6-year-old boy presents with acute cyclical abdominal pain, with his knees drawn to the chest, nonbilious vomiting, and a target sign on ultrasound, which is a constellation of symptoms most consistent with intussusception. The recurrence of the episode and the presence of anemia are suggestive of a particular pathologic lead point.

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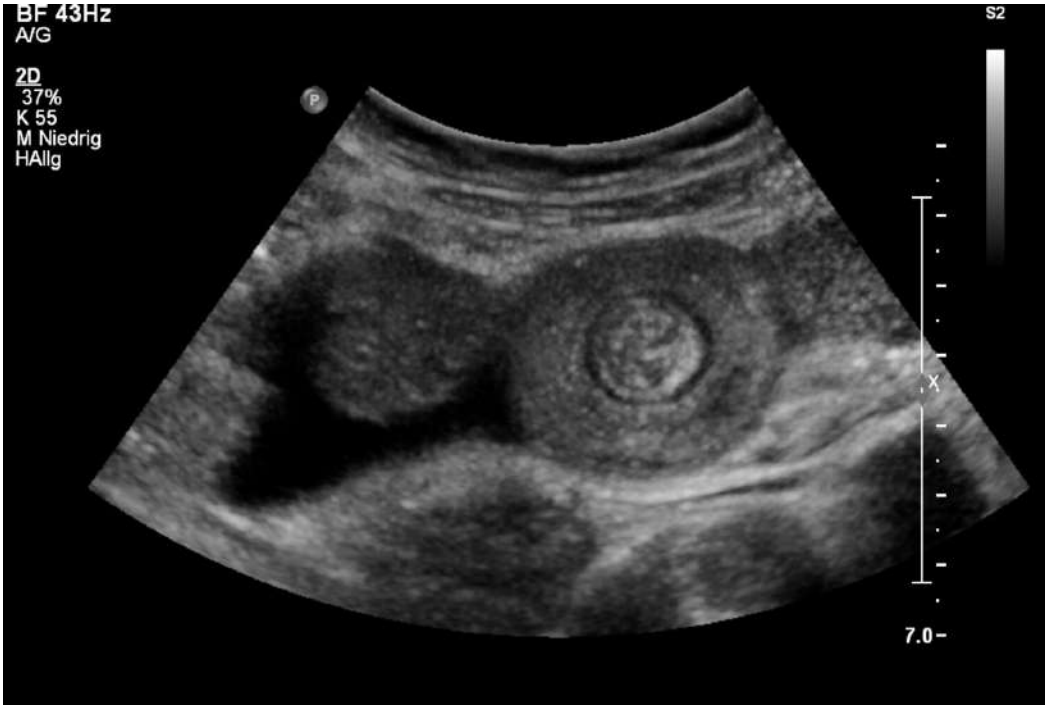
Correct Answer

A - Meckel diverticulum

Image



Explanation Why

Meckel diverticulum is the most common pathologic lead point causing intussusception. A pathological lead point should always be suspected in children older than 5 years of age who present with recurrent episodes of abdominal pain, especially if symptoms occur within 6 months of the last episode. Meckel diverticulum can cause bleeding if it contains ectopic gastric mucosal cells that secrete gastric acid and can so irritate the adjacent small bowel to the point of ulceration, which explains this child's anemia.

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B - Malrotation with volvulus

Explanation Why

Malrotation with volvulus typically presents with acute onset of abdominal pain and bloody stools. On abdominal ultrasound, the classic feature of volvulus is the whirlpool sign (whirl sign), which indicates a twisted mesentery and is easily distinguished from the target sign seen in this patient. Although the clinical features may be similar to those of this patient's condition, volvulus caused by a malrotation of the intestines usually occurs during early infancy and would be uncommon in a 6-year-old child.

C - Intestinal polyps

Explanation Why

Intestinal polyps are the second most common pathological lead point resulting in intussusception. While intestinal polyps cannot be entirely excluded, they are not the most common cause of intussusception in this age group. This patient appears to have had chronic blood loss that resulted in anemia, suggesting a different etiology.

D - Intestinal adhesions

Explanation Why

Intestinal adhesions may cause bowel obstruction or act as a pathologic lead point for intussusception. They usually form after abdominal surgery, intra-abdominal inflammation, or abdominal radiotherapy, none of which are mentioned in this patient's history.

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E - Acute appendicitis

Explanation Why

Acute appendicitis presents with diffuse, continuous abdominal pain migrating from the periumbilical region to the right lower quadrant, vomiting, and target sign on ultrasound, making it an important differential diagnosis for this patient's symptoms. However, repeated attacks of pain and the presence of anemia in this patient suggest a different diagnosis.

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Question # 7

Ten days after undergoing emergent colectomy for a ruptured bowel that she sustained in a motor vehicle accident, a 59-year-old woman has abdominal pain. During the procedure, she was transfused 3 units of packed red blood cells. She is currently receiving total parenteral nutrition. Her temperature is 38.9°C (102.0°F), pulse is 115/min, and blood pressure is 100/60 mm Hg. Examination shows tenderness to palpation in the right upper quadrant of the abdomen. Bowel sounds are hypoactive. Serum studies show:

Aspartate aminotransferase	142 U/L
Alanine aminotransferase	86 U/L
Alkaline phosphatase	153 U/L
Total bilirubin	1.5 mg/dL
Direct bilirubin	1.0 mg/dL
Amylase	20 U/L

Which of the following is the most likely diagnosis?

	Answer	Image
A	Acalculous cholecystitis	
B	Ischemic hepatitis	
C	Small bowel obstruction	
D	Hemolytic transfusion reaction	

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	Answer	Image
E	Cholecystolithiasis	
F	Acute pancreatitis	

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Hint

This patient's condition is usually only seen in hospitalized patients who are severely ill.

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Correct Answer

A - Acalculous cholecystitis

Explanation But

Imaging (ultrasonography or abdominal CT scan) would show a distended gallbladder with thickened walls, hyperdense bile (sludge), and pericholecystic fluid. Treatment includes antibiotics (with gram-negative and enteric coverage) and cholecystostomy for drainage, which is a less invasive approach for this critically ill patient. If the patient does not improve after initial management, then cholecystectomy is required.

Explanation Why

Acalculous cholecystitis should be suspected in critically ill and postoperative patients who present with fever, RUQ pain, slightly increased levels of serum aminotransferases, and laboratory evidence of biliary stasis (i.e., elevated bilirubin, and ALP), as observed in this patient. Conditions that result in biliary stasis and/or hypoperfusion of the gallbladder such as trauma, surgery, total parenteral nutrition, multiple transfusions, which are also seen here, are risk factors for acalculous cholecystitis.

B - Ischemic hepatitis

Explanation Why

Ischemic hepatitis, also known as “shock liver”, is typically caused by sudden hypotension and/or thromboses of the hepatic vasculature, both of which are potential intraoperative or postoperative complications of a major surgical procedure as the colectomy this patient has undergone. Ischemic hepatitis may manifest with RUQ pain and fever, which are also seen here. However, the characteristic feature is a very high elevation in serum transaminases of > 1000 IU/L (50 times the upper limit of normal), which this patient does not have.

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C - Small bowel obstruction

Explanation Why

Small bowel obstruction (SBO) is characterized by nausea, vomiting, and abdominal distention, as well as pain that is nonlocalized, periumbilical, cramping, and colicky, unlike what is reported in this patient. On physical examination, hyperactive, high-pitched bowel sounds are usually identified as peristalsis increases in an attempt to relieve the obstruction. This patient, however, presents with hypoactive bowel sounds, making SBO less likely. Moreover, localized RUQ tenderness, mild transaminitis, and increased alkaline phosphatase would not be explained by SBO.

D - Hemolytic transfusion reaction

Explanation Why

A delayed hemolytic transfusion reaction (DHTR) is seen in individuals with a previous history of transfusion or organ transplantation during which sensitization to specific RBC antigens would have occurred. Although DHTR manifests many days after the second transfusion with fever and jaundice, unconjugated hyperbilirubinemia would be expected. This patient has conjugated hyperbilirubinemia, elevated transaminases, localized RUQ pain, and signs of sepsis, all of which cannot be explained by DHTR. In addition, from the given history, this is the first transfusion this patient has received.

E - Cholecystolithiasis

Explanation Why

Symptomatic cholecystolithiasis typically manifests with postprandial RUQ pain associated with nausea and vomiting (biliary colic). Although liver enzyme parameters may be slightly abnormal in some patients, uncomplicated cholecystolithiasis would not cause the fever or hypotension seen in this patient.

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F - Acute pancreatitis

Explanation Why

Acute pancreatitis is an inflammatory disease of the pancreas most commonly caused by gallstones or alcohol abuse. Pancreatitis can cause fever, abdominal pain, tachycardia, hypotension, hypoactive bowel sounds, altered liver function parameters. Gallstone pancreatitis typically causes elevated bilirubin and ALP levels. Although this patient has all of these features, her serum amylase level is normal, making acute pancreatitis unlikely.

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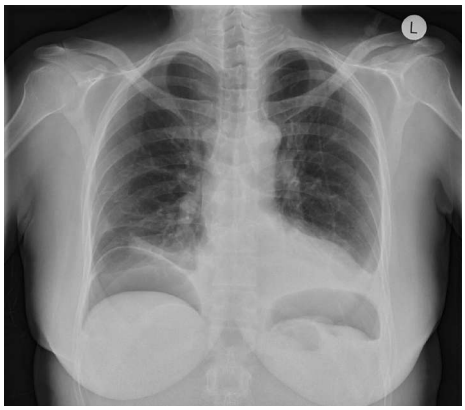
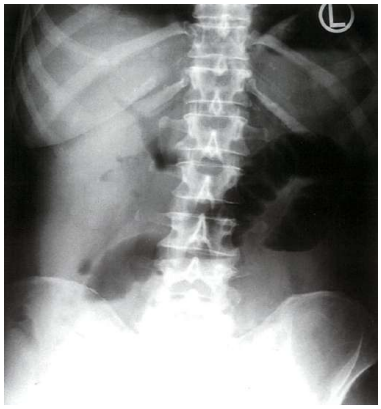
Question # 8

A 71-year-old woman with type 2 diabetes mellitus and hypertension comes to the emergency department because of a 3-day history of intermittent abdominal pain, vomiting, and obstipation. She has had multiple episodes of upper abdominal pain over the past year. She has smoked 1 pack of cigarettes daily for the past 30 years. Physical examination shows a distended abdomen with diffuse tenderness and high-pitched bowel sounds. An x-ray of the abdomen shows a dilated bowel, multiple air-fluid levels, and gas in the biliary tree. Which of the following is the most likely cause of this patient's condition?

	Answer	Image
A	Perforation of a peptic ulcer	
B	Inflammation of the gallbladder wall	

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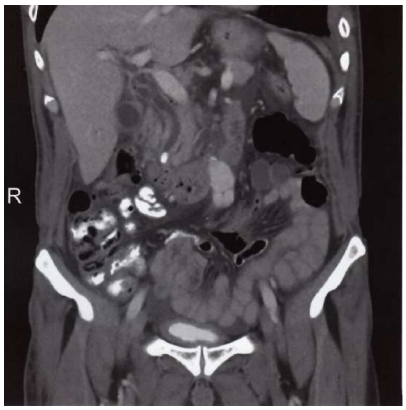
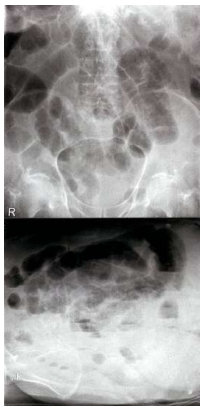
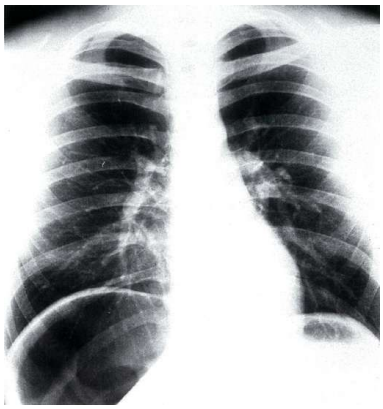
	Answer	Image
C	Obstruction of the common bile duct	
D	Occlusion of the superior mesenteric artery	
E	Torsion of the large intestine	

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Hint

This patient with a long-standing history of episodic upper abdominal pain now presents with features of mechanical obstruction (abdominal distention, vomiting, obstipation, high-pitched bowel sounds, and dilated bowel loops with multiple air-fluid levels) with pneumobilia on abdominal x-ray.

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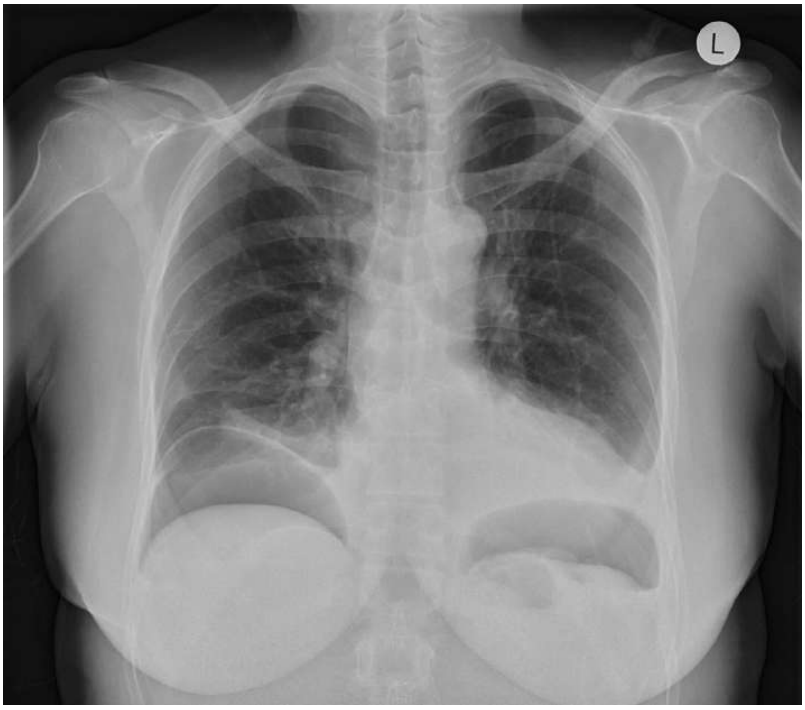
Correct Answer

A - Perforation of a peptic ulcer

Image



Explanation Why

A peptic ulcer perforation can manifest with acute onset abdominal pain, vomiting, and obstipation, which can be complicated by a paralytic ileus, demonstrated by a dilated bowel with multiple air-fluid levels on abdominal x-ray. However, air on an abdominal x-ray would be found in the peritoneum (due to perforation through the gastrointestinal tract) rather than in the biliary tree, as seen here. Moreover, individuals with a paralytic ileus would have decreased or absent bowel sounds rather than high-pitched bowel sounds.

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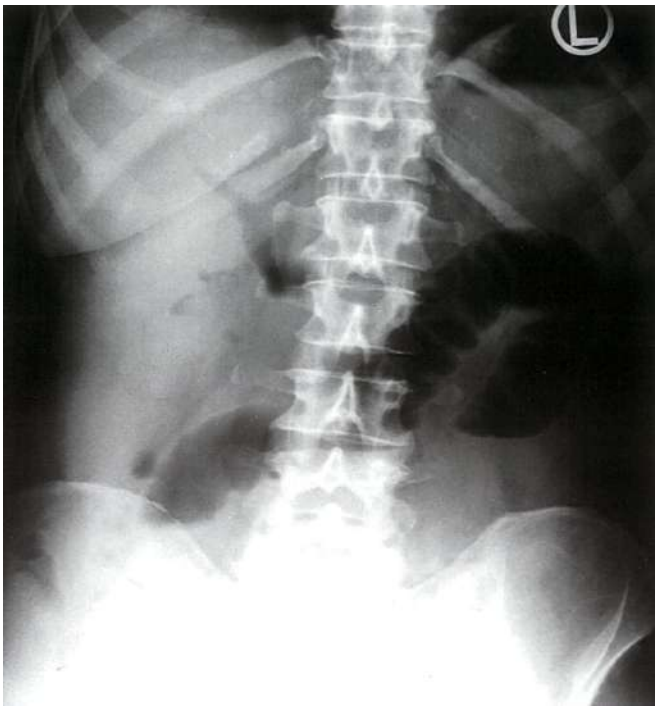
B - Inflammation of the gallbladder wall

Image



Explanation But

Treatment for gallstone ileus is usually surgical, involving removal of the stone (enterolithotomy) and possibly bowel resection to relieve the intestinal obstruction.

Explanation Why

Chronic inflammation of the gallbladder wall can lead to the formation of an abnormal connection between the gallbladder and the intestinal tract (i.e., a cholecystoenteric fistula), which provides a conduit for the passage of gallstones. A gallstone can subsequently become lodged in the distal ileum, the section of the intestine with the narrowest lumen, causing gallstone ileus. An abdominal x-ray will show pneumobilia, indicating that intra-intestinal air has moved through to the fistula into the biliary tree.

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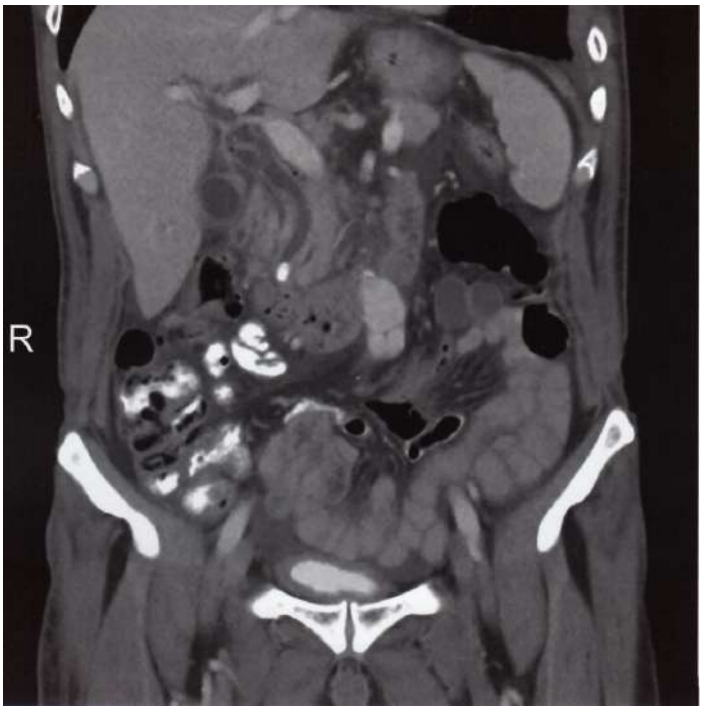
C - Obstruction of the common bile duct

Image



Explanation Why

Obstruction of the common bile duct (CBD) is most often caused by gallstone disease, which is associated with recurrent episodes of upper abdominal pain (chronic biliary colic). Acute cholangitis or acute pancreatitis associated with CBD obstruction can also cause vomiting. However, CBD obstruction would cause icterus, not mechanical bowel obstruction or pneumobilia. While this patient likely has a history of gallstone disease, she now presents with a different complication.

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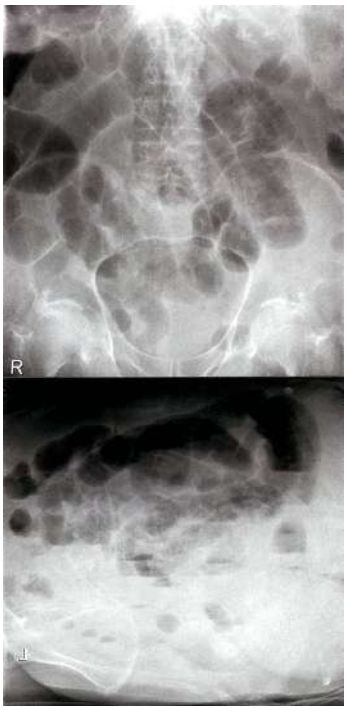
D - Occlusion of the superior mesenteric artery

Image



Explanation Why

This patient has risk factors for superior mesenteric artery (SMA) occlusion (e.g., diabetes mellitus, smoking). Acute SMA occlusion (acute mesenteric ischemia) can cause bowel infarction, which can lead to diffuse abdominal pain due to peritonitis, and vomiting and obstipation due to peritonitis-induced paralytic ileus. However, paralytic ileus manifests with decreased or absent bowel sounds rather than high-pitched bowel sounds. Moreover, pneumobilia would not be expected with acute mesenteric ischemia.

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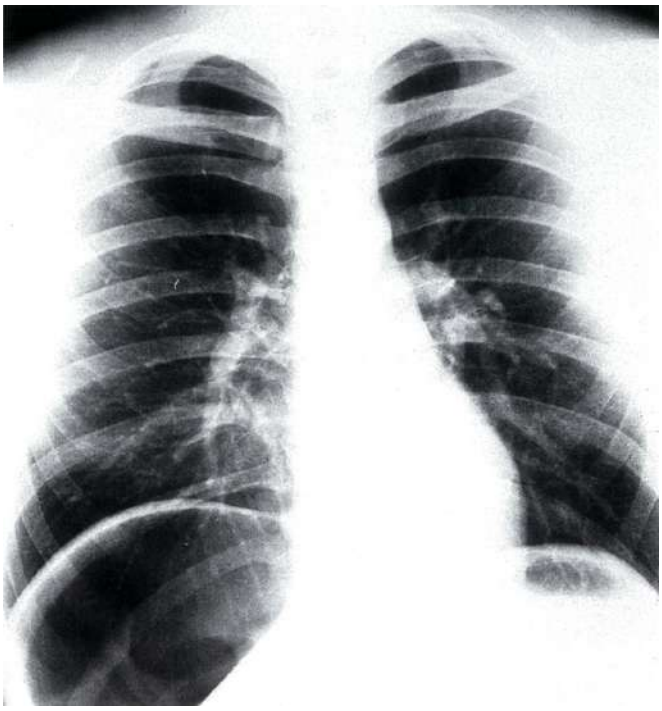
E - Torsion of the large intestine

Image



Explanation Why

Torsion of the large intestine causes volvulus, which may lead to a mechanical small bowel obstruction, as seen in this patient. Rarely, volvulus of the large intestine can manifest with a radiolucency in the right infra-diaphragmatic region (Chilaiditi sign). However, this patient's long history of upper abdominal pain and new finding of pneumobilia on abdominal x-ray suggest a different diagnosis.

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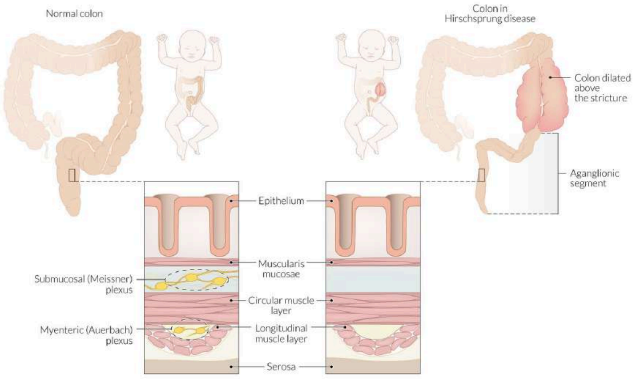
Question # 9

A 3-day-old newborn is brought to the physician because of abdominal distention, inconsolable crying, and 3 episodes of bilious vomiting since the previous evening. He was delivered at home at 40 weeks' gestation by a trained midwife. He has not passed meconium. Physical examination shows abdominal distention, a tight anal sphincter, and an explosive passage of air and feces on removal of the examining finger. Abnormal development of which of the following best explains this patient's condition?

	Answer	Image
A	Muscularis propria and adventitia	
B	Muscularis mucosae and serosa	
C	Epithelium and lamina propria	
D	Submucosa and muscularis externa	
E	Epithelium and submucosa	
F	Muscularis mucosae and lamina propria	

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Hint

This newborn's bilious vomiting, abdominal distention, failure to pass meconium in the first 48 hours of life, tight anal sphincter, and explosive passage of stool on examination are consistent with Hirschsprung disease.

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Correct Answer

A - Muscularis propria and adventitia

Explanation Why

The muscularis propria and adventitia are the outermost layers of the GI tract. The muscularis propria provides sympathetic and parasympathetic innervation, as well as motor innervation to the smooth muscle of the GI tract. The adventitia is the most superficial layer of the portion of the GI tract lying outside the peritoneal cavity (e.g., colon, esophagus) and is made up of connective tissue that acts to protect and create attachments to neighboring structures. However, Hirschsprung disease does not involve a joint defect of the muscularis propria and adventitia.

B - Muscularis mucosae and serosa

Explanation Why

The muscularis mucosae is the outermost layer of the GI mucosa, and the serosa is the outermost layer of the portion of the GI tract within the peritoneal cavity. The muscularis mucosae allows the mucosa to move, which facilitates glandular secretion and absorption. The serosa coats the intestines and secretes serous fluid that protects the GI tract against frictional damage, which might occur during movement within the abdomen. However, Hirschsprung disease involves other layers of the GI tract.

C - Epithelium and lamina propria

Explanation Why

The epithelium and lamina propria are the innermost layers of the GI tract mucosa. The epithelium contains glands that secrete digestive enzymes and also serves to absorb nutrients and water. It is attached via the lamina propria to the interior of the GI tract wall. However, Hirschsprung disease involves other layers of the GI tract.

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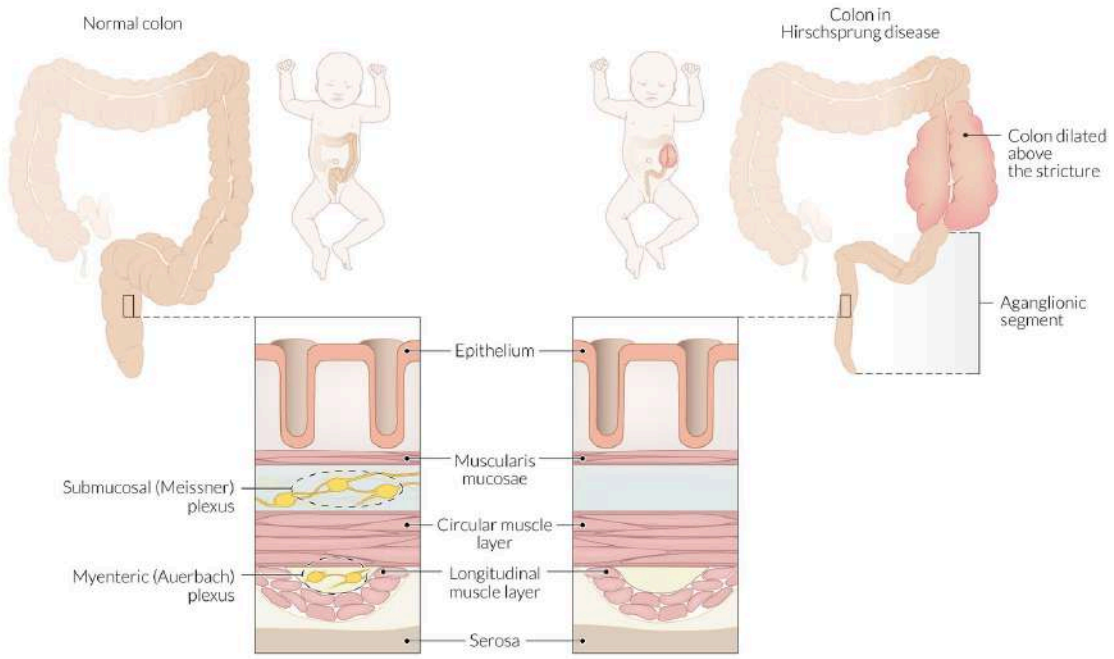
D - Submucosa and muscularis externa

Image



Explanation Why

The submucosa normally contains the Meissner (submucous) plexus, while the muscularis externa contains the Auerbach (myenteric) plexus. In Hirschsprung disease, these two plexuses are absent at the anorectal line. Hirschsprung disease is caused by defective migration of plexus ganglion cell precursors (neural crest cells), which ordinarily migrate to the distal colon during fetal development. Without the plexuses, peristalsis is uncoordinated, motility is slow, and relaxation is impeded, resulting in excessive contraction of intestinal muscles, constipation, and obstruction, as seen here. A biopsy of the distal colon showing absent ganglion cells is diagnostic.

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E - Epithelium and submucosa

Explanation Why

The epithelium is the innermost layer of the GI mucosa, and the submucosa lies just outside of the GI mucosa. The epithelium contains glands that secrete digestive enzymes and also serves to absorb nutrients and water. The submucosa provides parasympathetic innervation to glands and is responsible for secretomotor activity. However, Hirschsprung disease does not involve a joint defect of the epithelium and submucosa.

F - Muscularis mucosae and lamina propria

Explanation Why

The muscularis mucosae and lamina propria are the two outermost layers of the GI mucosa. The muscularis mucosae allows the mucosa to move, which facilitates glandular secretion and absorption and the lamina propria is the attachment site for the GI epithelium. However, Hirschsprung disease involves other layers of the GI tract.

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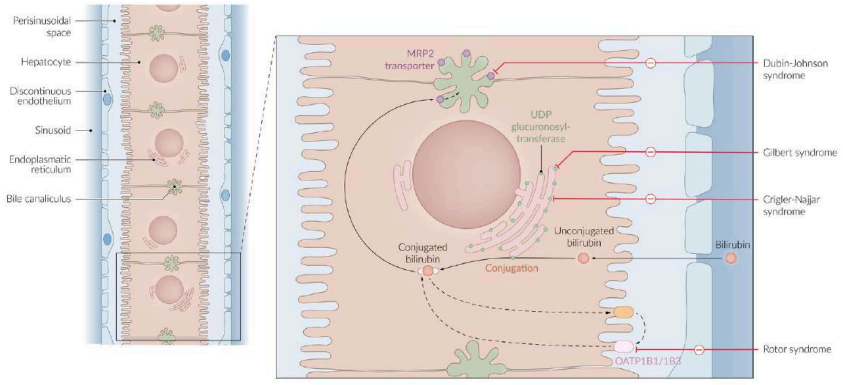
Question # 10

A 46-year-old man comes to the physician for a follow-up examination. Two weeks ago, he underwent laparoscopic herniorrhaphy for an indirect inguinal hernia. During the procedure, a black liver was noted. He has a history of intermittent scleral icterus that resolved without treatment. Serum studies show:

Aspartate aminotransferase	30 IU/L
Alanine aminotransferase	35 IU/L
Alkaline phosphatase	47 mg/dL
Total bilirubin	1.7 mg/dL
Direct bilirubin	1.1 mg/dL

Which of the following is the most likely diagnosis?

	Answer	Image
A	Type II Crigler-Najjar syndrome	
B	Dubin-Johnson syndrome	
C	Rotor syndrome	

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	Answer	Image
D	Gilbert syndrome	
E	Type I Crigler-Najjar syndrome	
F	Wilson disease	

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Hint

This patient has predominantly direct hyperbilirubinemia, which indicates defective excretion of conjugated bilirubin into the bile.

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Correct Answer

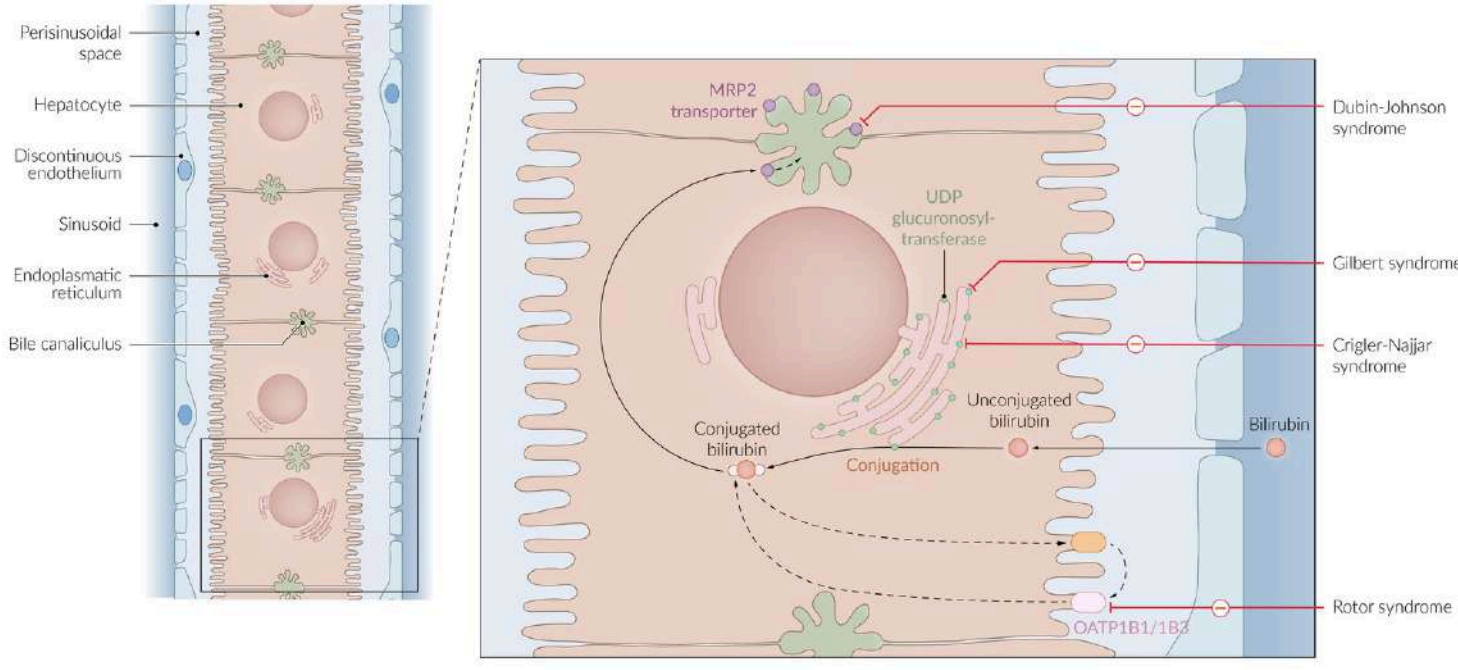
A - Type II Crigler-Najjar syndrome

Explanation Why

Type II Crigler-Najjar syndrome, which is caused by decreased UDP-glucuronosyltransferase synthesis, manifests with indirect hyperbilirubinemia as opposed to the direct hyperbilirubinemia seen in this patient. In addition, Crigler-Najjar syndrome would not result in hyperpigmentation of the liver.

B - Dubin-Johnson syndrome

Image



Explanation But

In women with Dubin-Johnson syndrome, hyperbilirubinemia can worsen during pregnancy or with

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the use of oral contraceptive pills, because the metabolites of estrogen and progesterone can inhibit the activity of this transport protein.

Explanation Why

Dubin-Johnson syndrome is caused by a hereditary defect in a transport protein of the biliary canaliculi. This defect impairs conjugated bilirubin excretion and causes direct hyperbilirubinemia. This defect also impairs the excretion of metabolites of epinephrine, which subsequently give the liver a black appearance. Dubin-Johnson syndrome is a benign condition that does not require treatment, as mild to moderate jaundice is typically the only clinical sign.

C - Rotor syndrome

Explanation Why

Rotor syndrome is caused by impaired bilirubin excretion and manifests with direct hyperbilirubinemia, which is also seen in this patient. However, Rotor syndrome does not cause hyperpigmentation of the liver.

D - Gilbert syndrome

Explanation Why

Gilbert syndrome, which is the most common type of inherited hyperbilirubinemia, is caused by impaired bilirubin uptake by hepatocytes and a mild decrease in UDP-glucuronosyltransferase activity. Gilbert syndrome would manifest with hyperbilirubinemia following stress (e.g., surgery), but it would also cause indirect hyperbilirubinemia, not direct hyperbilirubinemia. Moreover, Gilbert syndrome would not result in hyperpigmentation of the liver.

E - Type I Crigler-Najjar syndrome

Explanation Why

Type I Crigler-Najjar syndrome, which is caused by near absent UDP-glucuronosyltransferase

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activity, manifests with pure indirect hyperbilirubinemia as opposed to the direct hyperbilirubinemia seen in this patient. This condition usually manifests in newborns with persistent neonatal jaundice and neurological symptoms caused by kernicterus. In addition, Crigler-Najjar syndrome would not result in hyperpigmentation of the liver.

F - Wilson disease

Explanation Why

Wilson disease, which causes hepatic copper accumulation, can result in hyperbilirubinemia. However, the accumulation of copper occurs in focal deposits that can only be visualized on a liver biopsy with the help of special stains (e.g., rhodanine). Wilson disease would not cause the gross black discoloration of the liver seen in this patient. Furthermore, Wilson disease would manifest with elevated transaminases and mixed or indirect hyperbilirubinemia, whereas this patient has normal transaminases and purely direct hyperbilirubinemia.

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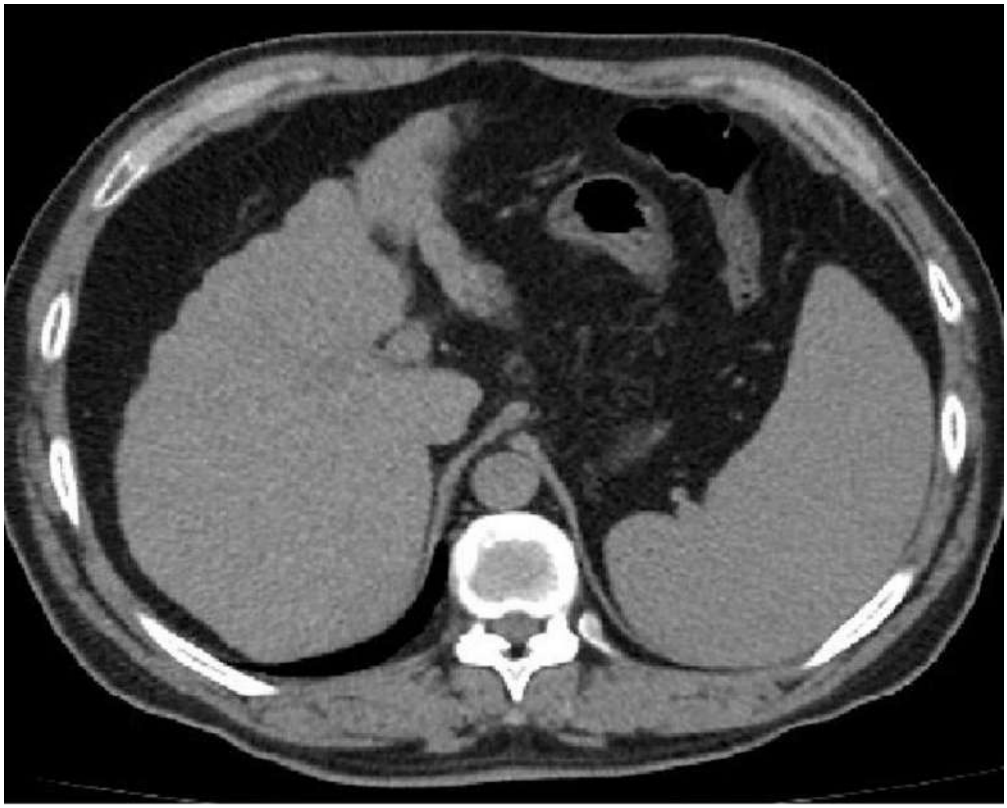
Question # 11

A 65-year-old man is brought to the emergency department because of a 1-day history of fever and disorientation. His wife reports that he had abdominal pain and diarrhea the previous day. He drinks 60 oz of alcohol weekly. His pulse is 110/min and blood pressure is 96/58 mm Hg. Examination shows jaundice, palmar erythema, spider nevi on his chest, dilated veins on the anterior abdominal wall, and 2+ edema of the lower extremities. The abdomen is soft and diffusely tender; there is shifting dullness to percussion. His albumin is 1.4 g/dL, bilirubin is 5 mg/dL, and prothrombin time is 31 seconds (INR = 3.3). Hepatitis serology is negative. A CT scan of the abdomen is shown. Which of the following processes is the most likely explanation for these findings?



	Answer	Image
A	Accumulation of iron in hepatocytes	
B	Hepatocyte swelling and necrosis with neutrophilic infiltration	

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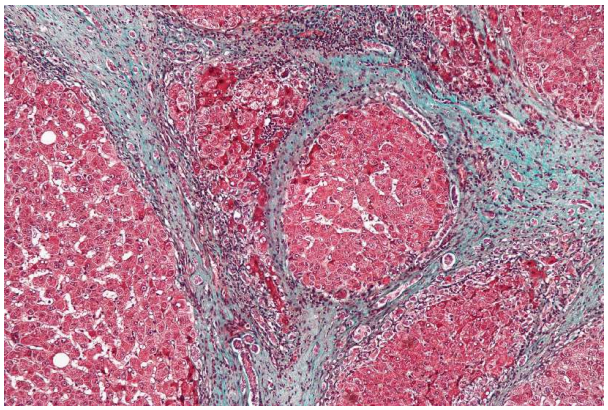
	Answer	Image
C	Ground-glass hepatocytes with cytotoxic T cells	
D	Fibrous bands surrounding regenerating hepatocytes	
E	Macrovesicular lipid accumulation in hepatocytes	
F	Hepatocyte swelling with Councilman bodies and monocyte infiltration	
G	Misfolded protein aggregates in hepatocellular endoplasmic reticulum	

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Hint

This patient presents with features of spontaneous bacterial peritonitis (e.g., fever, diffuse abdominal tenderness, diarrhea), likely due to advanced alcoholic cirrhosis. Cirrhosis is confirmed by the CT scan, which shows an atrophic nodular liver, an enlarged spleen, and ascites.

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Correct Answer

A - Accumulation of iron in hepatocytes

Explanation Why

Iron accumulation in hepatocytes is seen in patients with hemochromatosis, which can cause liver cirrhosis, as seen here. However, features of hemochromatosis also include diabetes mellitus, arthralgia, and bronze skin pigmentation, which have not been reported in this patient. Additionally, hemochromatosis is inherited or secondary to repeated blood transfusions in patients with hemolytic anemia. It is not a result of long-term alcohol abuse.

B - Hepatocyte swelling and necrosis with neutrophilic infiltration

Explanation Why

Hepatocyte swelling and necrosis with neutrophilic infiltration is seen in alcoholic hepatitis. Chronic alcoholic hepatitis would eventually lead to cirrhosis but in the stage of alcoholic hepatitis, the liver would be smoothly enlarged, not shrunken or nodular, as seen here. A different pathological process is responsible for this finding.

C - Ground-glass hepatocytes with cytotoxic T cells

Explanation Why

Ground-glass hepatocytes with cytotoxic T cells are seen in chronic liver disease secondary to hepatitis B infection. Although this patient has features of chronic liver disease, his hepatitis serology is negative, which makes HBV infection unlikely.

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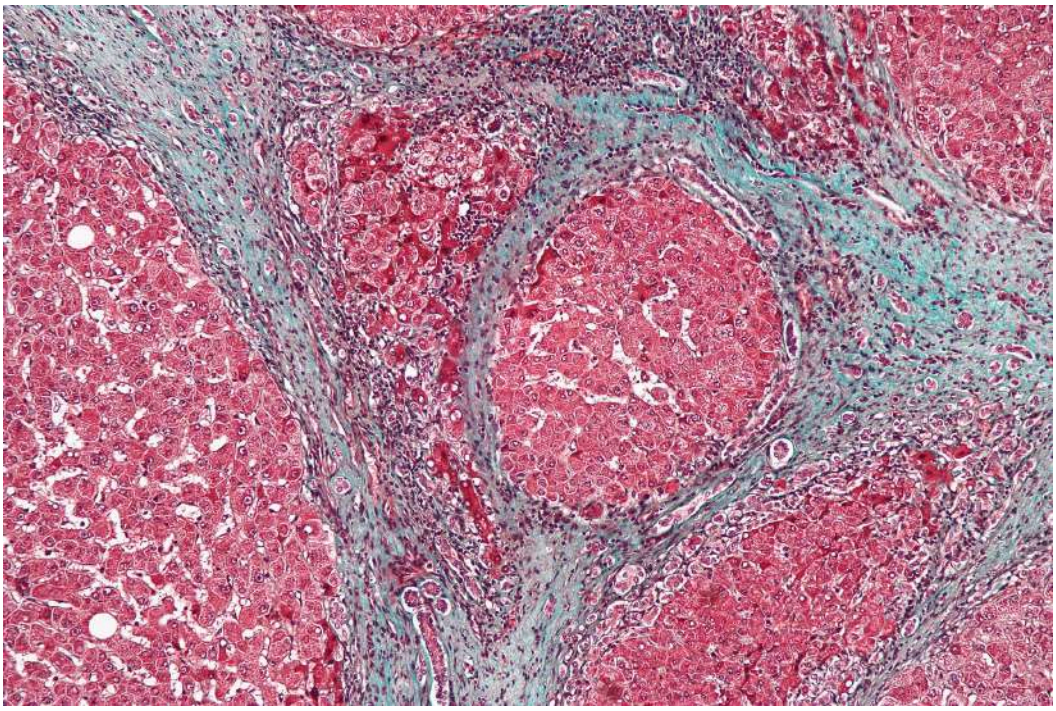
D - Fibrous bands surrounding regenerating hepatocytes

Image



Explanation Why

Hepatocyte destruction and hepatic stellate cell activation via inflammatory cytokines lead to excess collagen fiber production in the periportal and pericentral zones. The continuous formation of fibrous bands surrounding regenerating hepatocytes (i.e., fibrosis and nodular regeneration) destroy the normal architecture of the liver and result in the loss of normal liver metabolic function. Connective tissue formation in the periportal zones and other fibrotic changes lead to an increased intrahepatic vascular tone and subsequently, to portal hypertension, manifesting with splenomegaly, caput medusae, and/or esophageal varices.

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E - Macrovesicular lipid accumulation in hepatocytes

Explanation Why

Macrovesicular lipid accumulation in hepatocytes is a hallmark of hepatic steatosis (fatty liver disease), which can be caused by long-term alcohol abuse. Chronic hepatic steatosis would eventually lead to cirrhosis, as seen here, but in the stage of hepatic steatosis, the liver would be smoothly enlarged. The finding of a shrunken, nodular liver on CT is better explained by a different pathological process.

F - Hepatocyte swelling with Councilman bodies and monocyte infiltration

Explanation Why

The constellation of hepatocyte swelling with Councilman bodies and monocyte infiltration is characteristic of acute viral hepatitis, which would present with fever, jaundice, diarrhea, abdominal pain, and, rarely, features of acute hepatic failure (e.g., confusion, ascites, hypoalbuminemia, increased INR). Diarrhea is also a common prodromal symptom in patients with acute viral hepatitis due to HAV infection. However, the liver would be enlarged, not shrunken, and stigmata of chronic liver disease (e.g., spider nevi, palmar erythema, splenomegaly) would not be expected in acute viral hepatitis. Moreover, serological tests would usually be positive in viral hepatitis.

G - Misfolded protein aggregates in hepatocellular endoplasmic reticulum

Explanation Why

Misfolded protein aggregates in hepatocellular endoplasmic reticulum are characteristic of α1-antitrypsin deficiency. Affected patients can present with cirrhosis, as seen here. However, patients with α1-antitrypsin deficiency also develop panacinar emphysema, manifesting with dyspnea and cough, both of which have not been reported in this patient. Also, α1-antitrypsin deficiency is inherited and would not be caused by long-term alcohol abuse.

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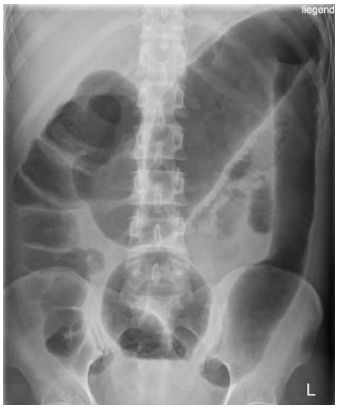
Question # 12

A 32-year-old woman comes to the emergency department because a 5-week history of abdominal pain and bloody diarrhea that has worsened in the past 24 hours. She was diagnosed with ulcerative colitis 1 year ago but has had difficulty adhering to her drug regimen. Her temperature is 38.2°C (100.8°F), pulse is 120/min, and blood pressure is 92/56 mm Hg. Examination shows a distended, rigid abdomen and hypoactive bowel sounds. Fluid resuscitation is initiated. Which of the following is the most appropriate next step in the diagnosis of this patient's current condition?

	Answer	Image
A	Double-contrast barium enema	
B	Abdominal CT scan with contrast	
C	CT angiography	
D	Abdominal x-ray	
E	Colonoscopy	

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Hint

Toxic megacolon should be suspected in a patient with a history of ulcerative colitis and medication nonadherence who presents with bloody diarrhea, severe abdominal pain and distention, and signs of sepsis (fever, tachycardia, hypotension).

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Correct Answer

A - Double-contrast barium enema

Explanation Why

Double-contrast barium enema is an imaging modality that can be used in the diagnosis of UC because it can identify fine mucosal changes (e.g., microulcerations, pseudopolyps) that may be missed on other imaging modalities. However, the diagnosis of UC has already been established in this patient. More importantly, barium enema is contraindicated in patients with suspected toxic megacolon because it would further increase colonic distension and thus risk colonic perforation.

B - Abdominal CT scan with contrast

Explanation Why

A contrast-enhanced CT scan (CECT) has a limited role in the diagnosis of toxic megacolon. CT scan can be considered if the first-line diagnostic modality is inconclusive, or to better identify possible complications of toxic megacolon, such as perforation and bowel ischemia.

C - CT angiography

Explanation Why

CT angiography is a confirmatory test used to diagnose acute mesenteric ischemia, which can present with an acute onset of bloody diarrhea, abdominal pain and distention, hypoactive bowel sounds, and, in case of bowel necrosis, signs of sepsis. However, AMI usually occurs in patients > 60 years with cardiovascular risk factors. This 32-year-old patient presents with a 5-week history of bloody diarrhea and she lacks risk factors for the development of AMI, such as a atrial fibrillation, valvular heart disease, or a recent history of critical illness.

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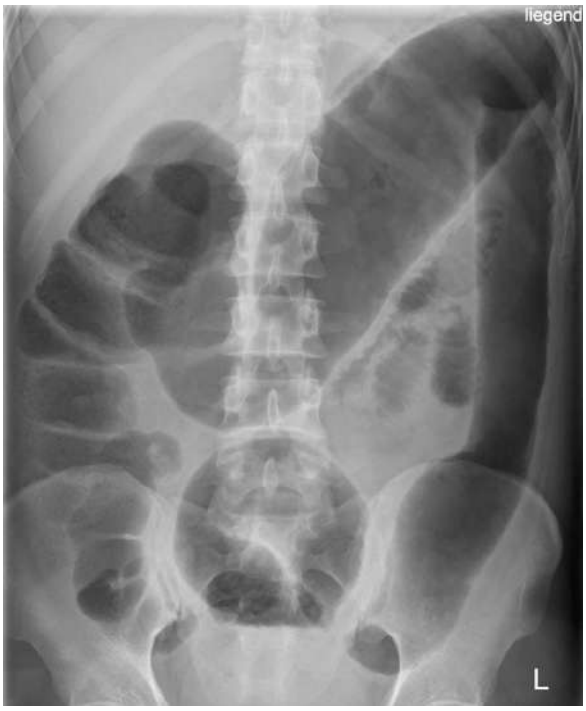
D - Abdominal x-ray

Image



Explanation But

Toxic megacolon is a cause of nonmechanical/functional colonic obstruction and dilation. Mechanical colonic obstruction (e.g., due to carcinoma colon, colonic volvulus) can also present with abdominal distention, radiological features of colonic obstruction, and, in case of bowel necrosis or perforation, features of sepsis. However, the preceding history of diarrhea (acute/chronic/bloody) is usually absent in mechanical colonic obstruction.

Explanation Why

Abdominal x-ray is the preferred diagnostic modality for toxic megacolon and should be ordered in all patients who present with bloody diarrhea, abdominal distention, and signs of sepsis. Dilation of the transverse colon > 6 cm on plain abdominal x-ray confirms the diagnosis. Loss of colonic haustration and multiple air-fluid levels indicate colonic dilation and paralytic ileus. Patients with inflammatory bowel disease, such as this patient, are at risk of developing toxic megacolon, especially early in the course of disease (~ 5% lifetime risk).

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E - Colonoscopy

Explanation But

Patients with UC are at increased risk of developing colorectal cancer. Screening colonoscopies with biopsies every 1–2 years are recommended 8–10 years after the initial diagnosis. Although colon cancer can also present with abdominal pain and distention, the features of sepsis in this 32-year-old patient are more consistent with toxic megacolon.

Explanation Why

Colonoscopy is useful for the diagnosis of inflammatory bowel diseases such as UC. However, patients with toxic megacolon have a grossly dilated colon that is often friable due to the transmural inflammation and bowel wall ischemia. This increases the risk of colonic perforation during colonoscopy, making it contraindicated in patients with suspected toxic megacolon.

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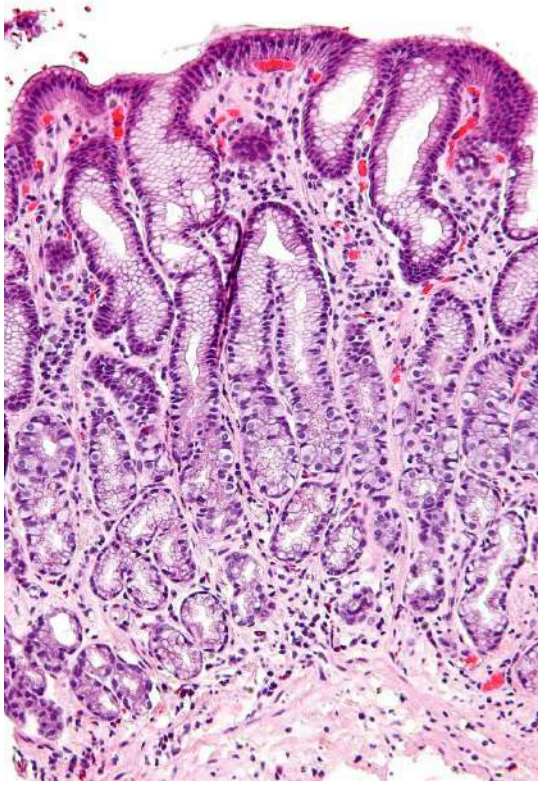
Question # 13

A 45-year-old woman with hypothyroidism comes to the physician because of progressive fatigue, lethargy, and epigastric pain after eating. Physical examination shows pale conjunctivae. Laboratory studies show decreased serum hemoglobin levels and increased serum gastrin levels. Esophagogastroduodenoscopy shows inflammation of the gastric body and fundus. A photomicrograph of a biopsy specimen taken from the gastric antrum is shown. Which of the following is the most likely cause of this patient's symptoms?



	Answer	Image
A	S cell hyperplasia	
B	Mucosal cell hyperplasia	
C	Enterochromaffin-like cell hyperplasia	

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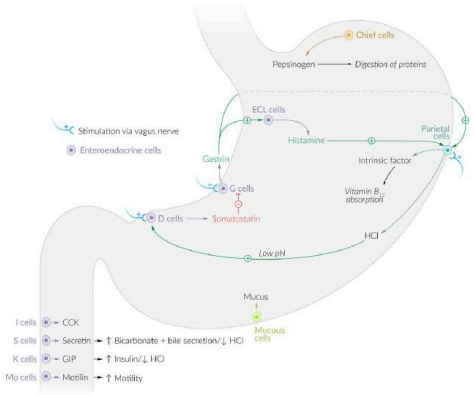
	Answer	Image
D	Parietal cell destruction	
E	Chief cell destruction	
F	I cell destruction	

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Hint

This patient's biopsy sample shows antral G cell hyperplasia, which is consistent with a diagnosis of atrophic gastritis.

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Correct Answer

A - S cell hyperplasia

Explanation Why

S cell hyperplasia would lead to an increased secretion of secretin, which normally increases pancreatic bicarbonate secretion and decreases gastric acid secretion by physiologically inhibiting gastrin secretion from G cells. Increased secretin would not cause anemia, inflammation of the gastric body and fundus, elevated gastrin production, or G-cell hyperplasia.

B - Mucosal cell hyperplasia

Explanation Why

Mucosal cell hyperplasia would lead to an increased secretion of bicarbonate, which increases gastric pH. While hypochlorhydria can result in microcytic anemia (due to decreased absorption of iron), mucosal cell hyperplasia would not explain the inflammation of the gastric body and fundus, an elevated gastrin production, or G-cell hyperplasia seen in this patient.

C - Enterochromaffin-like cell hyperplasia

Explanation Why

Enterochromaffin-like cell (ECL) hyperplasia would increase the secretion of histamine and subsequently gastric acid production, which can lead to inflammation of the gastric body and fundus. Gastrin stimulates histamine release from ECL cells but would not occur as a consequence of ECL hyperplasia. The combination of anemia, hypergastrinemia, and G-cell hyperplasia are more likely due to an alternate etiology.

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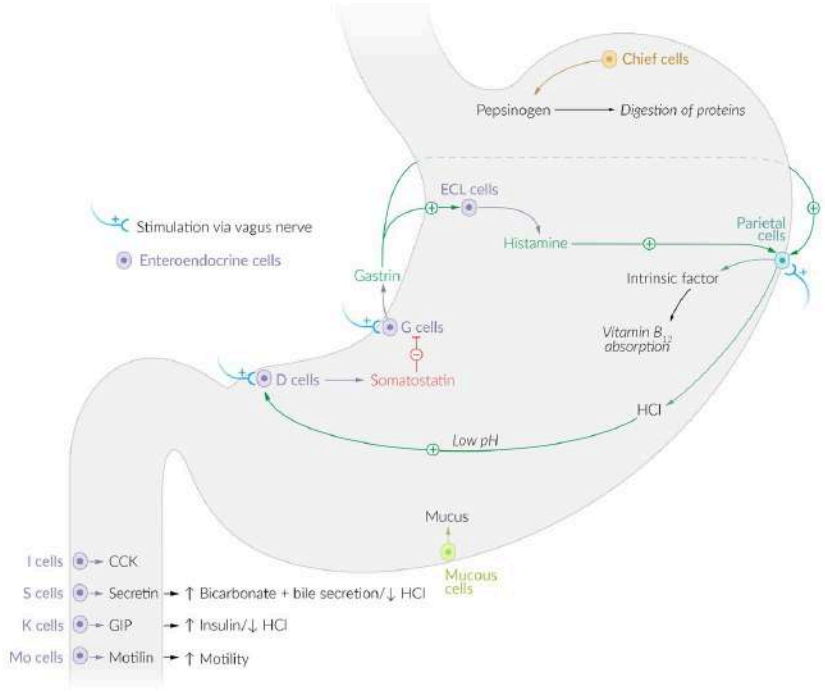
D - Parietal cell destruction

Image



Explanation But

Proton pump inhibitors (PPIs) can also cause G cell hyperplasia by inhibiting gastric acid secretion. However, elevated gastrin levels are usually not found.

Explanation Why

Parietal cell destruction in the gastric fundus is seen in autoimmune-mediated atrophic gastritis (AMAG), which results in reduced gastric acid production. The reduced acid production in AMAG leads to loss of negative feedback on G cells, which subsequently causes G cell hyperplasia in the gastric antrum and hypergastrinemia. Parietal cell destruction also impairs intrinsic factor production and causes decreased vitamin B12 absorption in the ileum, leading to vitamin B_{12} deficiency anemia (pernicious anemia). However, iron deficiency anemia may be present earlier in the disease course, due to the decreased solubility of iron in the setting of hypochlorhydria.

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E - Chief cell destruction

Explanation Why

Chief cell destruction is seen in chronic gastritis with mucosal atrophy and would lead to impaired protein digestion due to decreased production of pepsinogen (which is converted to pepsin). Since pepsin cleaves vitamin B_{12} from food proteins, a pepsin deficiency can impair the absorption of protein-bound vitamin B_{12}, which would manifest with macrocytic anemia. However, chief cell destruction would not affect gastrin production or cause the G-cell hyperplasia seen here.

F - I cell destruction

Explanation Why

I cell destruction would lead to a decreased secretion of cholecystokinin, which normally increases pancreatic secretion, mediates gallbladder contraction, and inhibits gastric emptying. Decreased secretion of cholecystokinin would not explain the anemia, inflammation of the gastric body and fundus, elevated gastrin production, or G-cell hyperplasia seen in this patient.

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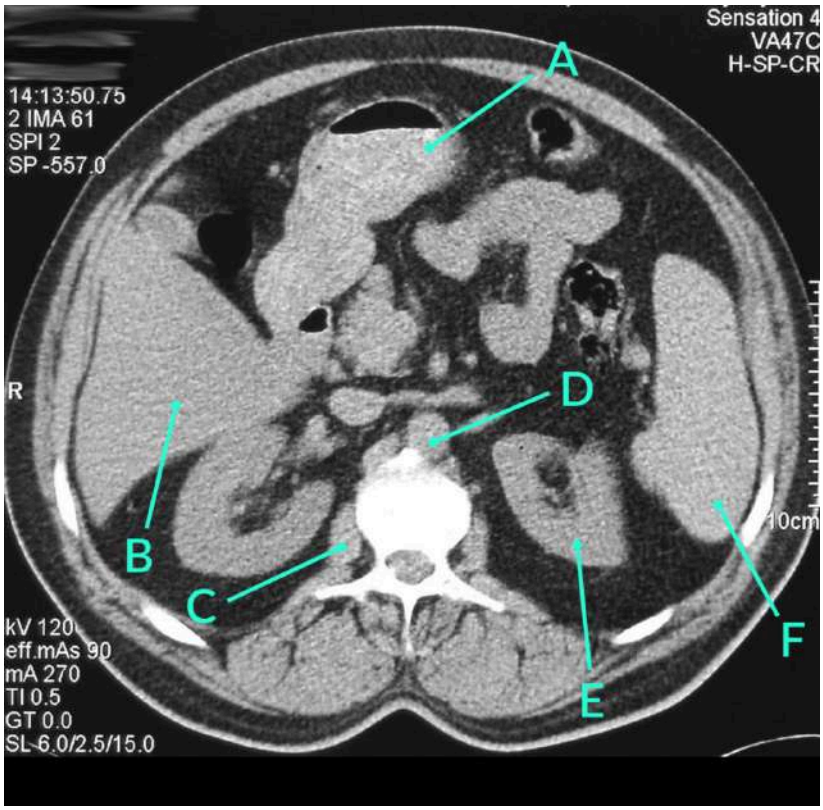
Question # 14

A 25-year-old woman comes to the physician for routine follow-up evaluation. She has a history of poorly-controlled asthma, for which she uses albuterol and fluticasone inhalers. Her mother died at 66 years of complications from emphysema. Laboratory analysis shows decreased levels of a protease inhibitor that inhibits elastin degradation. Which of the labeled abdominal organs is most likely to be involved in the pathogenesis of this patient's condition?



	Answer	Image
A	A	
B	B	
C	C	

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	Answer	Image
D	D	
E	E	
F	F	

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Hint

This woman's family history and decreased levels of α1-antitrypsin (protease inhibitor that inhibits elastin degradation) indicate a diagnosis of α1-antitrypsin deficiency (AATD).

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Correct Answer

A - A

Explanation Why

A, the stomach, is an intraperitoneal, midline, and anterior organ that often appears as a circular, grey tissue density with an inner air-fluid level on a CT scan. It is generally unaffected by AATD.

B - B

Explanation Why

B, the liver, is visible intraperitoneally as an often triangular, homogenous grey, soft tissue density on the patient's right side on an axial CT scan. The liver plays a central role in the pathogenesis of AATD. Mutations in the AAT gene lead to the production of a misfolded protein within hepatocytes. The defective AAT cannot be secreted and aggregates, which causes hepatic damage and possibly cirrhosis and/or primary liver cancer. Histopathology shows the protein aggregations as PAS-positive, spherical inclusion bodies in periportal hepatocytes.

C - C

Explanation Why

C, the psoas major muscle, is situated retroperitoneally along the vertebral bodies T12–L3 and appears as a circular, homogeneously grey, soft tissue density on an axial CT scan. It is generally unaffected by AATD.

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D - D

Explanation Why

D, the aorta, is situated retroperitoneally just left of the midline and anterior to the spine and appears as a circular, homogeneously grey tissue density. It is generally unaffected by AATD.

E - E

Explanation Why

E, the left kidney, appears retroperitoneally as a bean-shaped, gray, soft tissue density with central areas of hypodensity on a CT scan. It is generally unaffected by AATD.

F - F

Explanation Why

F, the spleen, is visible intraperitoneally on a CT scan as an oblong, homogeneously gray, soft tissue density on the patient's left side. It is generally unaffected by AATD.

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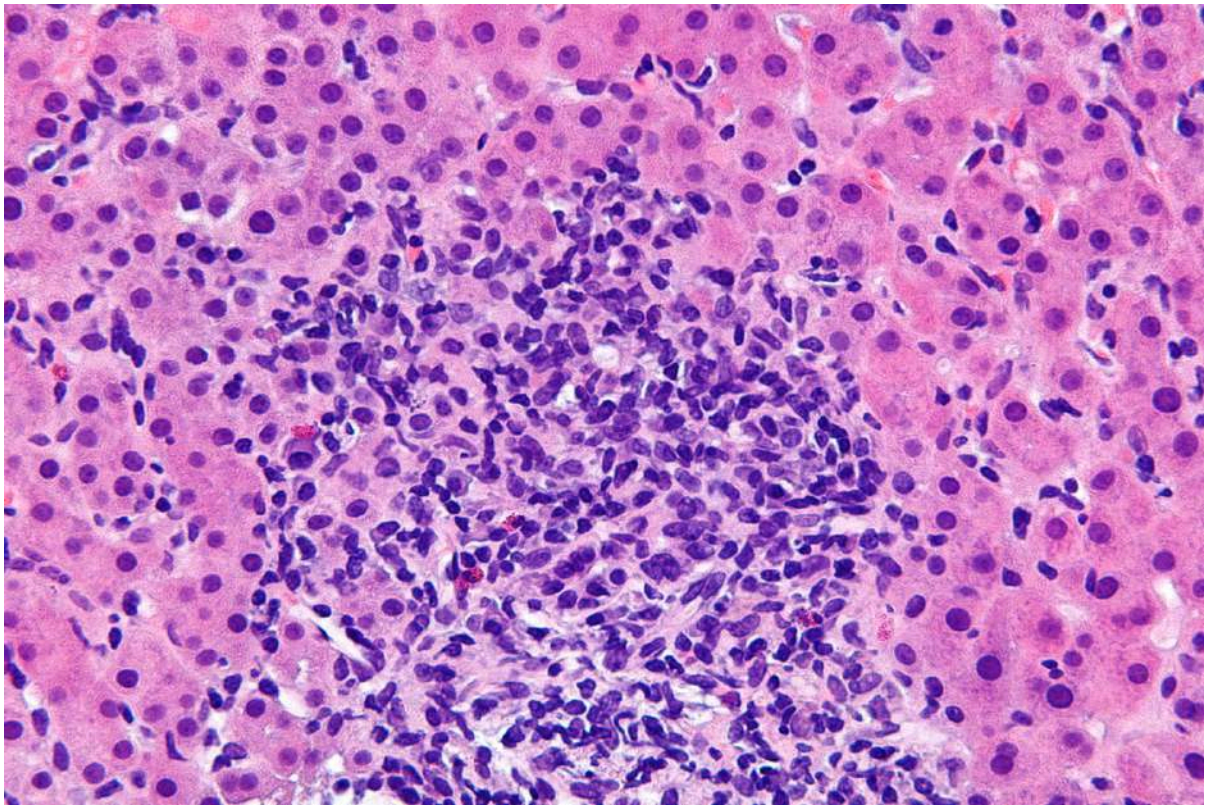
Question # 15

A 57-year-old man comes to the physician for a follow-up examination. Serum studies show:

Aspartate aminotransferase	134 U/L
Alanine aminotransferase	152 U/L
γ-Glutamyltransferase	83 U/L (N = 5–50)
Hepatitis B surface antigen	positive

A photomicrograph of a specimen obtained on liver biopsy is shown. These biopsy findings are most characteristic of which of the following types of inflammatory reactions?



	Answer	Image
A	Acute inflammation	

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	Answer	Image
B	Ischemic necrosis	
C	Malignant transformation	
D	Granulomatous inflammation	
E	Chronic inflammation	

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Hint

The patient's biopsy shows signs of tissue destruction and repair, with piecemeal necrosis and ground glass hepatocytes. Together with the serum studies positive for hepatitis B surface antigen (HBsAg), elevated AST/ALT, and elevated GGT, this suggests viral hepatitis.

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Correct Answer

A - Acute inflammation

Explanation Why

While this patient's serum findings, including the presence of HBsAg and elevated transaminases, could be seen in acute viral hepatitis, this patient's liver biopsy lacks key features such as eosinophilic single-cell necrosis (Councilman body), stellate cells, and diffuse apoptosis. The piecemeal necrosis seen here is not consistent with acute inflammation.

B - Ischemic necrosis

Explanation Why

Ischemic necrosis on liver biopsy is commonly seen in patients presenting with acute hepatitis and would appear as necrotic hepatocytes around the central venules. This patient's biopsy, however, shows piecemeal necrosis, which is not consistent with ischemic necrosis. Furthermore, serum studies are suggestive of viral hepatitis.

C - Malignant transformation

Explanation Why

Malignant transformation (e.g., development of hepatocellular carcinoma) may occur as a consequence of hepatitis B infection, which this patient has. However, expected biopsy findings would include signs of nuclear atypia or dedifferentiation, which are not present here.

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D - Granulomatous inflammation

Explanation Why

Hepatic granulomas would appear as organized collections of activated macrophages (epithelioid histiocytes) on biopsy. This finding is most commonly seen in TB and schistosomiasis infections. This patient's biopsy, however, does not show any granulomas and serum findings are suggestive of viral hepatitis.

E - Chronic inflammation

Explanation Why

The patient's biopsy shows lymphocytic infiltrates, piecemeal necrosis, and ground glass hepatocytes, which are typical of chronic viral hepatitis. Chronic inflammation of any tissue typically shows mononuclear cell infiltration (e.g., lymphocytes, plasma cells, macrophages) and fibrosis may be present simultaneously as well.

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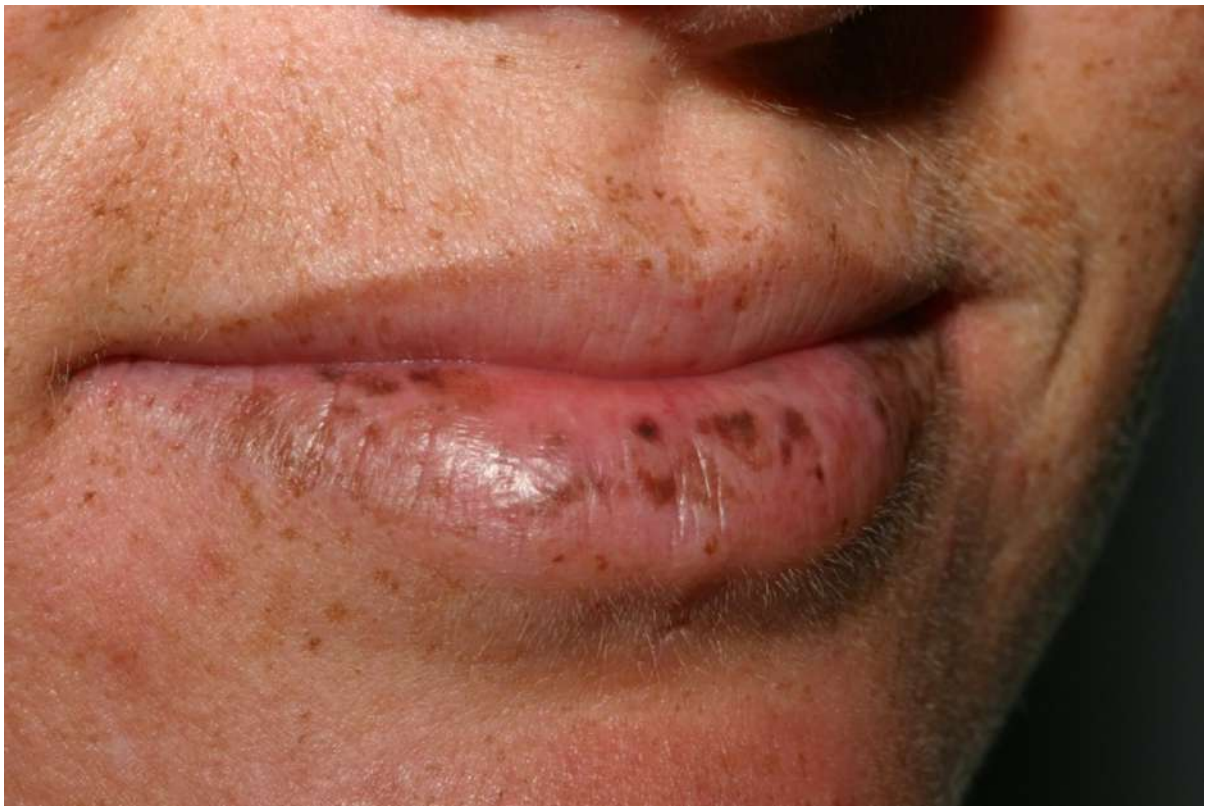
Question # 16

A 39-year-old woman comes to the physician for a follow-up examination after a colonoscopy showed 42 hamartomatous polyps. The physical examination findings are shown in the photograph. Which of the following conditions is most likely to develop in this patient?



	Answer	Image
A	Mandibular osteoma	
B	Pheochromocytoma	
C	Medulloblastoma	
D	Non-Hodgkin lymphoma	

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	Answer	Image
E	Pancreatic carcinoma	
F	Malignant melanoma	
G	Hepatocellular carcinoma	

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Hint

Hamartomatous tumors are disorganized growths of well-differentiated tissue in their native location. In combination with mucocutaneous hyperpigmentation, multiple hamartomatous polyps are consistent with Peutz-Jeghers syndrome (PJS).

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Correct Answer

A - Mandibular osteoma

Explanation Why

Peutz-Jeghers syndrome is not associated with an increased risk of mandibular osteomas. Mandibular osteomas and soft tissue tumors (e.g., desmoid tumors, sebaceous cysts) are associated with Gardner syndrome, a variant of familial adenomatous polyposis (FAP), which would present with colonic polyps. However, the polyps in FAP would be adenomatous rather than hamartomatous, and patients with FAP would typically have thousands of polyps.

B - Pheochromocytoma

Explanation Why

Peutz-Jeghers syndrome is not associated with an increased risk of pheochromocytoma. The risk of pheochromocytoma is increased in neurofibromatosis type 1 (NF1), von Hippel-Lindau disease (VHL), and multiple endocrine neoplasia (MEN) type 2. NF1 can cause hyperpigmented macules (café au lait spots), intestinal neuromas, and hamartomatous nodules in the iris (Lisch nodules), but the café au lait spots would be seen on the trunk in association with cutaneous neurofibromas, and hamartomatous intestinal polyps would not be expected. MEN type 2A can cause intestinal neuromas and VHL can cause intestinal cavernous hemangiomas, but neither MEN type 2A nor VHL would be associated with hamartomatous polyps or perioral hyperpigmented macules.

C - Medulloblastoma

Explanation Why

Peutz-Jeghers syndrome is not associated with an increased risk of medulloblastoma. Brain tumors such as medulloblastoma and gliomas are associated with Turcot syndrome, a variant of familial adenomatous polyposis (FAP), which would manifest with colonic polyps. However, the polyps in FAP would be adenomatous rather than hamartomatous and patients with FAP would typically have thousands of polyps.

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D - Non-Hodgkin lymphoma

Explanation Why

Peutz-Jeghers syndrome is not associated with an increased risk of non-Hodgkin lymphoma. Seborrheic keratosis can appear as a pigmented macule, and multiple seborrheic keratoses (Leser-Trelat sign) can be a harbinger of lymphoid malignancies (e.g., non-Hodgkin lymphoma) or gastrointestinal malignancies. However, seborrheic keratoses typically appear on the head, trunk, and extremities, in contrast to the perioral pigmented macules seen in this patient.

E - Pancreatic carcinoma

Explanation Why

Peutz-Jeghers syndrome (PJS) is a rare autosomal dominant condition caused by a hyperactive serine-threonine kinase due to a gain of function mutation on the *STK11* gene on chromosome 19. Patients with PJS develop melanotic macules on the lips, buccal mucosa, genitalia, palms, and soles as well as gastrointestinal hamartomatous polyps characterized by normal colonic epithelium and branching muscularis mucosae. Possible complications of the hamartomatous polyps include bleeding and intussusception. Individuals with PJS are also at increased risk of malignancies such as colorectal, pancreatic, ovarian, and breast cancer.

F - Malignant melanoma

Explanation Why

The melanotic macules associated with Peutz-Jeghers syndrome have not been known to develop into a melanoma or any other cutaneous malignancy. Lynch syndrome is associated with sebaceous cutaneous neoplasms and colorectal cancer, but Lynch syndrome does not manifest with intestinal polyposis.

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G - Hepatocellular carcinoma

Explanation Why

Peutz-Jeghers syndrome is associated with an increased risk of gallbladder carcinoma but not hepatocellular carcinoma. The risk of hepatocellular carcinoma is increased in conditions such as Wilson disease and hemochromatosis, both of which can cause hyperpigmentation. However, hyperpigmentation in Wilson disease predominantly affects the skin, and patients with hemochromatosis would have diffuse cutaneous hyperpigmentation, in contrast to the pigmented perioral macules seen here. Moreover, neither Wilson disease nor hemochromatosis is associated with intestinal polyposis.

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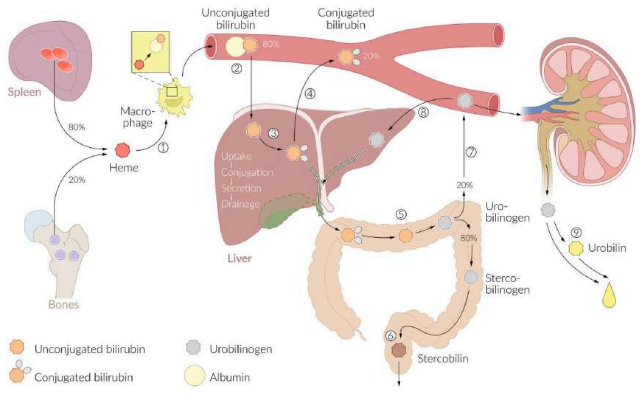
Question # 17

A 49-year-old man comes to the physician because of a 1-week history of yellowish discoloration of his skin and generalized pruritus. Examination shows jaundice of the skin and scleral icterus. Urinalysis shows an elevated concentration of bilirubin and a low concentration of urobilinogen. Which of the following is the most likely underlying cause of these findings?

	Answer	Image
A	Absent UDP-glucuronosyltransferase activity	
B	Increased hemoglobin breakdown	
C	Malignant growth in the pancreatic body	
D	Increased intestinal bilirubin reabsorption	
E	Defective hepatic bile excretion	
F	Presence of stones within the gallbladder	

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Hint

This patient's bilirubinuria suggests an underlying conjugated hyperbilirubinemia, as unconjugated bilirubin is tightly bound to albumin and cannot be filtered and excreted in the urine.

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Correct Answer

A - Absent UDP-glucuronosyltransferase activity

Explanation Why

Decreased UDP-glucuronosyltransferase activity leads to unconjugated hyperbilirubinemia, which is seen in Gilbert syndrome and Crigler-Najjar syndrome. While affected patients may present with jaundice and pruritus, bilirubin would not be detected in the urine. Moreover, the relatively acute course of this patient's symptoms makes this unlikely.

B - Increased hemoglobin breakdown

Explanation Why

Hemolysis can also cause jaundice and pruritus, which are seen here. In hemolysis, destruction of RBCs leads to excess unconjugated bilirubin in the serum and other laboratory signs of hemolysis, as well as increased excretion of conjugated bilirubin by the intestines. Urinalysis would be expected to show increased urobilinogen (due to increased conversion from conjugated bilirubin to urobilinogen in the gut, intestinal reabsorption, and renal excretion) and normal bilirubin, unlike with this patient.

C - Malignant growth in the pancreatic body

Explanation Why

Pancreatic head tumors commonly present with jaundice, given their proximity to the biliary tree and subsequent potential for biliary duct obstruction. However, pancreatic body tumors are uncommon and much less likely to affect the liver or cause bile duct obstruction. This pathology is therefore an unlikely cause of this patient's features.

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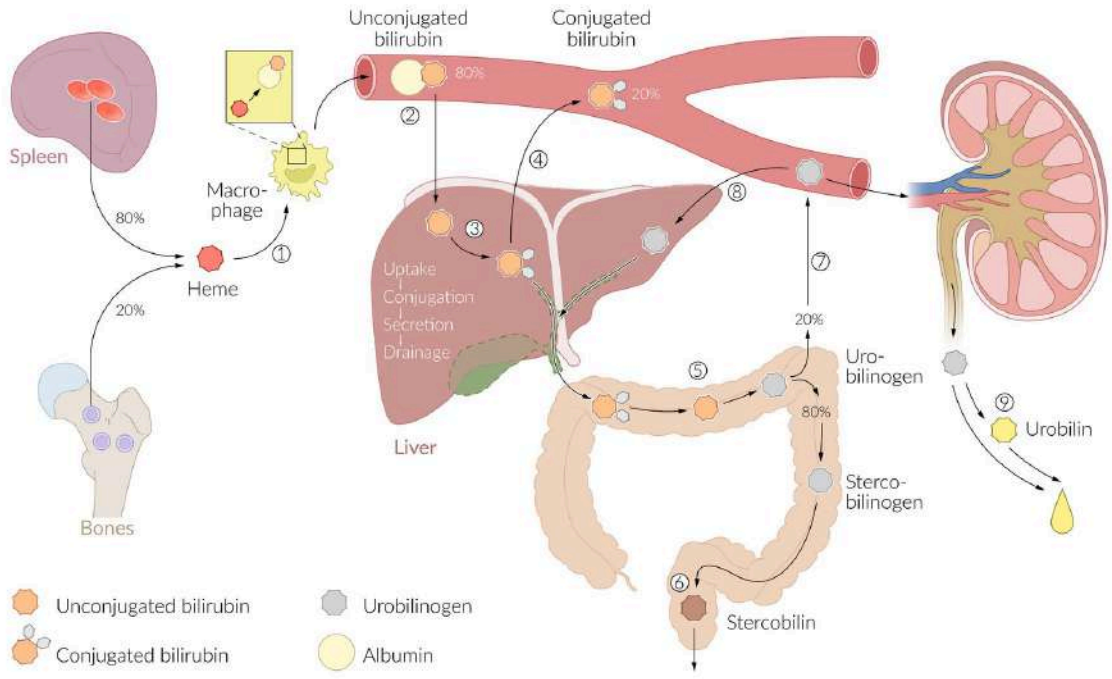
D - Increased intestinal bilirubin reabsorption

Explanation Why

Increased intestinal bilirubin reabsorption would result in increased levels of conjugated bilirubin (conjugated hyperbilirubinemia). While this excess of bilirubin can lead to acute jaundice and pruritus, urinalysis would show both increased bilirubin and urobilinogen excretion. This patient's urinalysis shows a low concentration of urobilinogen, which implies his conjugated hyperbilirubinemia is due to a different cause.

E - Defective hepatic bile excretion

Image



Explanation Why

Normally, unconjugated bilirubin is absorbed by the liver and conjugated with glucuronic acid. It is then secreted via the bile and converted to urobilinogen by intestinal bacteria. In cases of defective

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hepatic bile excretion (i.e., due to a bile duct stenosis or choledocholithiasis), conjugation continues to take place (i.e., unconjugated bilirubin concentration remains normal) but conjugated bilirubin cannot be secreted. Conjugated bilirubin accumulates in the blood (conjugated hyperbilirubinemia) and is excreted by the kidneys (increased bilirubin in urinalysis).

F - Presence of stones within the gallbladder

Explanation Why

Gallstones located in the gallbladder do not lead to hyperbilirubinemia. Only a patient with a gallstone obstructing biliary outflow would be symptomatic, in which case jaundice, pruritus, and conjugated hyperbilirubinemia would be expected.

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Question # 18

A 28-year-old woman with a history of intravenous drug use is brought to the emergency department because of a 1-day history of fatigue, yellow eyes, confusion, and blood in her stools. She appears ill. Her temperature is 38.1°C (100.6°F). Physical examination shows pain in the right upper quadrant, diffuse jaundice with scleral icterus, and bright red blood in the rectal vault. Further evaluation demonstrates virions in her blood, some of which have a partially double-stranded DNA genome while others have a single-stranded RNA genome. They are found to share an identical lipoprotein envelope. This patient is most likely infected with which of the following pathogens?

	Answer	Image
A	Picornavirus	
B	Calicivirus	
C	Flavivirus	
D	Filovirus	
E	Hepevirus	
F	Herpesvirus	
G	Deltavirus	

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Hint

This patient presents with features of acute viral hepatitis (e.g., fever, jaundice, right upper quadrant tenderness) and hepatic failure (e.g., confusion due to encephalopathy, rectal bleeding due to coagulopathy). Her history of intravenous drug use puts her at risk of infection with hepatitis B virus (HBV), which is an enveloped partially double-stranded DNA virus. The presence of virions with a single-stranded RNA genome and an envelope with identical lipoproteins as the HBV virus indicates that the patient is concurrently infected with the hepatitis D virus.

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Correct Answer

A - Picornavirus

Explanation Why

Picornaviruses are single-stranded RNA viruses and include the hepatitis A virus (HAV), which would cause acute hepatitis. However, picornaviruses do not have an envelope, and liver failure occurs in <1% of HAV infection. Moreover, HAV is transmitted via the fecal-oral route (contaminated food or water), not via injection drug use.

B - Calicivirus

Explanation Why

Caliciviruses are single-stranded RNA viruses. Norovirus, which is the most clinically relevant calicivirus, causes gastroenteritis. It does not cause hepatitis. Additionally, noroviruses are non-enveloped viruses, unlike the enveloped RNA virus in this patient, and norovirus is transmitted via the fecal-oral route (contaminated food or water), not via injection drug use.

C - Flavivirus

Explanation Why

Flaviviridae are enveloped single-stranded RNA viruses. Hepatitis C virus (HCV), which is a flavivirus, can cause acute hepatitis. Also, coinfection of HBV (a double-stranded DNA virus) with HCV can occur because both HCV and HBV are be transmitted by the use of contaminated needles, and the risk of fulminant hepatic failure due to acute HCV hepatitis is increased if the patient has an underlying HBV infection. However, flaviviruses and HBV do not share an identical envelope.

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D - Filovirus

Explanation Why

Filoviruses (e.g., Ebola virus, Marburg virus) are enveloped single-stranded RNA viruses can cause fever, hepatitis, and rectal bleeding (viral hemorrhagic fever) and can be transmitted via needle sticks contaminated with body fluids. However, filoviruses do not have a lipoprotein envelope that is identical to any DNA virus. Moreover, filovirus infections occur in sub-Saharan Africa. Filoviruses are not endemic to the continental US. The few cases that have been reported in the US were attributed to travel to an endemic region.

E - Hepevirus

Explanation Why

Hepeviruses are single-stranded RNA viruses. Hepatitis E virus (HEV), which is the most clinically relevant hepevirus, would cause acute viral hepatitis. However, HEV does not have a lipoprotein envelope. Moreover, HEV is transmitted via the fecal-oral route (contaminated food or water), not via injection drug use, and hepatic failure does not typically occur with HEV hepatitis unless the patient is pregnant.

F - Herpesvirus

Explanation Why

Herpesviruses are enveloped double-stranded DNA viruses. Certain herpesviruses such as CMV, EBV, and HSV would cause fever and, rarely, hepatitis, especially when associated with coinfection by HIV, which is an enveloped single-stranded RNA virus. However, HIV and herpesviruses do not share an identical lipoprotein envelope. Moreover, patients who have been infected acutely by any of the aforementioned herpesviruses would also have other characteristic clinical features (e.g., pharyngitis and lymphadenopathy in the case of EBV infection, vesicular rash in the case of HSV infection).

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G - Deltavirus

Explanation Why

Hepatitis B virus (HBV) and hepatitis D virus (HDV) are transmitted sexually, parenterally (e.g., contaminated shared needles), or perinatally. Acute HBV infection is usually mild or asymptomatic and resolves within a few weeks or months. However, 5% of adult patients will develop chronic HBV infection. HDV, on the other hand, is a defective virus that is dependent on the HBsAg coat of HBV for entry into hepatocytes. Therefore, HDV can only cause infection if simultaneous infection with HBV occurs or if the patient already has a chronic HBV infection. Simultaneous infection of HBV with HDV usually has a protracted course but superinfection by HDV in a patient with pre-existing HBV infection often has a rapid course characterized by fulminant hepatic failure, as seen here.

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Question # 19

A 23-year-old man comes to the physician because of a 2-day history of profuse watery diarrhea and abdominal cramps. Four days ago, he returned from a backpacking trip across Southeast Asia. Physical examination shows dry mucous membranes and decreased skin turgor. Stool culture shows gram-negative, oxidase-positive, curved rods that have a single polar flagellum. The pathogen responsible for this patient's condition most likely has which of the following characteristics?

	Answer	Image
A	Requires low infectious dose to establish infection	
B	Acts by activation of guanylate cyclase	
C	Causes necrosis of Peyer patches of distal ileum	
D	Infection commonly precedes Guillain-Barré syndrome	
E	Grows well in medium with pH of 9	
F	Forms spores in unfavorable environment	

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Hint

This patient's stool microscopy findings correspond with the morphological appearance of *Vibrio cholerae*.

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Correct Answer

A - Requires low infectious dose to establish infection

Explanation Why

Shigella is an example of a bacterium that is highly resistant against stomach acid, and thus it requires a very low infectious dose to establish gastroenteritis. However, bloody diarrhea would be expected, whereas this patient reported profuse watery diarrhea. Furthermore, although *Shigella* bacteria would appear as gram-negative rods on stool culture, they are not curved, do not have flagella, and are oxidase-negative.

B - Acts by activation of guanylate cyclase

Explanation Why

Enterotoxigenic *E. coli* (ETEC) causes traveler's diarrhea. It produces heat labile toxin and heat stable toxin, which respectively activate adenylate cyclase and guanylate cyclase, resulting in watery diarrhea. However, although ETEC would appear as a gram-negative rod on stool culture, it is not curved, has no flagella, and is oxidase-negative. *Vibrio cholerae* permanently activates adenylate cyclase, not guanylate cyclase.

C - Causes necrosis of Peyer patches of distal ileum

Explanation Why

Salmonella typhi and *Yersinia enterocolitica* are examples of gram-negative bacteria that are known to migrate into Peyer patches of the distal ileum, which can lead to necrosis and result in bloody diarrhea. Patients with *Salmonella typhi* infection present with fever and constipation followed by diarrhea, while patients with *Yersinia enterocolitica* infection present with gastroenteritis and/or mesenteric lymphadenitis, which may mimic acute appendicitis. These organisms do not match the profuse watery diarrhea reported in this patient. Furthermore, unlike the pathogen isolated from this patient's stool, both *S. typhi* and *Y. enterocolitica* are oxidase-negative organisms with peritrichous flagella.

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D - Infection commonly precedes Guillain-Barré syndrome

Explanation Why

Guillain-Barré syndrome typically follows gastroenteritis due to *Campylobacter jejuni*. Although *C. jejuni* appear as gram-negative and oxidase-positive bacteria with polar flagella under the microscope, they are s-shaped rather than curved, and patients often have bloody rather than profuse watery diarrhea.

E - Grows well in medium with pH of 9

Explanation Why

Vibrio cholerae is a gram-negative, oxidase-positive, curved rod. It produces an enterotoxin, which permanently activates a G_S protein and thereby results in increased intracellular cAMP levels. This leads to secretion of chloride ions and water in the intestines, resulting in the typical rice-water diarrhea. *V. cholerae* is acid-labile, growing well in an alkaline medium (e.g. with a pH of 9). Accordingly, stomach acidity provides a natural barrier against *V. cholera*, so that a high amount of pathogens are required to cause infection (high infectious dose). A decrease in gastric acidity (e.g., due to treatment with proton pump inhibitors) reduces the infectious dose significantly.

F - Forms spores in unfavorable environment

Explanation Why

Clostridioides difficile is an obligate anaerobe that can form spores in unfavorable environments. It can cause pseudomembranous colitis, which commonly manifests with abdominal cramps and watery diarrhea. However, *C. difficile* is a gram-positive rod, as opposed to the gram-negative pathogen isolated. Moreover, *C. difficile* infection typically follows antibiotic treatment.

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Question # 20

A 59-year-old man comes to the physician for the evaluation of generalized fatigue, myalgia, and a pruritic skin rash for the past 5 months. As a child, he was involved in a motor vehicle accident and required several blood transfusions. Physical examination shows right upper abdominal tenderness, scleral icterus, and well-demarcated, purple, polygonal papules on the wrists bilaterally. Laboratory studies show an elevated replication rate of a hepatotropic virus. Further analysis shows high variability in the genetic sequence that encodes the glycosylated envelope proteins produced by this virus. Which of the following is the most likely explanation for the variability in the genetic sequence of these proteins?

	Answer	Image
A	Neutralizing host antibodies induce viral genome mutations	
B	Viral RNA polymerase lacks proofreading ability	
C	Incorporation of envelope proteins from a second virus	
D	Integration of viral genes into host cell genome	
E	Infection with multiple viral genotypes	

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Hint

This patient presents with signs and symptoms of viral hepatitis. His history of blood transfusions before 1992, the year in which screening for the hepatitis C virus (HCV) in donor blood began, suggests chronic infection with hepatitis C. The pruritic skin rash on the wrists is most likely lichen planus, a common extrahepatic manifestation of chronic infection.

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Correct Answer

A - Neutralizing host antibodies induce viral genome mutations

Explanation Why

Because HCV continuously produces antigenically unique virions, host antibodies cannot confer immunity to the virus. Meanwhile, the production of host antibodies does not drive the virus to create antigenically unique virions. These antibodies are unable to exert selection pressure, which would otherwise encourage viral mutations. Instead, the virus innately mutates and produces antigenically unique virions that drive the continued production of unique antibodies by the host.

B - Viral RNA polymerase lacks proofreading ability

Explanation Why

Hepatitis C virus RNA-dependent RNA polymerase has a very poor proofreading mechanism, leading to frequent errors in viral genes. These errors manifest as variations in the structure of viral proteins. Mutations in the viral glycoprotein envelope allow for antigenic variation and evasion of the host antibody response to these envelope proteins. In addition, HCV replicates very quickly, which enhances the effect of poor proofreading and accelerates the production of antigenically distinct envelopes.

C - Incorporation of envelope proteins from a second virus

Explanation Why

Incorporation of envelope proteins from a second virus does not affect the ability of hepatitis C virions to evade the host immune system. Hepatitis D virus, for example, lacks the genes required to synthesize an envelope, so it relies on the envelope of the hepatitis B virus for entry into host hepatocytes. Therefore, hepatitis D viral infection can only occur as a coinfection (both hepatitis D and B simultaneously) or superinfection (hepatitis D after hepatitis B) with hepatitis B.

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D - Integration of viral genes into host cell genome

Explanation Why

Integration of viral genes into the host cell genome is not a feature of the HCV lifecycle or pathophysiology.

E - Infection with multiple viral genotypes

Explanation Why

Infection with multiple viral genotypes is possible in patients with HCV because there are six genotypes of the virus. Patients infected with multiple strains most commonly have a history of intravenous drug use. It is unlikely that this patient contracted more than one genotype of HCV from his previous blood transfusions. Also, infection with more than one viral strain does not explain the variability in the genetic sequence of these viral proteins.

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Question # 21

A 43-year-old man comes to the physician because of a 2-week history of nonbloody diarrhea, abdominal discomfort, and bloating. When the symptoms began, several of his coworkers had similar symptoms but only for about 3 days. Abdominal examination shows diffuse tenderness with no guarding or rebound. Stool sampling reveals a decreased stool pH. Which of the following is the most likely underlying cause of this patient's prolonged symptoms?

	Answer	Image
A	Intestinal type 1 helper T cells	
B	Anti-endomysial antibodies	
C	Heat-labile toxin	
D	Bacterial superinfection	
E	Lactase deficiency	

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Hint

A localized outbreak of nonbloody diarrhea that only lasts a few days is most likely due to viral gastroenteritis. A small intestine biopsy of the patient would show a loss of intestinal brush border.

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Correct Answer

A - Intestinal type 1 helper T cells

Explanation Why

Activation of intestinal type 1 helper T cells is involved in the pathogenesis of Crohn disease, which can manifest with nonbloody diarrhea, abdominal discomfort, bloating, and loss of the intestinal brush border (villous atrophy) on small intestine biopsy. However, affected individuals usually have certain genetic markers (e.g., mutation of the NOD2 gene, HLA-B27 association), and Crohn disease would not occur secondarily to viral gastroenteritis. Furthermore, stool sampling would not reveal a decreased stool pH.

B - Anti-endomysial antibodies

Explanation Why

Anti-endomysial antibodies are seen in celiac disease, which causes nonbloody diarrhea, abdominal discomfort, and bloating. Celiac disease would also manifest with loss of the intestinal brush border (villous atrophy) on small intestine biopsy. However, it usually also presents with symptoms of malabsorption (e.g., vitamin deficiencies, anemia, fatigue, delayed growth, osteoporosis or weight loss) and would not be secondary to viral gastroenteritis. Furthermore, stool sampling would not reveal a decreased stool pH.

C - Heat-labile toxin

Explanation Why

Heat-labile toxin is produced by enterotoxigenic *E. coli* (ETEC), which can cause nonbloody diarrhea, abdominal discomfort, and bloating, and, in some severe cases, loss of the intestinal brush border (villous atrophy) on small intestine biopsy. However, it usually occurs in patients with a history of recent travel (traveler's diarrhea), not secondarily to viral gastroenteritis. Moreover, stool sampling would not reveal a decreased stool pH.

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D - Bacterial superinfection

Explanation Why

Bacterial superinfection, e.g., with *C. difficile*, can cause *Clostridioides difficile* colitis, which would manifest with nonbloody diarrhea, abdominal discomfort, bloating, and potential loss of the intestinal brush border (villous atrophy) on small intestine biopsy. However, it is usually caused by antibiotic use, not viral gastroenteritis. Moreover, stool sampling would not reveal a decreased stool pH.

E - Lactase deficiency

Explanation Why

Lactase deficiency is the most likely cause of this patient's prolonged symptoms of abdominal discomfort, diarrhea, and bloating. Secondary lactase deficiency can be due to underlying disorders of the small intestine that result in mucosal damage, e.g., viral gastroenteritis. Lactase is found distally in the intestinal villi, which are particularly affected by mucosal damage. Lactose intolerance results in the passing of undigested, osmotically active lactose to the large intestine, where it binds water and is degraded by the native flora of the intestine, causing increased gas (flatulence) and short-chain fatty acid formation (diarrhea).

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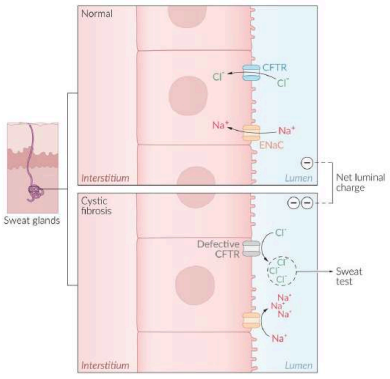
Question # 22

A 2720-g (6-lb) female newborn delivered at 35 weeks' gestation starts vomiting and becomes inconsolable 48 hours after birth. The newborn has not passed her first stool yet. Examination shows abdominal distention and high-pitched bowel sounds. A water-soluble contrast enema study shows microcolon. Serum studies show increased levels of immunoreactive trypsinogen. Which of the following is the most likely additional laboratory finding?

	Answer	Image
A	Decreased hydrogen ion concentration in renal collecting duct	
B	Increased chloride concentration in alveolar fluid	
C	Increased serum calcium concentration	
D	Increased bicarbonate concentration in pancreatic secretions	
E	Increased sodium concentration in sweat	

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Hint

This newborn's inability to pass her first stool (most likely caused by meconium ileus) and increased serum immunoreactive trypsinogen are indicative of cystic fibrosis as the underlying disease.

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Correct Answer

A - Decreased hydrogen ion concentration in renal collecting duct

Explanation Why

Decreased hydrogen ion concentration in the renal collecting duct would not be expected in this patient. As a result of this neonate's vomiting, she is most likely hypovolemic with a contraction alkalosis. In cases of contraction alkalosis, aldosterone acts on the distal tubule to increase secretion of hydrogen and potassium ions in exchange for increased reabsorption of sodium ions. Therefore, she would be expected to have an increased, not decreased hydrogen ion concentration. Cystic fibrosis itself does not affect renal electrolyte concentrations because the CFTR protein is not expressed in the kidneys.

B - Increased chloride concentration in alveolar fluid

Explanation Why

Increased chloride concentration in alveolar fluid is not expected in cases of cystic fibrosis. Chloride concentration in the alveolar fluid is established through the action of CFTR channels, which actively transport chloride ions into the alveoli. A defect of the CFTR protein in cystic fibrosis impairs the transport of chloride ions into the alveoli and leads to a decrease (not an increase) in alveolar chloride concentration. As a result of the diminished chloride transport, water molecules are not secreted and the resulting mucus is hyperviscous, leading to mucus plug formation.

C - Increased serum calcium concentration

Explanation Why

Increased serum calcium concentration is not expected in cystic fibrosis. Instead, patients with (advanced) cystic fibrosis often present with signs and symptoms of malabsorption, including impaired absorption of vitamin D. Because vitamin D is essential for renal and intestinal reabsorption of calcium, vitamin D deficiency results in decreased serum calcium concentrations. In this neonate, serum calcium concentrations are most likely within the reference range.

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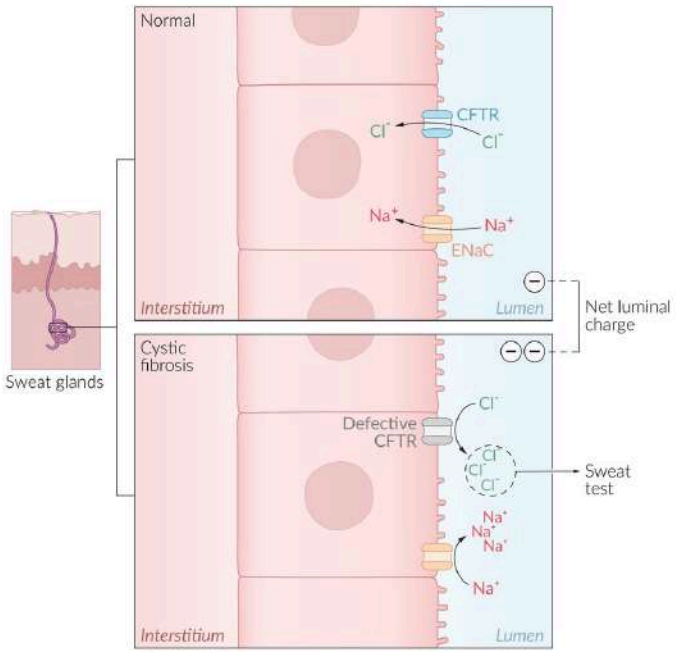
D - Increased bicarbonate concentration in pancreatic secretions

Explanation Why

An increase in bicarbonate concentration in pancreatic secretions occurs as a normal response to food intake; it would not be expected in cystic fibrosis. The defective CFTR protein in cystic fibrosis impairs the secretion of chloride, sodium, and bicarbonate ions from the pancreas, decreasing the water content of pancreatic secretions. In newborns with cystic fibrosis, decreased water content of pancreatic secretions contributes to the development of recalcitrant meconium. As patients with this condition age, the hyperviscous pancreatic secretions lead to sclerosis of the pancreatic ducts and, ultimately, exocrine pancreatic insufficiency.

E - Increased sodium concentration in sweat

Image



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Explanation But

Levels of immunoreactive trypsinogen (IRT) are measured as part of neonatal screening for cystic fibrosis. Elevated levels of IRT in heel-prick blood indicate that it has not been converted to its active form (trypsin), as a result of impaired release of pancreatic enzymes.

Explanation Why

Increased sodium concentration in sweat is a result of impaired chloride ion transport; chloride transport is mediated by the CFTR channel and the gene for this channel is mutated in cystic fibrosis. In the most common CFTR gene mutation, the membrane transporter misfolds, causing it to be retained in the rough endoplasmic reticulum. As a result, chloride is not properly reabsorbed and remains in the lumen of the apocrine sweat gland. Positively charged sodium ions are also pathologically trapped in sweat by the negatively charged chloride ions in order to balance the net electric charge, resulting in hypertonic sweat.

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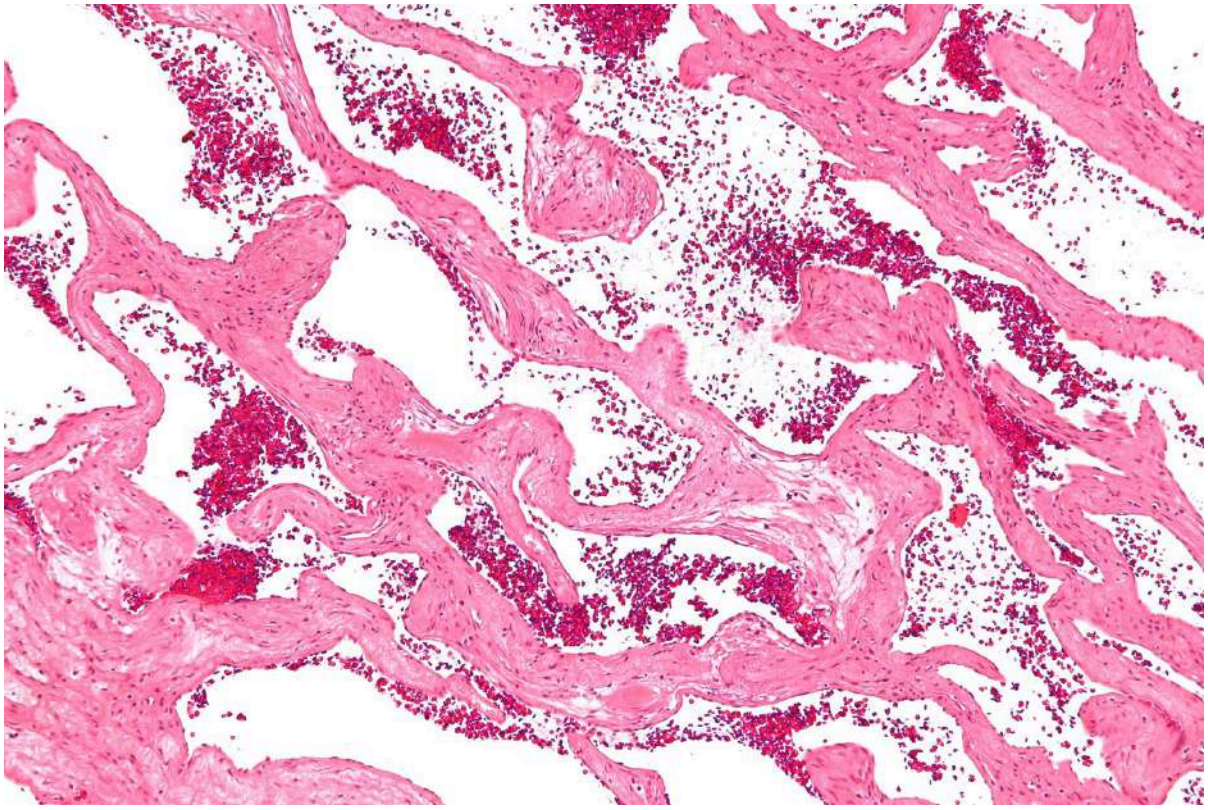
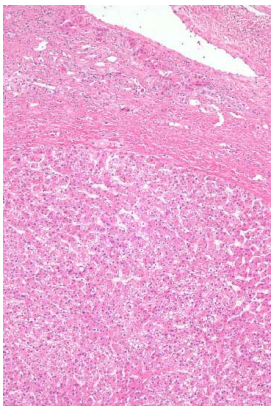
Question # 23

A 49-year-old woman comes to the physician with a 2-month history of mild abdominal pain, nausea, and several episodes of vomiting. She often feels full after eating only a small amount of food. Abdominal examination shows mild right upper quadrant tenderness and a liver span of 16 cm. Ultrasonography shows a 5 x 4 cm hyperechoic mass in the left lobe of the liver. The mass is surgically excised. A photomicrograph of the resected specimen is shown. Which of the following is the most likely diagnosis?



	Answer	Image
A	Hepatocellular adenoma	

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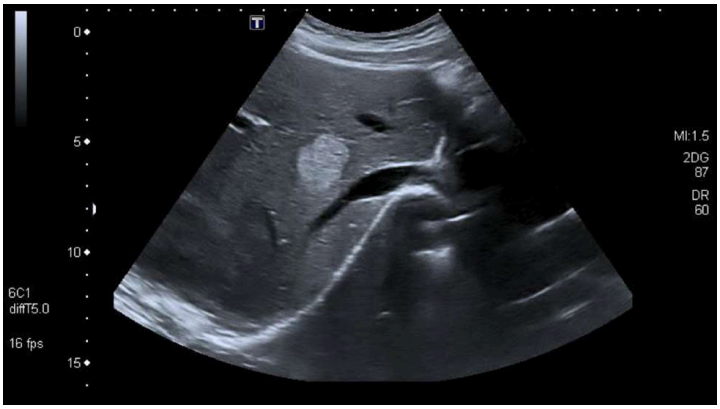
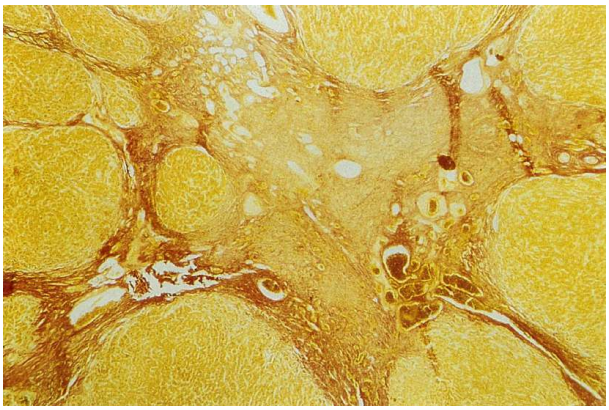
	Answer	Image
B	Alveolar echinococcosis	
C	Polycystic kidney disease	
D	Cavernous hemangioma	
E	Focal nodular hyperplasia	
F	Angiosarcoma	

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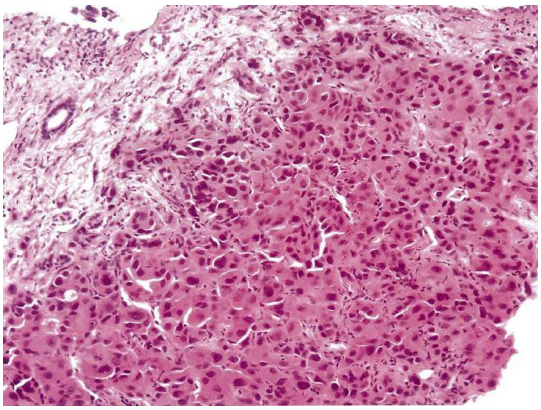
	Answer	Image
G	Hepatocellular carcinoma	

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Hint

The photomicrograph shows numerous cystic spaces lined by a single layer of endothelium. The cysts contain erythrocytes and multiple thromboses. There is no evidence of normal hepatic parenchyma.

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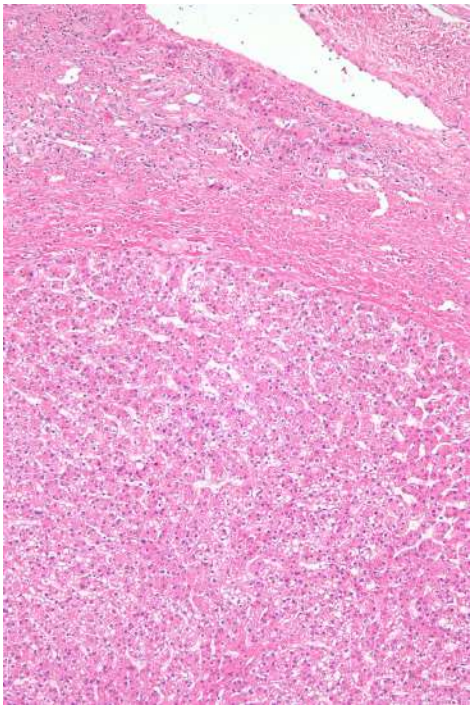
Correct Answer

A - Hepatocellular adenoma

Image



Explanation Why

Hepatocellular adenoma (HA) is a benign tumor of the liver that is typically seen in women aged 20–45 years. HA mainly occurs in individuals on long-term use of oral contraceptives or steroids. HA is usually asymptomatic and is often detected incidentally. On sonography, HA is seen as a well-demarcated, heteroechoic intraparenchymal lesion. Histopathological features of HA include enlarged benign hepatocytes that contain glycogen and lipid deposits, which are not seen in this specimen.

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B - Alveolar echinococcosis

Explanation Why

Alveolar echinococcosis is a rare parasitic infection that mostly affects the liver and causes intraparenchymal lesions. Hepatic lesions can manifest with upper abdominal pain and hepatomegaly, which are seen in this patient. Imaging would show anechoic cysts with or without septae and areas of calcification. On histopathology, the walls of echinococcal cysts are seen as lamellated membranes, surrounded by chronically inflamed hepatic parenchyma, and areas of calcification. Both of these features are absent in this specimen.

C - Polycystic kidney disease

Explanation Why

Most individuals (75–90%) with polycystic kidney disease (PKD) also have multiple hepatic cysts that typically manifest with right upper abdominal pain and hepatomegaly, which are seen in this patient. Unlike the specimen here, however, hepatic cysts in PKD are seen as multiple anechoic unilocular cysts on sonography, and histopathology would show cysts lined with cuboidal biliary epithelium and surrounded by normal hepatic parenchyma.

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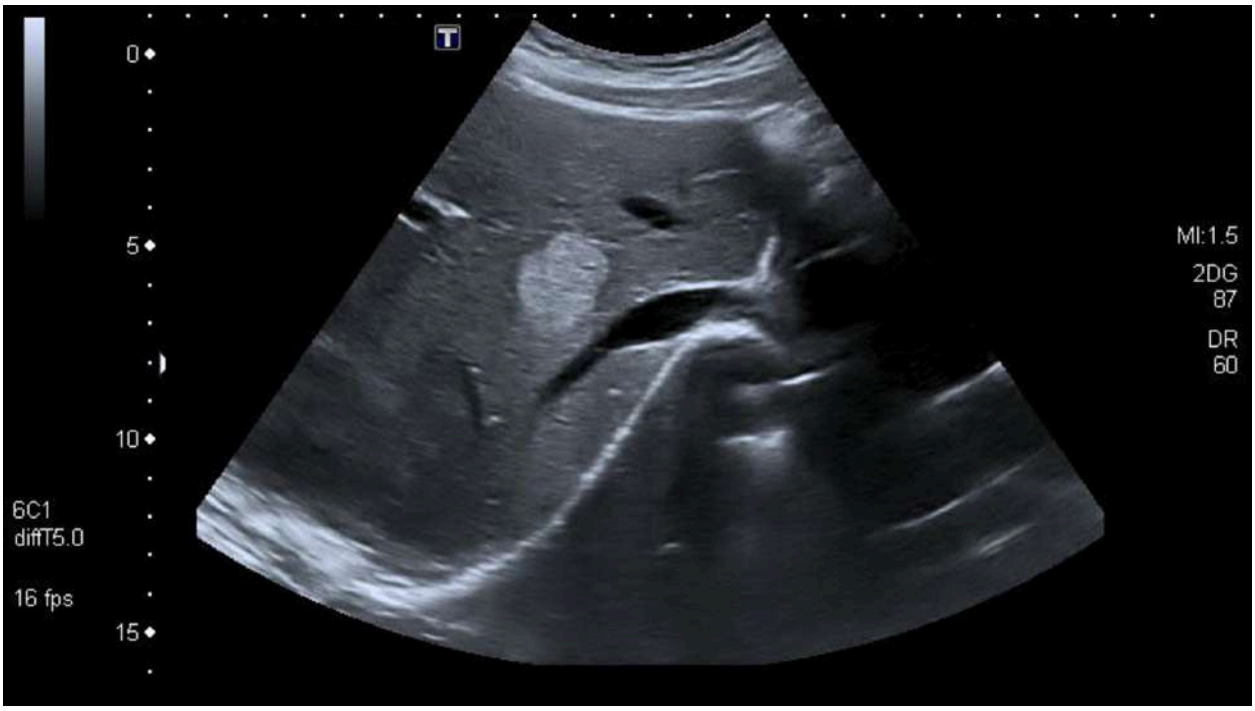
D - Cavernous hemangioma

Image



Explanation Why

This patient's biopsy specimen shows a benign vascular tumor, which confirms the diagnosis of cavernous hepatic hemangioma. Cavernous hemangioma of the liver is the most common benign hepatic tumor and is typically seen in women aged 30–50 years. While most patients with hepatic hemangiomas are asymptomatic, a large hepatic hemangioma can compress the adjacent bowel (causing early satiety) and stretch the Glisson capsule (causing upper abdominal pain). Because hepatic hemangiomas are highly vascular, they typically appear as hyperechoic masses on ultrasonography. Needle aspiration or biopsy should be avoided in the diagnostic workup of hepatic hemangiomas due to the risk of hemorrhage.

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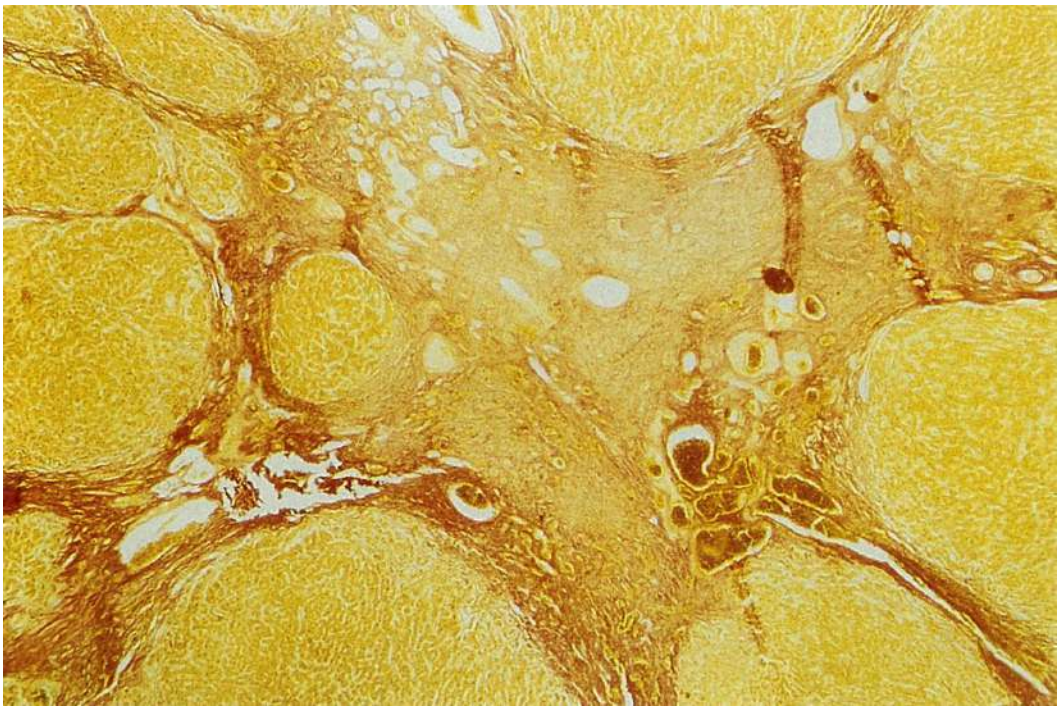
E - Focal nodular hyperplasia

Image



Explanation Why

Focal nodular hyperplasia (FNH) is a benign tumor of the liver that is typically seen in women aged 20–50 years. A large FNH tumor can cause hepatomegaly, abdominal pain, and early satiety, similar to the features seen in this patient. However, on imaging, FNH is seen as an intrahepatic mass of variable echogenicity, often with a central scar. In addition, a biopsy of FNH would show benign hepatocytes arranged in nodules. These nodules would be separated by fibrous septa containing aberrant blood vessels. Bile ductules and Kupffer cells would also be seen.

F - Angiosarcoma

Explanation Why

Hepatic angiosarcoma is a rare tumor of the liver that is typically seen in men > 60 years of age who

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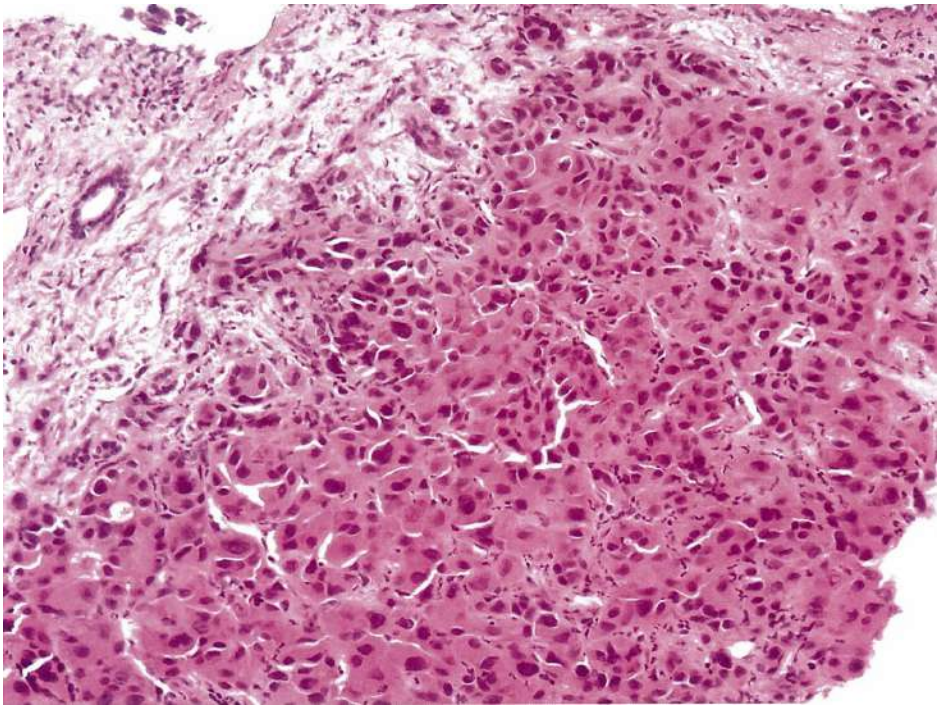
have been exposed to arsenic, vinyl chloride, or thorium dioxide. Hepatic angiosarcoma can manifest with upper abdominal pain, early satiety, and hepatomegaly, which are seen in this patient, but usually also causes weight loss, fatigue, or ascites. Unlike the specimen here, hepatic angiosarcoma usually appears as multiple, large, intraparenchymal lesions with necrotic areas on sonography. Histopathology would show vascular spaces lined with dysplastic endothelium that infiltrates the hepatic cords and sinusoids.

G - Hepatocellular carcinoma

Image



Explanation Why

Hepatocellular carcinoma (HCC) is the most common primary liver cancer. While HCC can manifest with upper abdominal pain, early satiety, and hepatomegaly, the most important risk factor for HCC is chronic liver disease (e.g., liver cirrhosis, chronic hepatitis B, chronic hepatitis C, hemochromatosis), which this patient does not have. On sonography, HCC appears as an intraparenchymal mass of variable echogenicity with areas of necrosis and calcification. Histopathology would show pleomorphic hepatocytes with eosinophilic cytoplasm, prominent nucleoli, and mitotic figures, as well as areas of necrosis and neovascularization, which is not consistent with this patient's biopsy findings.

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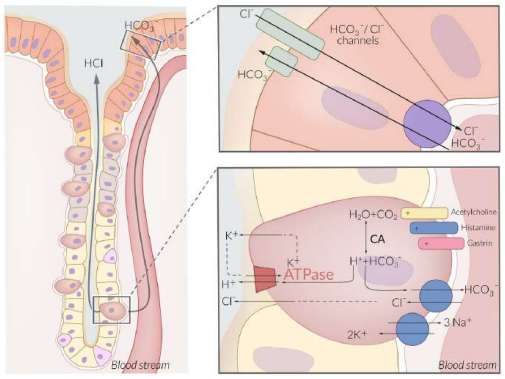
Question # 24

A 33-year-old man comes to the physician because of a 2-month history of burning epigastric pain, dry cough, and occasional regurgitation. The pain is aggravated by eating and lying down. Physical examination shows a soft, non-tender abdomen. Upper endoscopy shows hyperemia in the distal third of the esophagus. Which of the following drugs is most likely to directly inhibit the common pathway of gastric acid secretion?

	Answer	Image
A	Pirenzepine	
B	Ranitidine	
C	Aluminum hydroxide	
D	Lansoprazole	
E	Sucralfate	
F	Octreotide	

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Hint

This patient presents with classical features of gastroesophageal reflux disease, e.g., heartburn that is aggravated by eating and lying down. ATP-dependent secretion of H^+ ions into the gastric lumen is mediated by the H^+/K^+ ATPase located on gastric parietal cells and represents the common final pathway of gastric acid secretion.

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Correct Answer

A - Pirenzepine

Explanation Why

Anticholinergics such as pirenzepine reduce gastric acid secretion by blocking acetylcholine-mediated gastric secretion. However, anticholinergics do not block acid secretion stimulated via other routes, such as gastrin or histamine.

B - Ranitidine

Explanation Why

H2 receptor blockers such as ranitidine may be used for mild GERD symptoms as they inhibit histamine-dependent gastric acid secretion by antagonizing H2 receptors in gastric parietal cells. However, they do not block acid secretion stimulated via other routes, such as gastrin or acetylcholine.

C - Aluminum hydroxide

Explanation Why

Antacids such as aluminum hydroxide are used for symptomatic relief in mild, intermittent GERD as they directly neutralize gastric acid. However, antacids do not affect gastric acid secretion.

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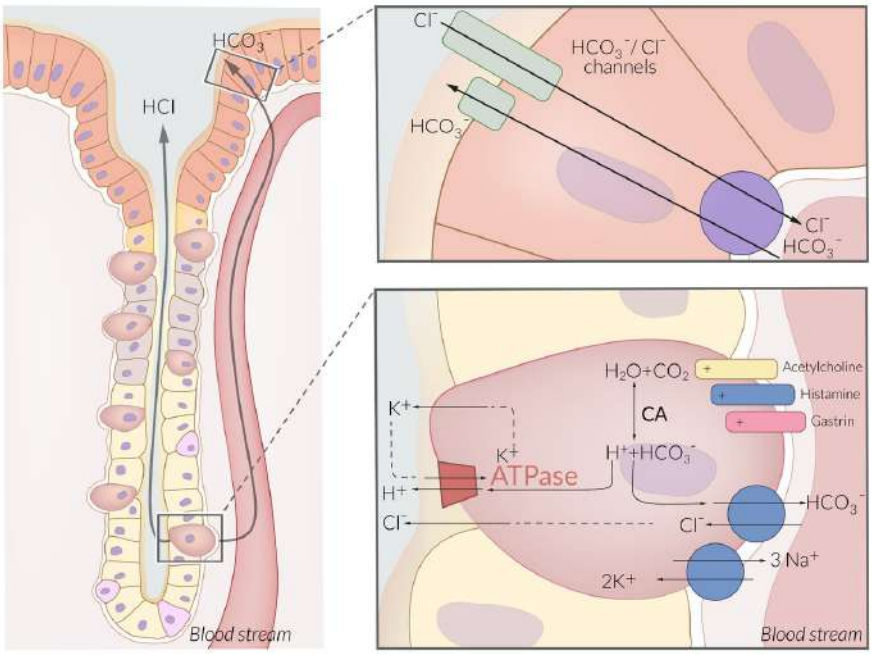
D - Lansoprazole

Image



Explanation Why

Proton pump inhibitors (PPIs) like lansoprazole are the first-line treatment for moderate to severe GERD. PPIs directly inhibit the H^+/K^+ ATPase, making them the most effective agents for the treatment of GERD.

E - Sucralfate

Explanation Why

Sucralfate is used as an adjunct treatment for peptic ulcer disease as it enhances the mucosal barrier in particularly acidic areas of the stomach and duodenum, acting as an acid buffer and promoting $HCO3^-$ production. However, sucralfate does not affect gastric acid secretion.

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F - Octreotide

Explanation Why

Octreotide, a somatostatin analog, is used in the management of gastric acid secretion secondary to hypergastrinemia (e.g, Zollinger- Ellison syndrome). Octreotide significantly reduces gastrin secretion, which decreases gastric acid secretion. However, it does not block acid secretion stimulated via other routes, such as histamine and acetylcholine.

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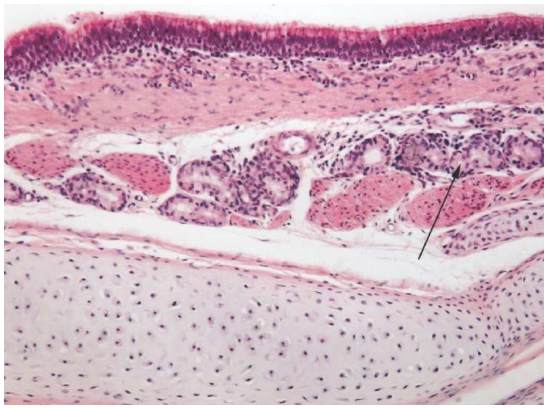
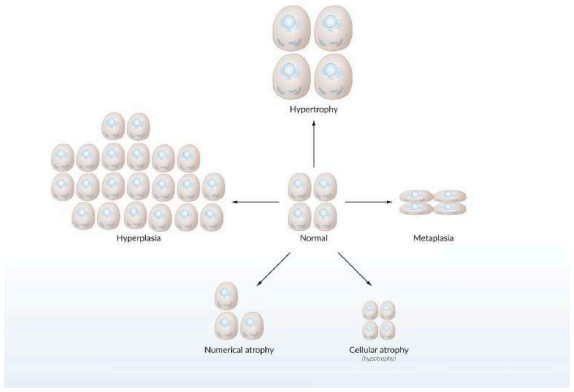
Question # 25

A 57-year-old man comes to the physician for a follow-up evaluation of chronic, retrosternal chest pain. The pain is worse at night and after heavy meals. He has taken oral pantoprazole for several months without any relief of his symptoms. Upper endoscopy shows ulcerations in the distal esophagus and a proximally dislocated Z-line. A biopsy of the distal esophagus shows mature columnar epithelium with goblet cells. Which of the following microscopic findings underlies the same pathomechanism as the cellular changes seen in this patient?

	Answer	Image
A	Pseudostratified columnar epithelium in the bronchi	
B	Squamous epithelium in the bladder	

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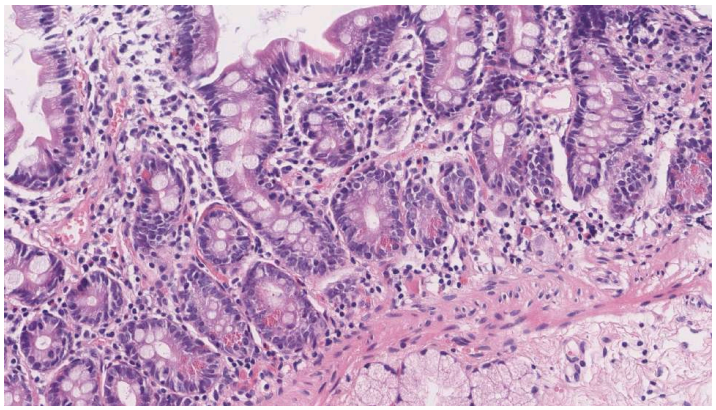
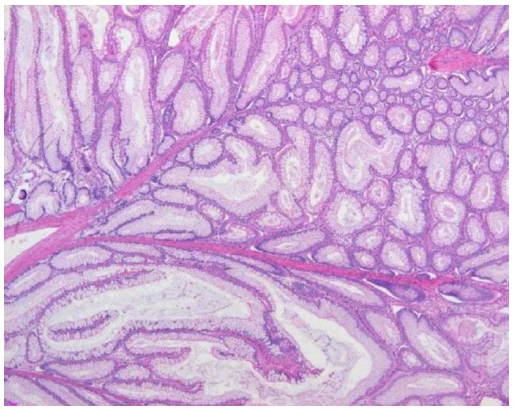
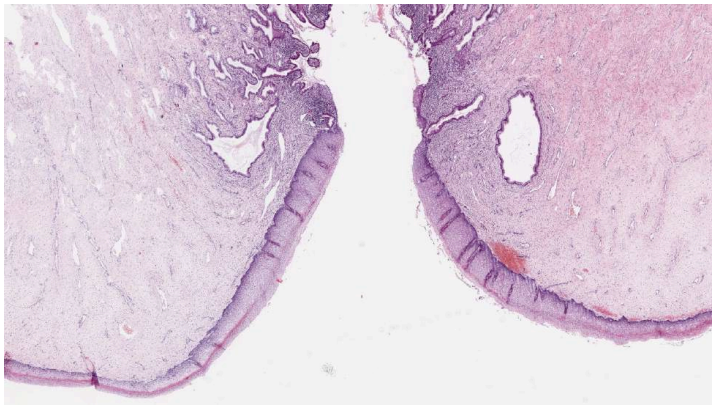
	Answer	Image
C	Paneth cells in the duodenum	
D	Branching muscularis mucosa in the jejunum	
E	Chief cells in the ileum	
F	Simple columnar epithelium in the endocervix	

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Hint

The biopsy findings in this patient (columnar epithelium with goblet cells) confirm a diagnosis of Barrett esophagus, which is characterized by metaplasia from squamous epithelium to intestinal columnar epithelium as a result of chronic gastric acid exposure.

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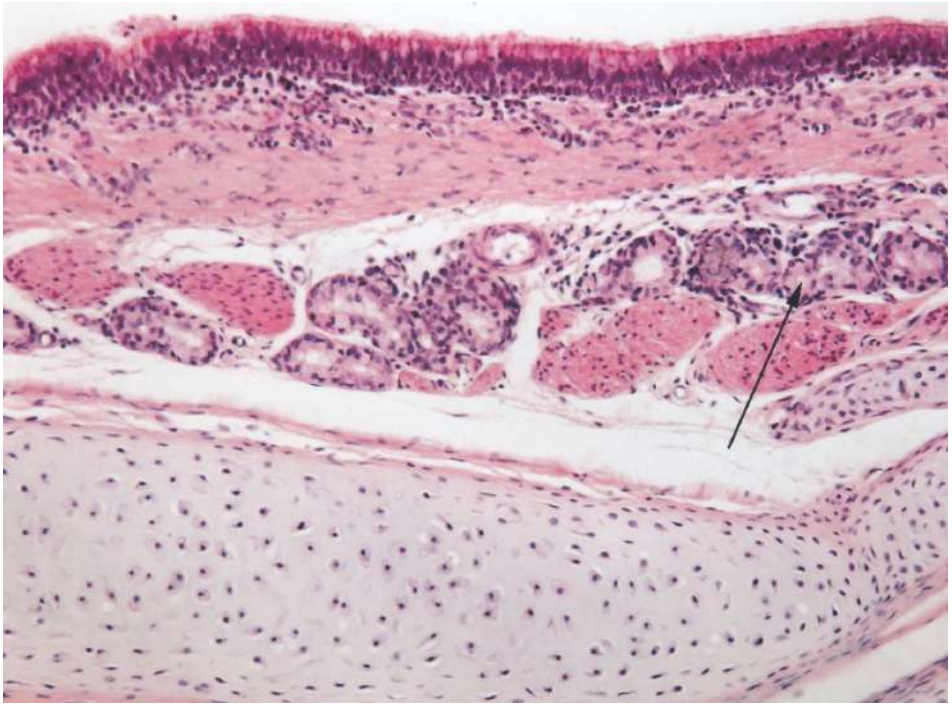
Correct Answer

A - Pseudostratified columnar epithelium in the bronchi

Image



Explanation Why

The presence of pseudostratified columnar epithelium in the bronchi (and the trachea) is a normal finding. In contrast, Barrett esophagus is an example of metaplasia. The presence of stratified squamous epithelium in the bronchi (e.g., from chronic smoke exposure) would be an example of metaplasia.

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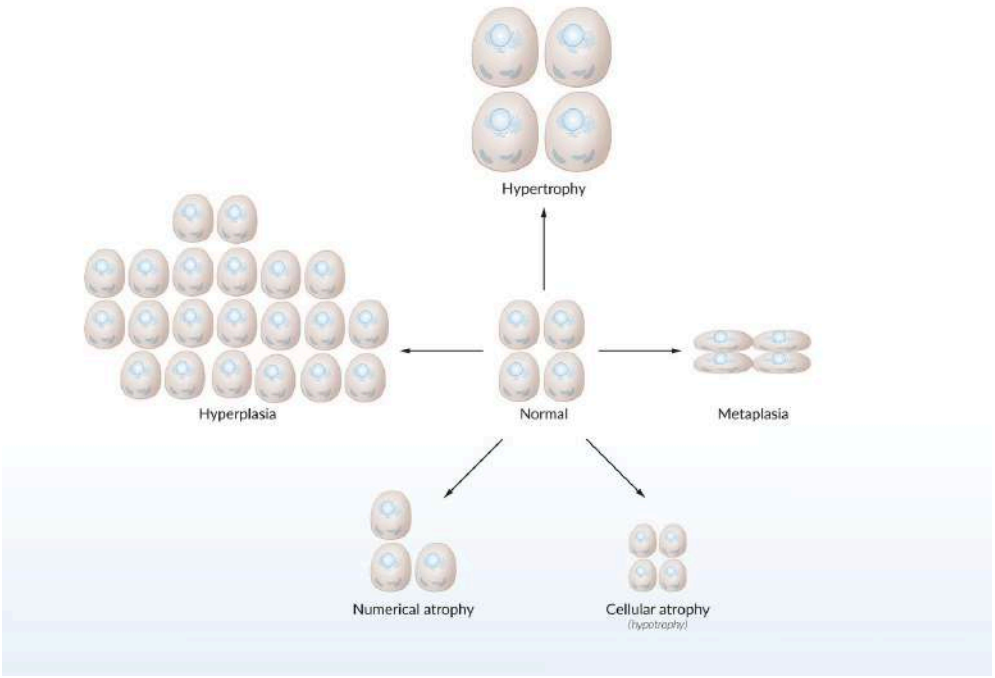
B - Squamous epithelium in the bladder

Image



Explanation But

Another example of metaplasia is the transformation of the respiratory ciliated columnar epithelium to a stratified squamous epithelium as a result of chronic smoke exposure.

Explanation Why

The bladder is normally lined by transitional epithelium. Chronic irritation of the bladder wall (e.g., from *Schistosoma* infection, urinary calculi, or indwelling catheters) can result in a transformation of transitional to squamous epithelium. Cellular transformation due to chronic stress (metaplasia) occurs when stem cells reprogram to replace one mature cell type with another that adapts to the chronic stress. Early metaplastic changes are reversible if exposure to the irritant stops. However, dysplastic changes can occur if chronic irritation persists.

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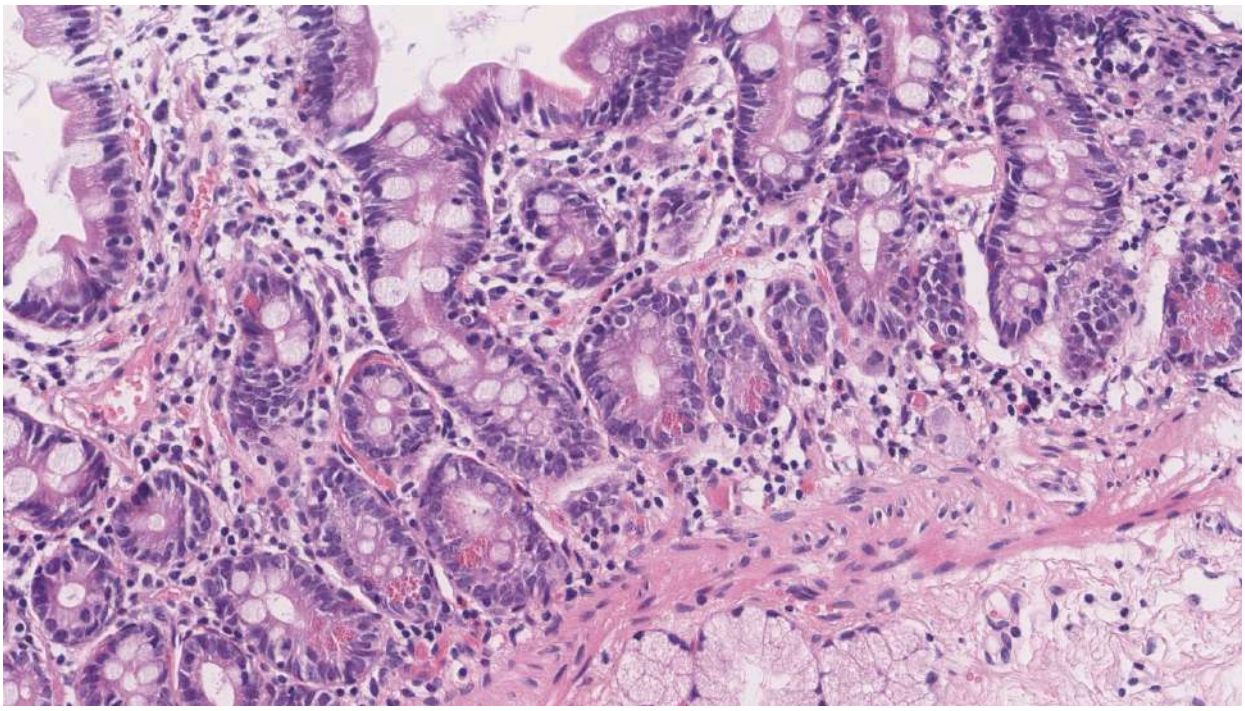
C - Paneth cells in the duodenum

Image



Explanation Why

The presence of Paneth cells in the duodenum is a normal finding. In contrast, Barrett esophagus is an example of metaplasia. The presence of Paneth cells in the stomach (e.g., as a result of chronic *H. pylori* infection) would be an example of metaplasia.

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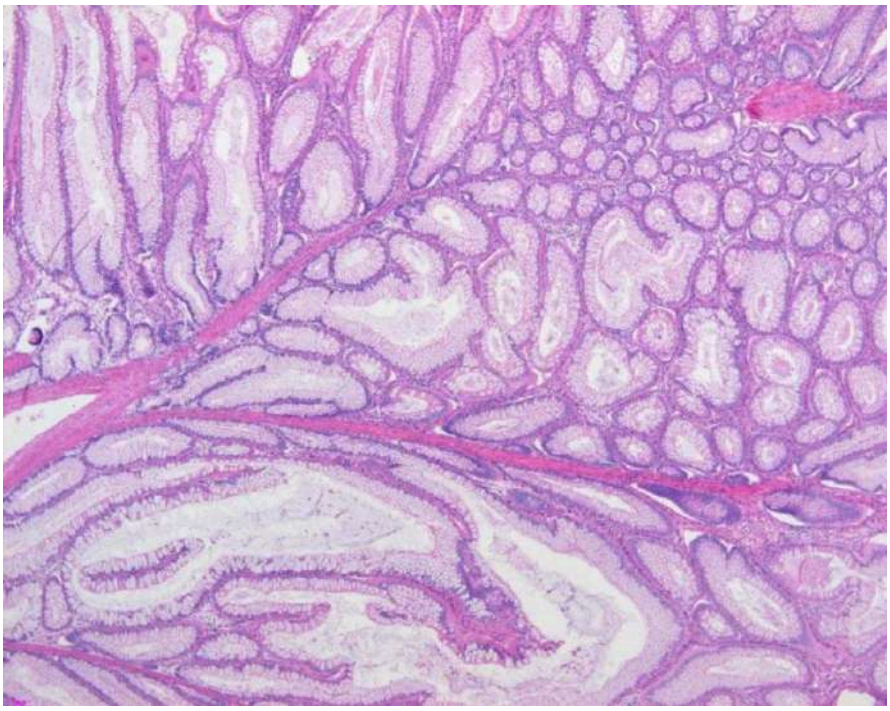
D - Branching muscularis mucosa in the jejunum

Image



Explanation Why

Branching of the muscularis mucosa is a characteristic feature of hamartomatous polyps, which are associated with Peutz-Jeghers syndrome and can occur at any location along the gastrointestinal tract. Hamartomas are disorganized overgrowths of tissue in their native location. Barrett esophagus is characterized by metaplasia, not hamartomas.

E - Chief cells in the ileum

Explanation Why

The presence of gastric chief cells in the ileum can be seen in some forms of Meckel diverticulum. A Meckel diverticulum with gastric tissue is an example of a choristoma, which refers to an ectopic island of normal tissue in an abnormal location. Choristomas are the result of metaplastic changes

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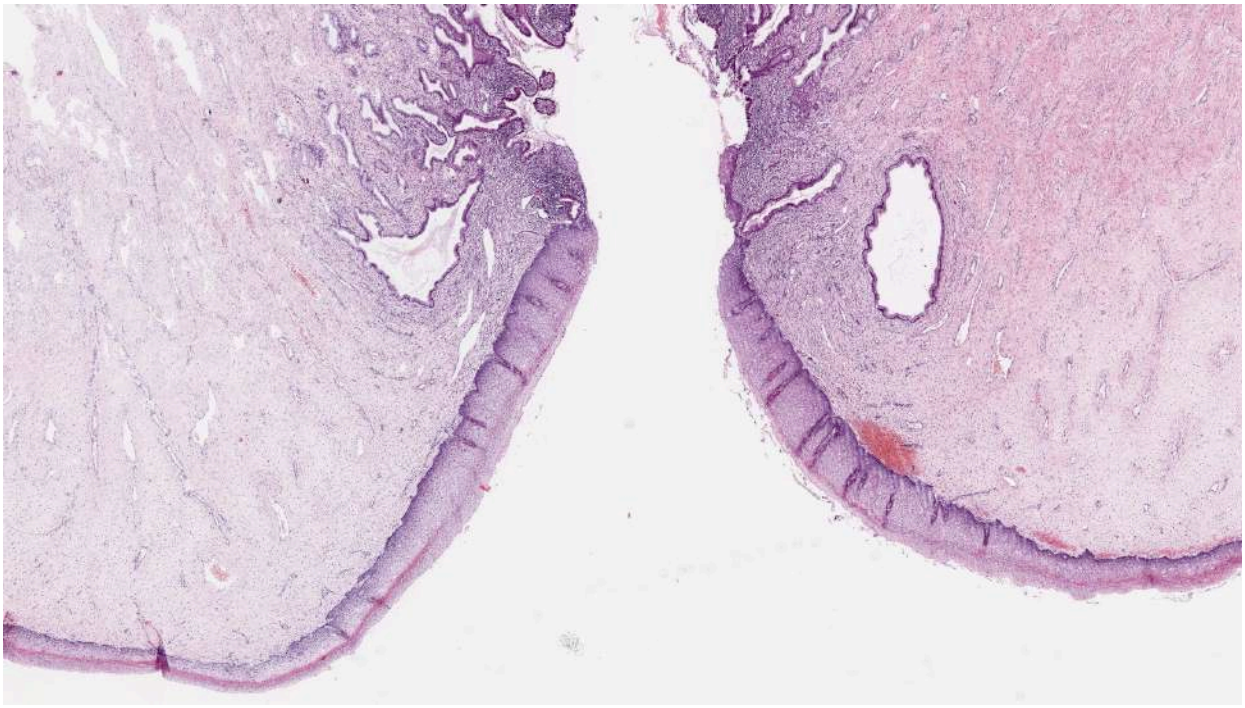
during embryonic development. In contrast, Barrett esophagus is characterized by postnatal metaplasia.

F - Simple columnar epithelium in the endocervix

Image



Explanation Why

The presence of simple columnar epithelium in the endocervix is a normal finding. In contrast, Barrett esophagus is an example of metaplasia. The endocervix physiologically undergoes metaplasia in the cervical transformation zone (squamocolumnar junction), where the simple columnar epithelium develops into squamous epithelium as a result of exposure to the acid vaginal pH.

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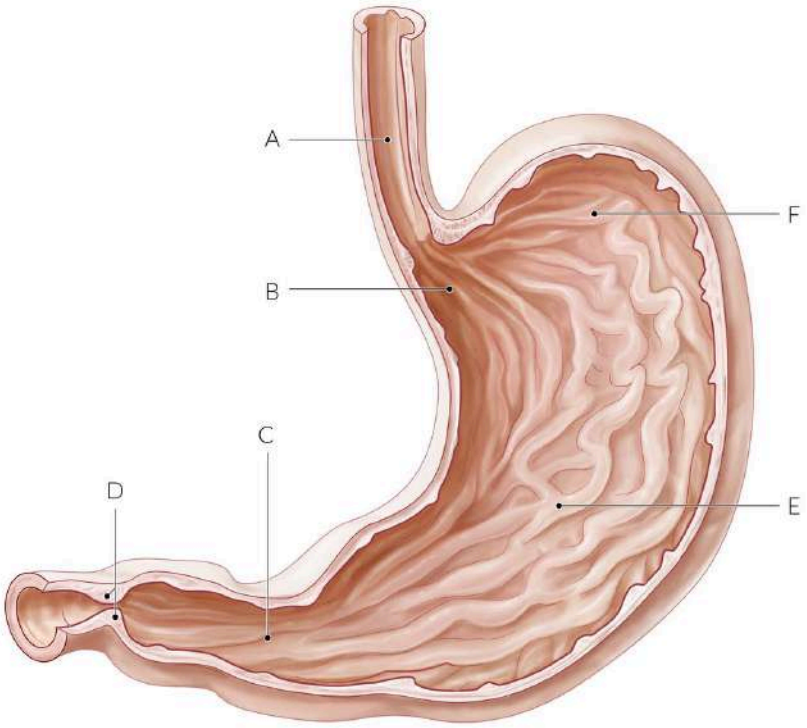
Question # 26

A 54-year-old woman comes to the physician for a routine follow-up examination. She was diagnosed with peptic ulcer disease one year ago and takes pantoprazole daily. Serum studies show a fasting gastrin level of 315 pg/mL (N < 100). This laboratory finding is most likely caused by increased hormone production from cells that are predominantly located in which of the following labeled areas?



	Answer	Image
A	A	
B	B	

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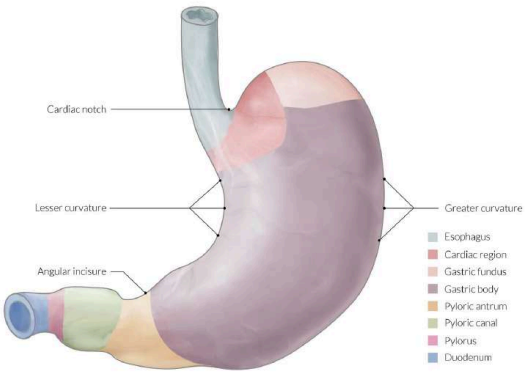
	Answer	Image
C	C	
D	D	
E	E	
F	F	

Hint

Longterm PPI use stimulates the production of gastrin by G cells.

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Correct Answer

A - A

Explanation Why

This region is the distal esophagus, which is normally lined by nonkeratinized stratified squamous epithelium. It does not have G cells.

B - B

Explanation Why

This region is the gastric cardia, which has mucous cells, parietal cells, gastric chief cells, and certain enteroendocrine cells (e.g., ECL cells, ghrelin cells). It does not contain G cells.

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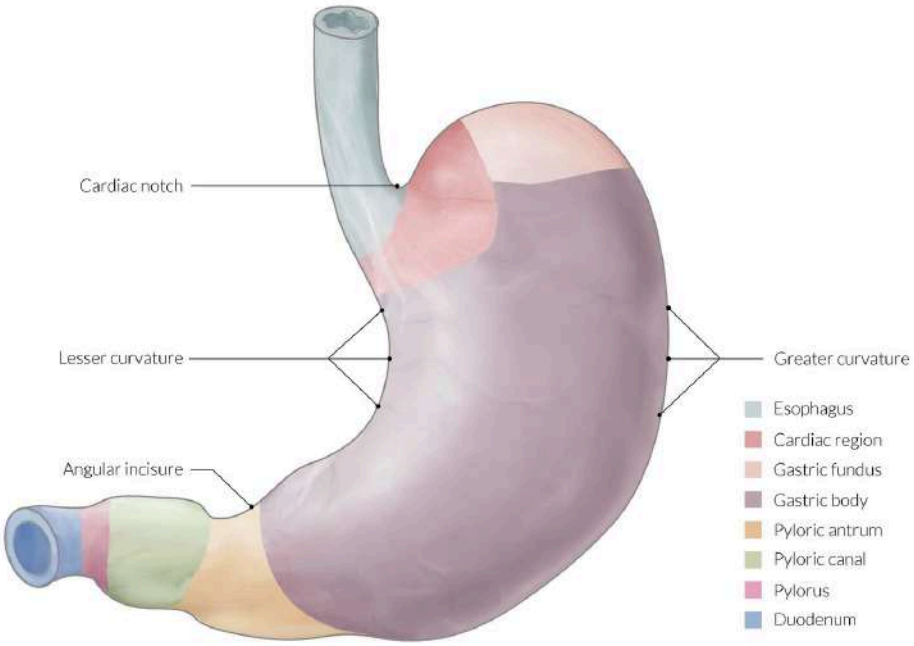
C - C

Image



Explanation Why

This region is the gastric antrum, which contains most of the gastrin-secreting G cells in the body. Smaller numbers of G cells are found in the pyloric canal, duodenum, and pancreas. Factors that increase gastrin secretion include distention of the stomach, gastrin-releasing peptide, increase in gastric pH (e.g., chronic atrophic gastritis, PPI use), and the presence of amino acids in the stomach. Increased gastrin secretion is also seen with gastrin-secreting tumors (gastrinoma). Gastrin increases gastric acid secretion, gastric mucosal growth, and gastric motility. Although the gastric antrum also has significant numbers of mucous-secreting cells and D cells, it is relatively deficient in parietal cells, gastric chief cells, and certain other enteroendocrine cells (e.g., ECL cells, ghrelin cells) when compared to more proximal regions of the stomach.

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D - D

Explanation Why

This region is the pyloric canal. Although some G cells are located here, they are predominantly located in a different region.

E - E

Explanation Why

This region is the gastric body, which has mucous-secreting cells, parietal cells, gastric chief cells, and certain enteroendocrine cells (e.g., ECL cells, ghrelin cells). It does not contain G cells.

F - F

Explanation Why

This region is the gastric fundus, which has mucous-secreting cells, parietal cells, gastric chief cells, and certain enteroendocrine cells (e.g., ECL cells, ghrelin cells). It does not contain G cells.

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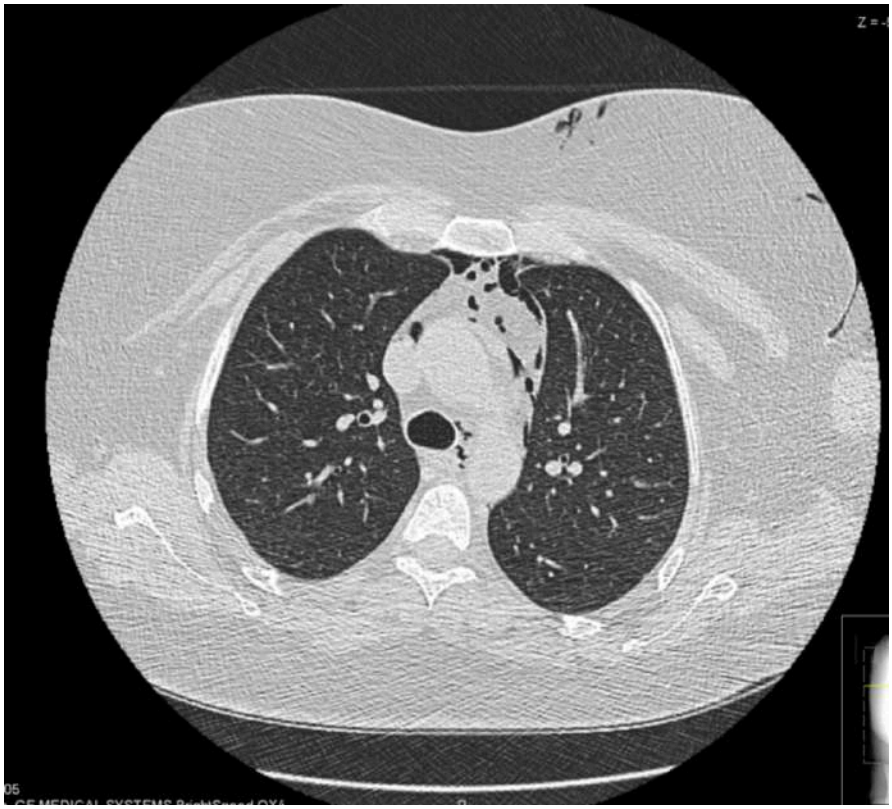
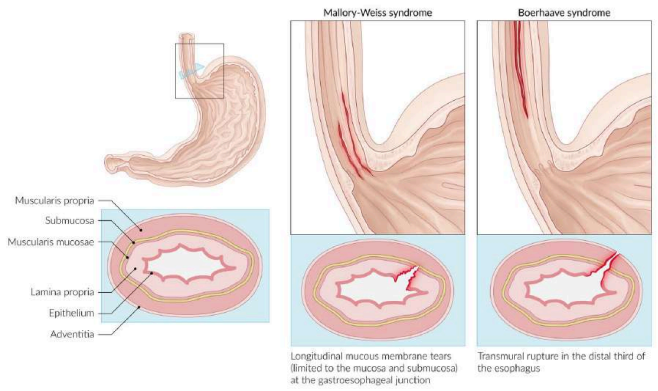
Question # 27

A 64-year-old woman is brought to the emergency department because of a 2-hour history of nausea, vomiting, and retrosternal pain that radiates to the back. Abdominal examination shows tenderness to palpation in the epigastric area. A CT scan of the patient's chest is shown. Which of the following is the most likely diagnosis?



	Answer	Image
A	Esophageal rupture	

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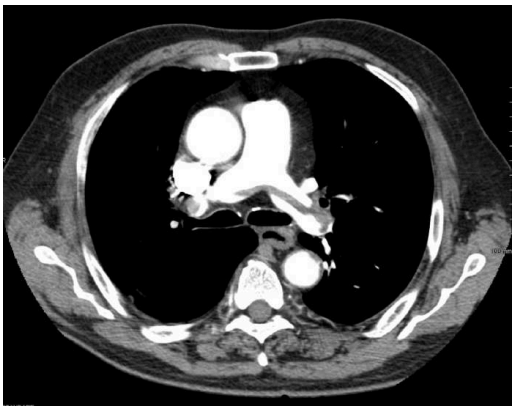
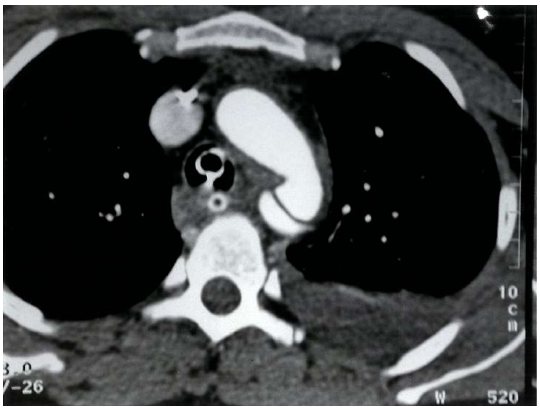
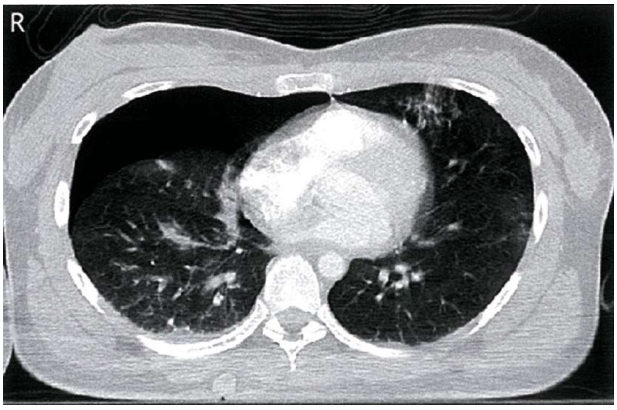
	Answer	Image
B	Pulmonary embolism	
C	Aortic dissection	
D	Acute myocardial infarction	
E	Pneumothorax	

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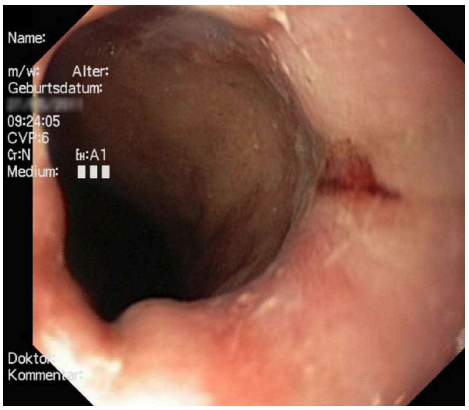
	Answer	Image
F	Mallory-Weiss syndrome	
G	Aspiration pneumonia	

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Hint

The CT scan shows extraluminal gas in the mediastinum (i.e., pneumomediastinum).

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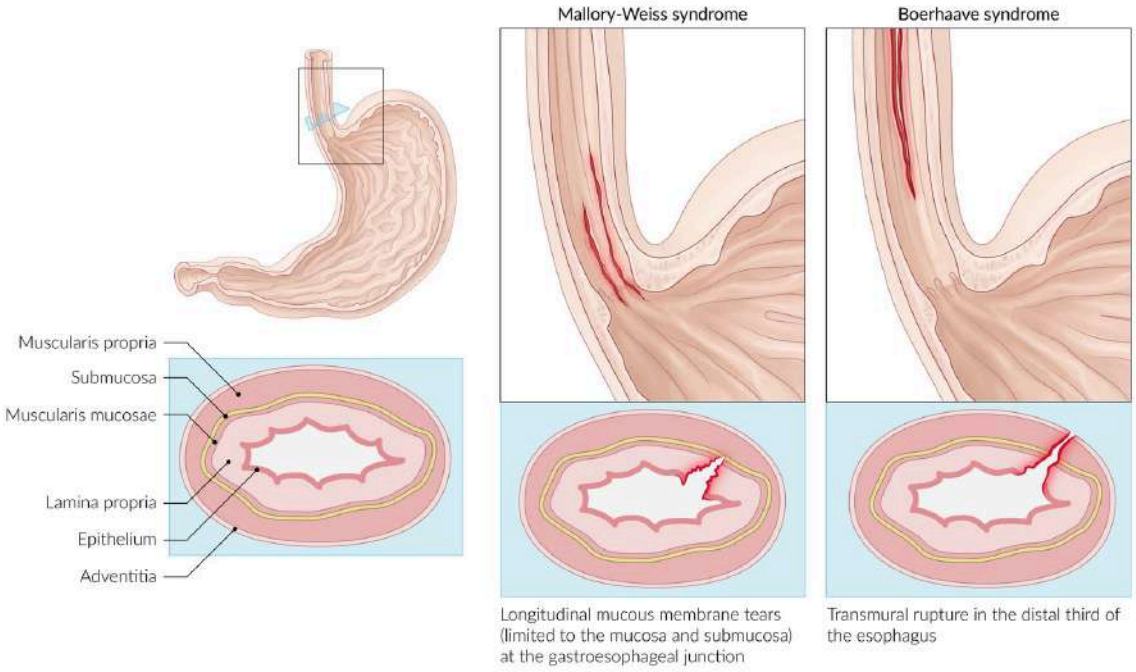
Correct Answer

A - Esophageal rupture

Image



Explanation Why

Boerhaave syndrome is most commonly caused by excessive vomiting and retching (e.g., as a result of high alcohol intake). Increased intrathoracic pressure results in elevated intraesophageal pressure that can lead to full-thickness rupture of the esophageal wall. Patients typically have a history of vomiting and develop severe, retrosternal pain that radiates to the back. Chest auscultation often reveals a crackling or crunching sound (Hamman sign) due to the presence of air in soft tissue spaces. This patient's history, symptoms, and chest CT scan that shows extraluminal gas in the mediastinum (i.e., pneumomediastinum) are consistent with a diagnosis of full-thickness esophageal rupture.

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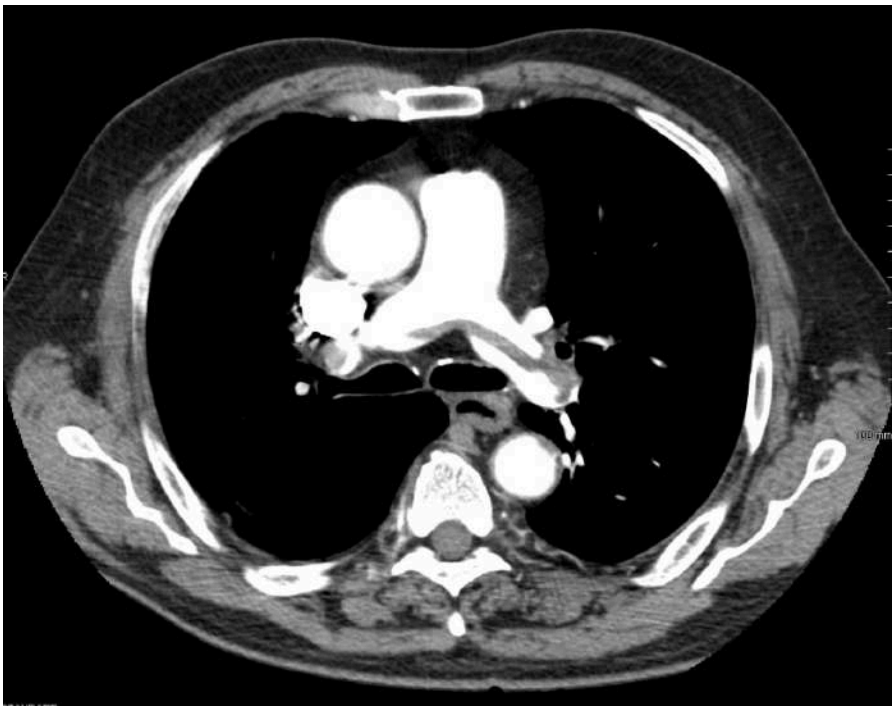
B - Pulmonary embolism

Image



Explanation Why

Pulmonary embolism can cause sudden-onset, severe chest pain as seen in this case. Additional manifestations include dyspnea, cough, tachycardia, and hypotension. CT imaging (helical spiral CT/ CT pulmonary angiography) classically shows an intraluminal filling defect of the pulmonary arteries; the presence of a wedge-shaped infarction with pleural effusion is a highly specific finding. Radiologic studies would not show pneumomediastinum.

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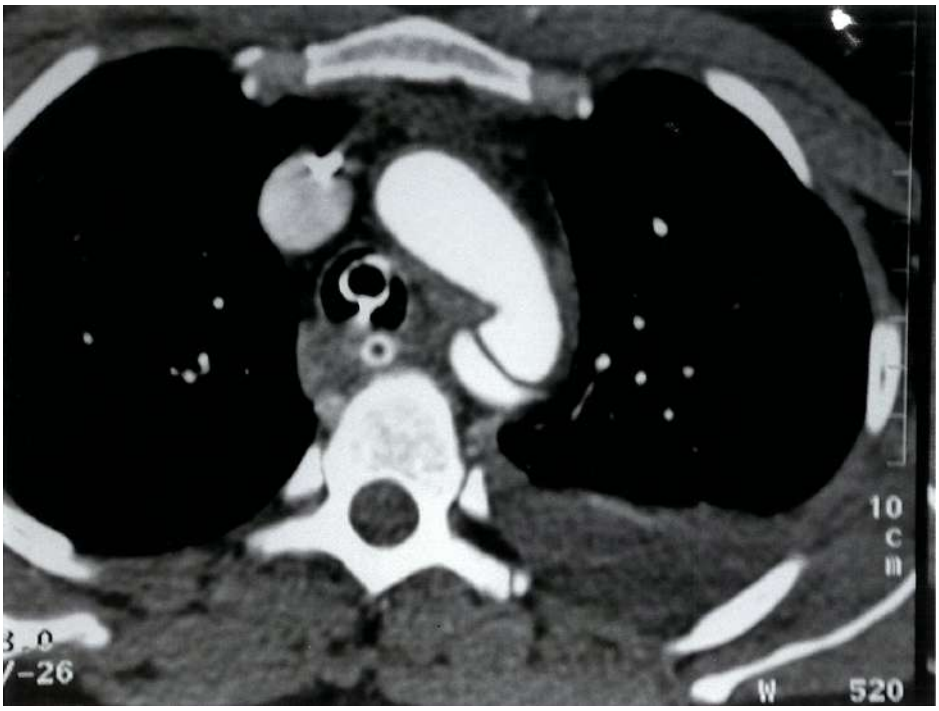
C - Aortic dissection

Image



Explanation Why

Aortic dissection can cause retrosternal pain that radiates to the back as seen in this case. Patients typically have a history of hypertension and usually present with severely elevated blood pressure (or hypotension in cases of shock and/or cardiac tamponade). Additional manifestations include asymmetrical blood pressure readings between the arms and syncope. CT scan of patients with aortic dissection shows an intimal flap that separates a true and false lumen, not pneumomediastinum.

D - Acute myocardial infarction

Explanation Why

Acute myocardial infarction can cause nausea, vomiting, and retrosternal pain as seen in this case. Though the use of CT imaging (e.g., coronary CT angiography) is not commonly used to evaluate

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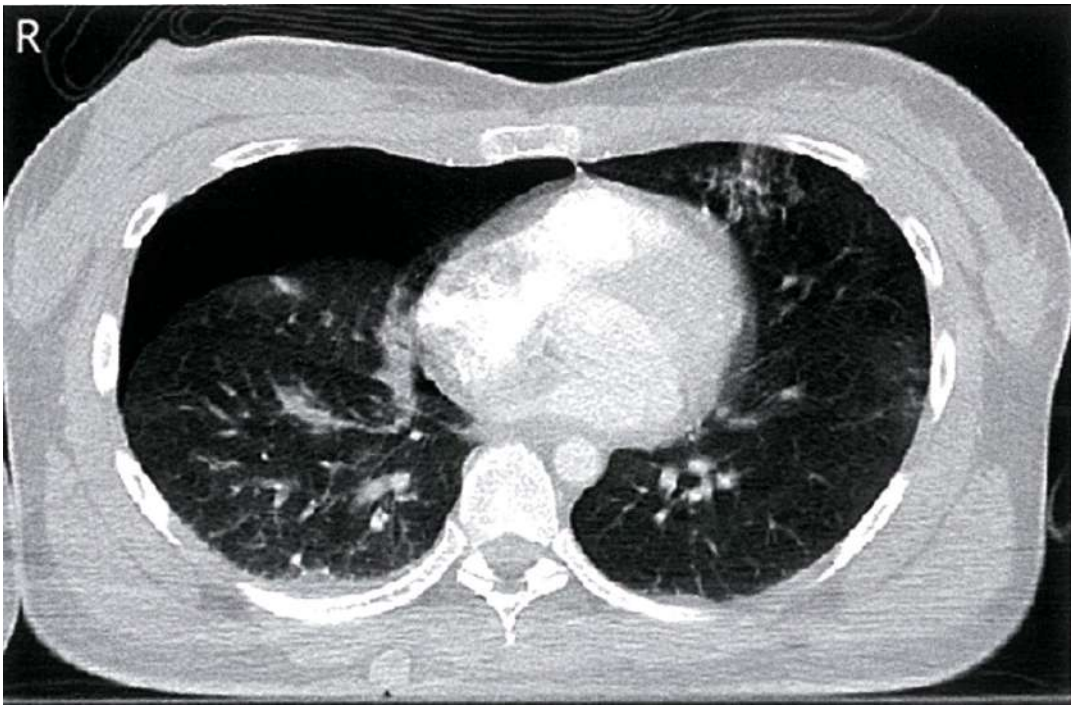
acute coronary syndrome, it can show atherosclerotic plaques and coronary artery stenosis. It would not pneumomediastinum.

E - Pneumothorax

Image



Explanation Why

Pneumothorax can cause sudden-onset, severe chest pain as seen in this case, but patients also typically have severe dyspnea. In addition, physical examination of patients with pneumothorax shows reduced or absent breath sounds, hyperresonance on percussion, and decreased fremitus on the ipsilateral side, not epigastric tenderness. Moreover, CT scan shows air pockets in the pleural space, not pneumomediastinum.

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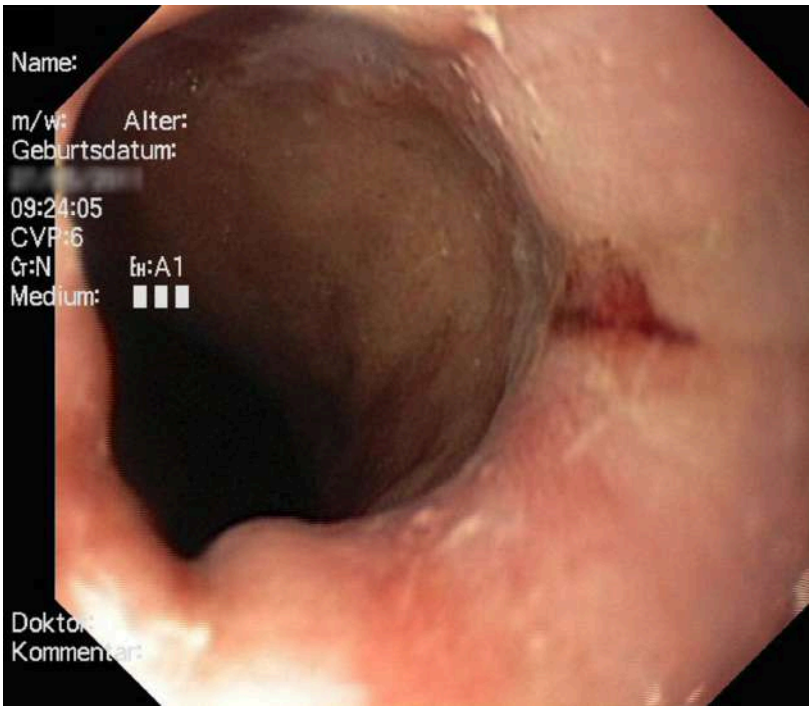
F - Mallory-Weiss syndrome

Image



Explanation Why

Mallory-Weiss syndrome can develop in patients with a history of forceful vomiting (e.g., from alcohol use disorder) and cause retrosternal chest pain and epigastric tenderness as seen in this case. However, patients typically have hematemesis. In addition, the preferred radiologic study to diagnose Mallory-Weiss syndrome is esophagogastroduodenoscopy, which typically shows a single, longitudinal tear in the mucosa at the esophagogastric junction. Radiologic studies would not show pneumomediastinum.

G - Aspiration pneumonia

Explanation Why

Aspiration pneumonia (e.g., due to aspiration of vomit) can cause chest pain as seen in this case.

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However, this condition also typically manifests with dyspnea, cough, fever, crackles on auscultation, and hypoxemia, not epigastric tenderness. Moreover, radiologic studies of aspiration pneumonia often show infiltrates in the dependent parts of the lung, not pneumomediastinum.

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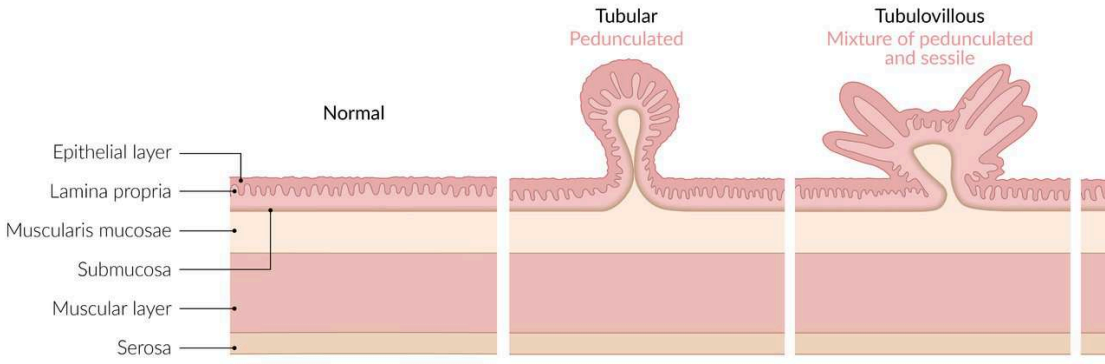
Question # 28

A previously healthy 35-year-old woman comes to the physician for a 3-week history of alternating constipation and diarrhea with blood in her stool. She has not had any fevers or weight loss. Her father died of gastric cancer at 50 years of age. Physical examination shows blue-gray macules on the lips and palms of both hands. Colonoscopy shows multiple polyps throughout the small bowel and colon with one ulcerated polyp at the level of the sigmoid colon. Multiple biopsy specimens are collected. These polyps are most likely to be characterized as which of the following histological subtypes?

	Answer	Image
A	Hyperplastic	
B	Adenomatous	
C	Mucosal	
D	Serrated	
E	Hamartomatous	

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Hint

The combination of multiple gastrointestinal polyps, mucocutaneous discoloration, and a family history of gastrointestinal malignancy is consistent with Peutz-Jeghers syndrome (PJS).

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Correct Answer

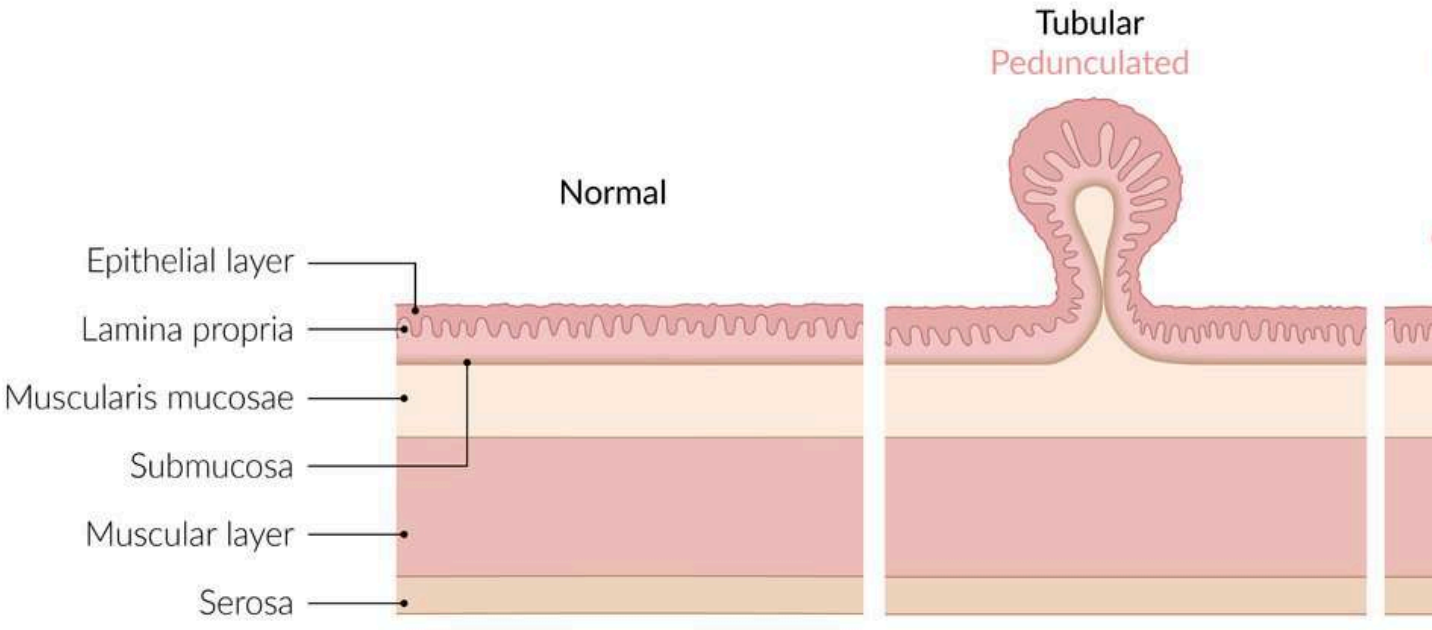
A - Hyperplastic

Explanation Why

Hyperplastic polyps are small growths that are most commonly found in the rectosigmoid colon. Although most hyperplastic polyps are benign, some may evolve into premalignant serrated polyps; therefore, removal is recommended. Hyperplastic polyps are not associated with mucocutaneous discoloration or a family history of gastrointestinal malignancy, both of which are present in this patient.

B - Adenomatous

Image



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Explanation Why

Adenomas are the most common type of neoplastic mucosal polyp. They include tubular adenomas, tubulovillous adenomas, and villous adenomas (with villous features indicating a higher malignant potential). In patients with multiple colorectal adenomas or those who have developed multiple adenomas at an early age, familial adenomatous polyposis syndrome should be suspected. This patient's clinical exam findings are more concerning for PJS, which is characterized by colonic polyps of a different histologic type.

C - Mucosal

Explanation Why

Mucosal polyps are small, usually < 5 mm in size, and benign. They are not associated with PJS.

D - Serrated

Explanation Why

Serrated polyps, which can be classified as either traditional serrated adenomas or sessile serrated polyps, have moderate potential to undergo malignant transformation. Although serrated polyps are associated with oncogenic mutations, such as BRAF, there is no known connection to PJS.

E - Hamartomatous

Explanation Why

Hamartomatous polyps are the most likely type to be found in this patient with PJS, a condition that is characterized by numerous hamartomatous colonic polyps, mucocutaneous hyperpigmentation, and an increased risk of gastrointestinal malignancy. In PJS, polyps commonly occur in the small intestine but can be found in any part of the GI tract. Although hamartomas are often benign, a small risk of malignant transformation is present. On histopathology, hamartomas contain a proliferation of smooth muscle extending into the lamina propria with normal overlying epithelium.

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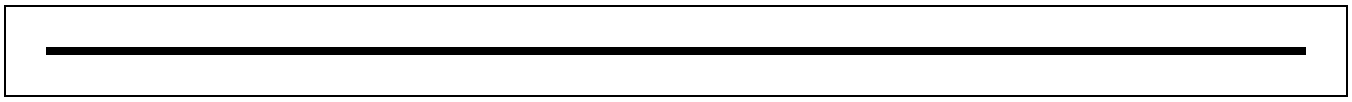

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Question # 29

An investigator is studying the secretion of gastrointestinal hormones before and after food intake. She isolates a hormone that accelerates the emptying of gastric contents into the duodenal bulb. The isolated hormone is most likely which of the following?

	Answer	Image
A	Glucagon-like peptide	
B	Gastrin	
C	Cholecystokinin	
D	Vasoactive intestinal peptide	
E	Secretin	

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Hint

The cells secreting this hormone are predominantly located in the duodenum and gastric antrum.

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Correct Answer

A - Glucagon-like peptide

Explanation Why

Glucagon-like peptide (GLP) is secreted by L cells located throughout the intestine. Unlike the hormone isolated here, GLP promotes gastric relaxation and pyloric contraction, thereby reducing gastric emptying. GLP also plays an important role as an incretin, helping to reduce serum glucose levels.

B - Gastrin

Explanation Why

Gastrin is a hormone produced by the G cells of the gastric antrum and duodenum. It enhances gastric motility by increasing antral contractions and propelling stomach contents towards the pylorus while simultaneously relaxing the pyloric sphincter so that gastric contents are mobilized into the duodenum. Other functions of gastrin include increased secretion of hydrochloric acid via parietal cell stimulation, stimulation of pepsin release from chief cells, and promotion of gastric mucosal growth.

C - Cholecystokinin

Explanation Why

The presence of food material in the duodenum and jejunum causes I cells to secrete cholecystokinin (CCK), which reduces gastric contractions and promotes pyloric closure, thereby decreasing gastric emptying. Other major functions of CCK include increasing pancreatic and biliary secretions and relaxing the sphincter of Oddi.

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D - Vasoactive intestinal peptide

Explanation Why

Vasoactive intestinal peptide (VIP) increases bicarbonate and water secretion in the small intestine. In general, VIP causes widespread smooth muscle relaxation, including gastric relaxation. As a result, VIP decreases, rather than increases, gastric motility and acid secretion.

E - Secretin

Explanation Why

Secretin is released by S cells of the duodenum in response to the presence of acidic gastric content in the small intestine. Secretin reduces acid secretion, gastric motility, and gastric emptying while increasing the secretion of bicarbonate-rich fluid from the pancreas.

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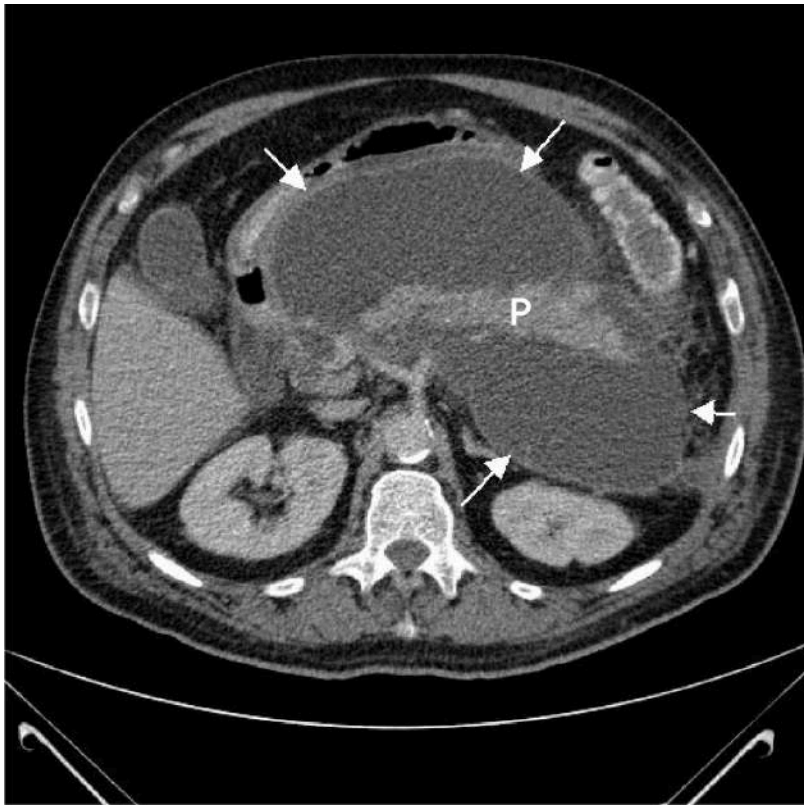
Question # 30

A 49-year-old man comes to the physician because of a 1-week history of diarrhea and abdominal bloating. His stools are bulky, foul-smelling, and difficult to flush. Over the past 6 months, he has had recurrent dull epigastric pain that is triggered by meals and lasts for a few days. He drinks 6 to 8 beers daily. Abdominal examination shows mild epigastric tenderness with no rebound or guarding. A CT scan of the abdomen is shown. The structure indicated by the arrows is most likely lined by which of the following?



	Answer	Image
A	Simple ductal epithelium	
B	Calcified ductal cells	
C	Granulation tissue	

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	Answer	Image
D	Pyogenic membrane	
E	Columnar mucinous epithelium	

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Hint

The large cystic lesion found on CT scan of this patient with a history of chronic alcohol abuse, steatorrhea (bulky, foul-smelling, difficult-to-flush stools), and recurrent epigastric pain is most likely a pancreatic pseudocyst that has formed as a result of chronic pancreatitis.

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Correct Answer

A - Simple ductal epithelium

Explanation Why

Simple ductal epithelium lining a cystic lesion on the pancreas is a pancreatic retention cyst. These are most often slow-growing, small, asymptomatic, benign lesions. The large cyst-like lesion found in this patient with a history of alcohol use is much more likely to be a pancreatic pseudocyst.

B - Calcified ductal cells

Explanation Why

Calcified ductal cells within the pancreas are strongly associated with chronic pancreatitis due to heavy alcohol consumption. Signs of chronic pancreatitis include pancreatic insufficiency (leading to steatorrhea and fat-soluble vitamin deficiencies) and endocrine pancreas insufficiency (resulting in diabetes mellitus). Although this patient's pseudocyst formation is most likely related to chronic pancreatitis and there are likely calcified ductal cells within the pancreas itself, these cells would not be found lining the pseudocyst.

C - Granulation tissue

Explanation Why

Granulation tissue encapsulates pancreatic pseudocysts, retaining enzyme-rich pancreatic fluids. These pseudocysts lack proper epithelial lining (in contrast to true cysts) and are instead walled off by adjacent intraperitoneal structures (e.g., stomach or omentum). Such lesions are due to a disruption of the pancreatic ductal system and extravasation of fluids, usually as a result of acute or chronic pancreatitis. Most pseudocysts remain asymptomatic but large lesions can cause mass effect, resulting in abdominal pain, biliary obstruction, and potentially gastrointestinal bleeds if nearby blood vessels are involved.

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D - Pyogenic membrane

Explanation Why

Pyogenic membranes form the outer wall of abscesses, enclosing pus and bacteria. Pancreatic abscesses typically occur as a complication of acute pancreatitis, whereby leakage of pancreatic enzymes leads to surrounding tissue necrosis that is subsequently infected. Pancreatic pseudocysts may become superinfected and progress into abscesses, but this progression would be accompanied by clinical evidence of infection such as fever or chills, neither of which this patient has.

E - Columnar mucinous epithelium

Explanation Why

The columnar mucinous epithelium comprises the lining of mucinous cystadenoma of the pancreas, a benign tumor that preferentially occurs on the body or tail of the pancreas and does not communicate with the pancreatic ductal system. Most of these lesions are asymptomatic and slow-growing, though very large lesions may exhibit symptoms of mass effect (e.g., epigastric fullness, nausea, and vomiting) and pose some threat of malignant transformation. The large fluid collection on this patient's imaging does not emanate from the body or tail of the pancreas, and his long history of alcohol use makes a pancreatic pseudocyst much more likely.

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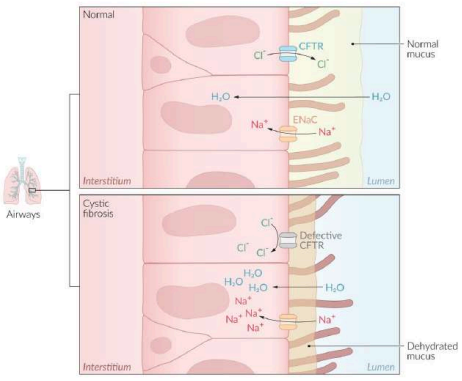
Question # 31

A 15-year-old boy is brought to the emergency department by his mother because of a 5-hour history of right lower quadrant pain, vomiting, and abdominal distention. Examination shows a palpable mass in the right lower quadrant of the abdomen. An x-ray of the abdomen shows a dilated ascending colon with an air-fluid level in the small intestine. A test is performed in which electrodes are placed on the nasal epithelium and the nose is perfused with several different solutions. When a chloride-free solution is administered, hyperpolarization across the nasal epithelium is absent. Which of the following is the most common cause of mortality in patients with the condition described here?

	Answer	Image
A	Liver cirrhosis	
B	Pulmonary embolism	
C	Diabetes mellitus	
D	Pulmonary infection	
E	Nephrolithiasis	

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Hint

This patient has clinical findings consistent with distal intestinal obstruction syndrome (abdominal distention, RLQ pain, and a RLQ mass), most likely due to abnormal chloride transmembrane transport.

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Correct Answer

A - Liver cirrhosis

Explanation Why

The liver is often affected in cystic fibrosis, with manifestations including cholestasis, hepatic steatosis, portal hypertension, and liver cirrhosis. However, liver cirrhosis is not a common cause of death in this patient group.

B - Pulmonary embolism

Explanation Why

Patients with cystic fibrosis are at a higher risk of developing pulmonary embolism compared to the general population, but it is not a common cause of death in this patient group.

C - Diabetes mellitus

Explanation Why

Pancreatic tissue involvement is common in cystic fibrosis. Progressive destruction of pancreatic beta cells can result in a significant proportion of adult patients manifesting with diabetes mellitus. However, diabetes mellitus is not a common cause of death in patients with cystic fibrosis.

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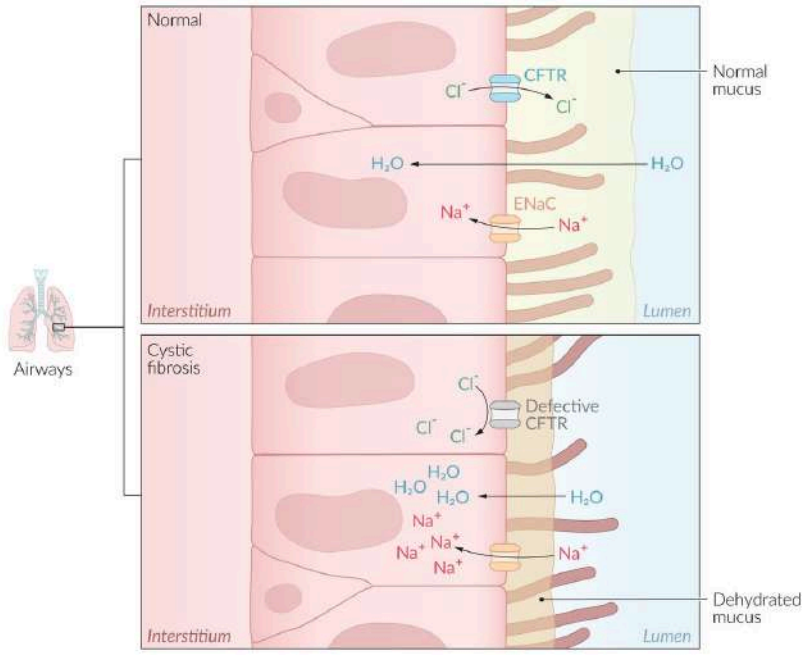
D - Pulmonary infection

Image



Explanation Why

The nasal potential difference test conducted here confirms the diagnosis of cystic fibrosis in this patient. Patients with cystic fibrosis have hyperviscous exocrine gland secretions, which can thicken stool and cause distal intestinal obstruction, as seen here. Hyperviscous respiratory secretions and deficient mucociliary clearance lead to recurrent pulmonary infections. This, combined with multiple episodes of antibiotic therapy, leads to the development of more severe, resistant infections (e.g., *Pseudomonas aeruginosa*) and structural lung changes (e.g., bronchiectasis, emphysema), with eventual progression to respiratory failure.

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E - Nephrolithiasis

Explanation Why

Nephrolithiasis is more common in patients with cystic fibrosis than in the general population, and chronic nephrolithiasis can lead to renal failure and/or urosepsis. However, it is not a common cause of death in this patient group.

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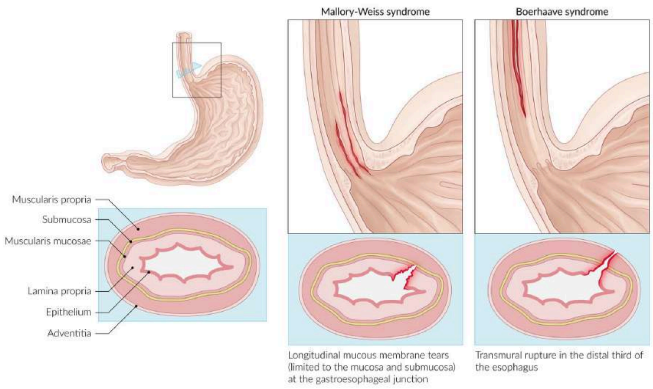
Question # 32

A 4-year-old girl is brought to the emergency department by her father for the evaluation of abdominal pain for 1 hour after drinking a bottle of rust remover. The father reports that she vomited once on the way to the hospital and that her vomit was not bloody. The patient has pain with swallowing. She appears uncomfortable. Oral examination shows mild erythema of the epiglottis and heavy salivation. Which of the following is the most likely long-term complication in this patient?

	Answer	Image
A	Esophageal webs	
B	Esophageal strictures	
C	Barrett esophagus	
D	Thyroglossal fistula	
E	Mallory-Weiss tears	
F	Oral cavity cancer	

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Hint

This patient's symptoms (abdominal pain, nausea, vomiting, odynophagia, and heavy salivation) began shortly after the ingestion of rust remover, suggesting caustic liquid poisoning.

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Correct Answer

A - Esophageal webs

Explanation Why

Esophageal webs are thin membranes of normal esophageal tissue that protrude into the esophagus. These webs can cause symptoms such as dysphagia, odynophagia, and food impaction. Esophageal webs may be congenital (Plummer-Vinson syndrome) or acquired (e.g., nutritional deficiencies), but they are not caused by caustic agent injury.

B - Esophageal strictures

Explanation Why

The most common long-term complication of caustic liquid ingestion is the development of esophageal strictures. Most strictures develop approx. 2 months after the initial injury. Esophageal dysmotility caused by strictures and neuromuscular damage can lead to severe dysphagia. Other complications of caustic liquid ingestion include esophageal ulcers and esophageal cancer.

C - Barrett esophagus

Explanation Why

Barrett esophagus is a complication of chronic gastroesophageal reflux. Chronic gastroesophageal reflux may occur secondary to caustic agent injury but Barrett esophagus is not a common complication.

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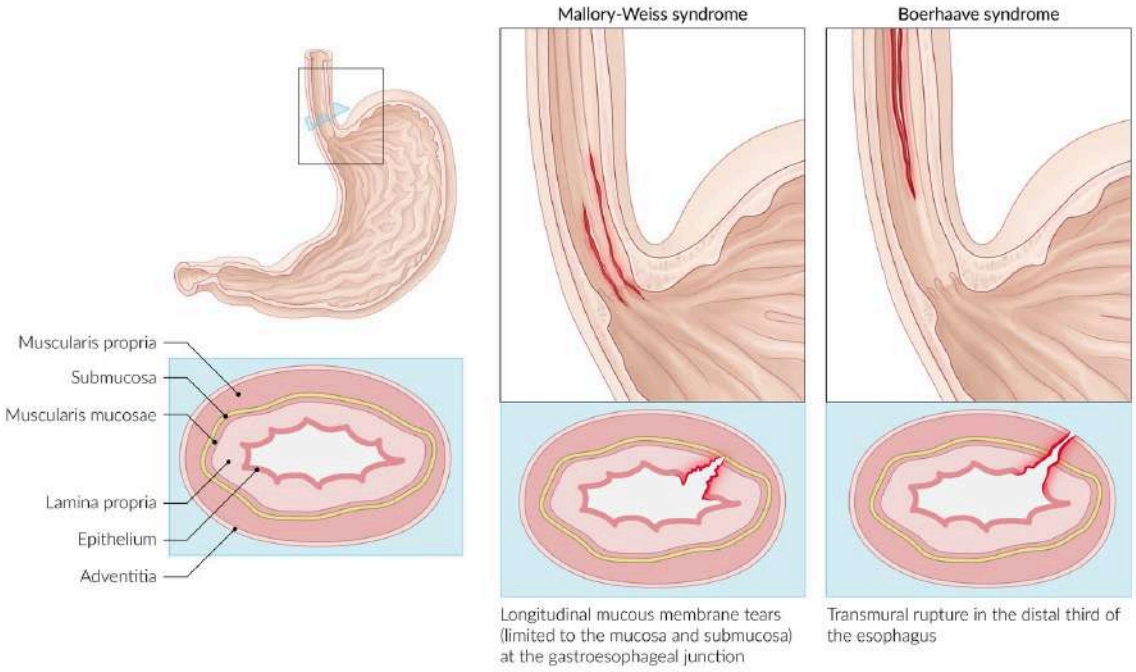
D - Thyroglossal fistula

Explanation Why

A thyroglossal fistula is a congenital remnant of the thyroid diverticulum. It would not be expected to develop as a result of caustic liquid injury. Mediastinal and tracheoesophageal fistulas may develop in patients with severe caustic liquid injury, especially in those with esophageal perforation.

E - Mallory-Weiss tears

Image



Explanation Why

Mallory-Weiss tears are traumatic mucosal and submucosal esophageal tears at the gastroesophageal junction. These tears usually manifest with hematemesis, and they are typically the result of severe, repeated retching and/or vomiting. In most affected individuals, Mallory-Weiss tears heal spontaneously. Conditions that predispose individuals to Mallory-Weiss tears include alcoholism,

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bulimia nervosa, and gastroesophageal reflux disease, but not caustic agent injury.

F - Oral cavity cancer

Explanation Why

Oral cavity cancer is associated with long-term oral tobacco use, smoking, or alcohol consumption as well as poor oral hygiene and/or human papillomavirus (e.g., HPV 16, 18, 31, and 33) infection. Caustic agent injury is associated with an increased risk of esophageal cancer rather than oral cavity cancer.

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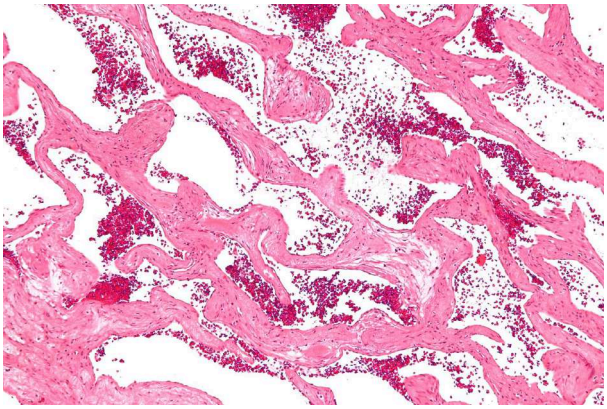
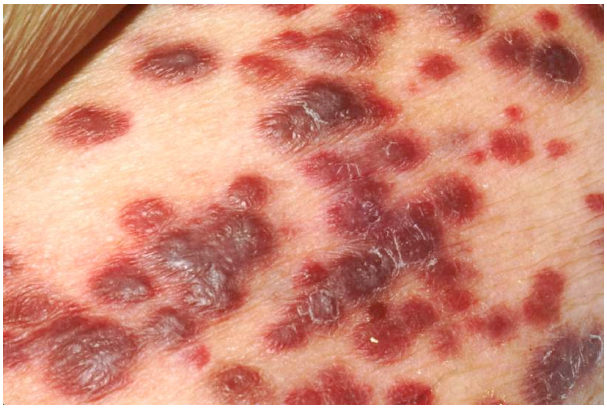
Question # 33

A previously healthy 75-year-old man comes to the physician with a 6-month history of fatigue, weight loss, and abdominal pain. He drinks 2 oz of alcohol on the weekends and does not smoke. He is retired but previously worked in a factory that produces plastic pipes. Abdominal examination shows right upper quadrant tenderness; the liver edge is palpable 2 cm below the ribs. A liver biopsy specimen shows pleomorphic spindle cells that express PECAM-1 on their surface. Which of the following is the most likely diagnosis?

	Answer	Image
A	Cavernous hemangioma	
B	Kaposi sarcoma	
C	Angiosarcoma	

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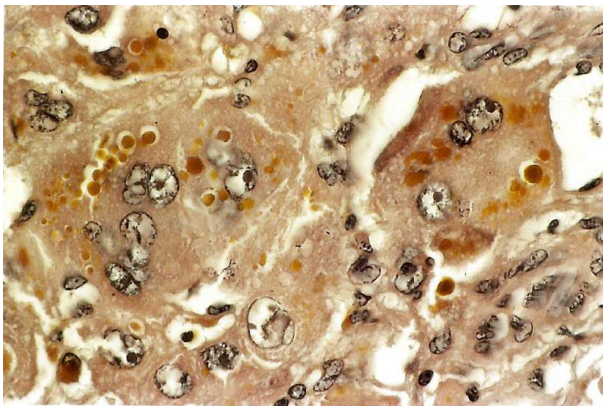
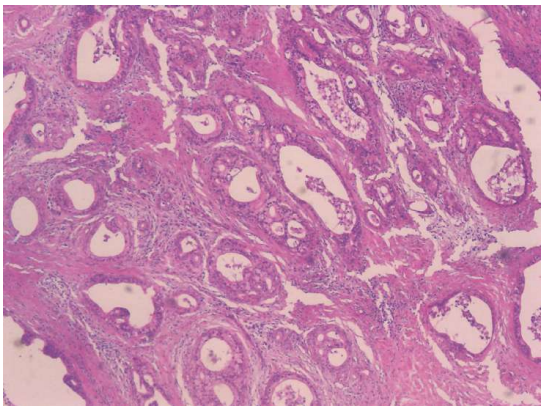
	Answer	Image
D	Hepatocellular carcinoma	
E	Hepatic adenoma	
F	Cholangiocarcinoma	

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Hint

This patient's symptoms together with his history of working at a plastic factory suggests a type of liver cancer associated with occupational exposure to vinyl chloride. Vinyl chloride is used to make various polyvinyl chloride (PVC) plastic products, including pipes.

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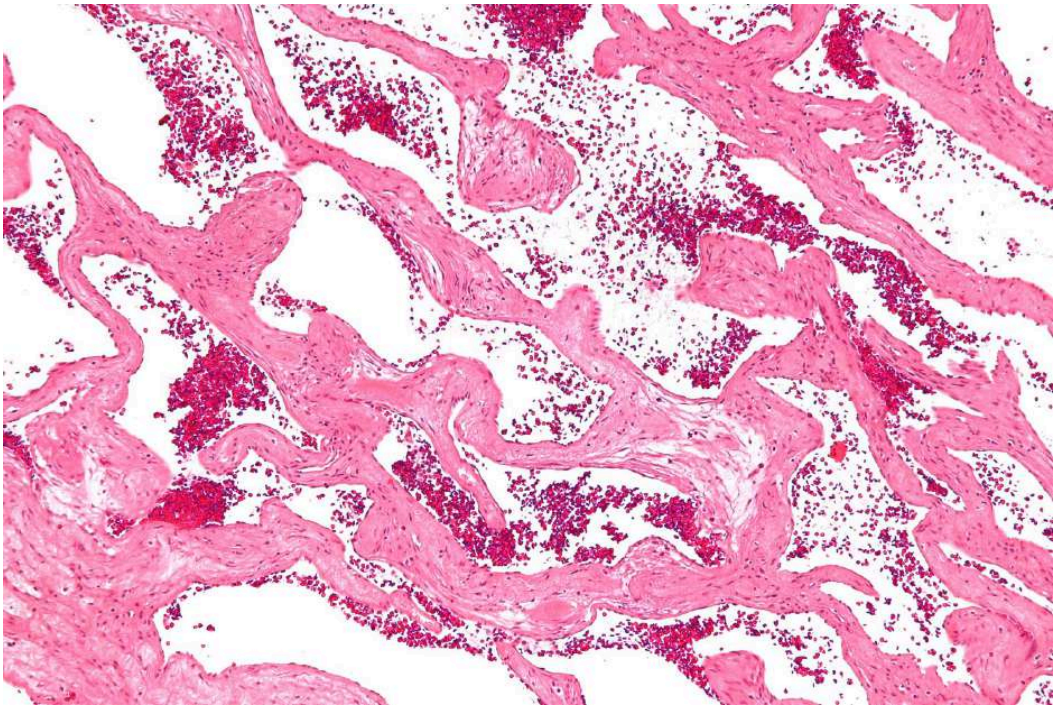
Correct Answer

A - Cavernous hemangioma

Image



Explanation Why

Cavernous hemangioma is the most common type of benign tumor of the liver. It is typically asymptomatic, but large hepatic hemangiomas can cause nonspecific symptoms (e.g., abdominal discomfort, early satiety, nausea). On histology, endothelium-lined blood-filled sinuses that stain positive for endothelial markers, including PECAM-1, are characteristic. However, normal flat endothelial cells rather than pleomorphic spindle cells would be seen. Moreover, cavernous hemangiomas are most common in adults between 30–50 years of age and, given their benign nature, would be unlikely to cause significant weight loss or hepatomegaly.

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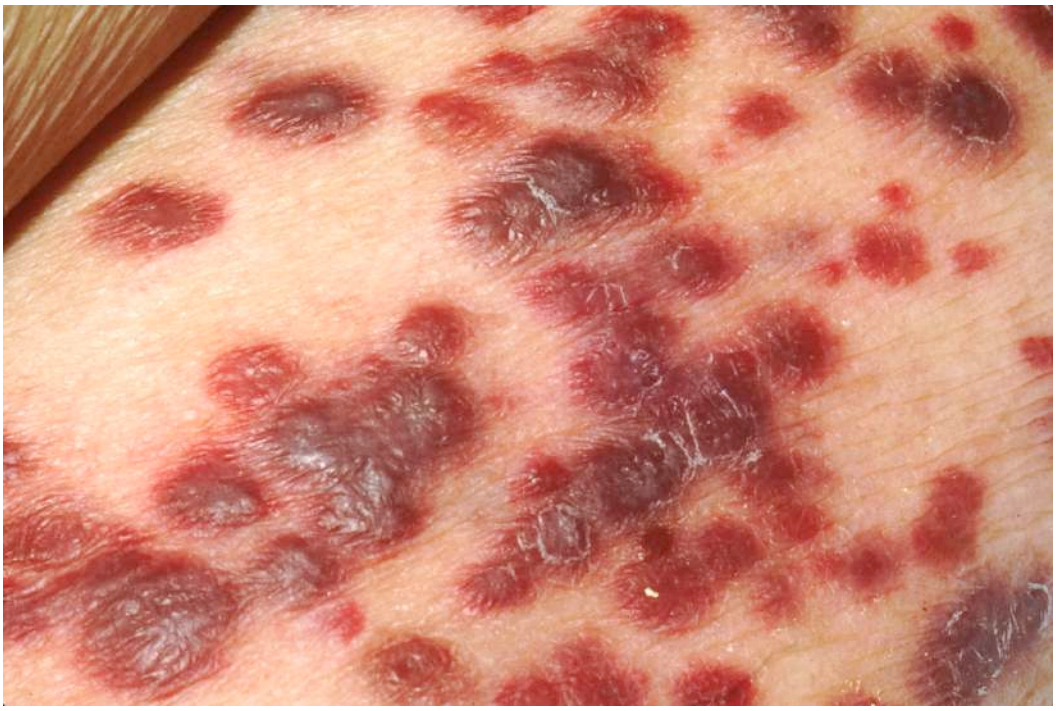
B - Kaposi sarcoma

Image



Explanation Why

Kaposi sarcoma is a malignant spindle cell tumor associated with human herpesvirus 8 that typically affects the skin but may occasionally also involve the gastrointestinal tract, oral cavity, or the respiratory system. Patients generally present with solitary or multiple purplish, nodular, submucosal, and painless plaques, none of which are present here. In addition, Kaposi sarcoma occurs predominantly in immunosuppressed individuals (e.g., AIDS patients). Finally, vinyl chloride exposure is not a known risk factor for Kaposi sarcoma.

C - Angiosarcoma

Explanation But

In contrast, nonhepatic angiosarcomas are particularly rare.

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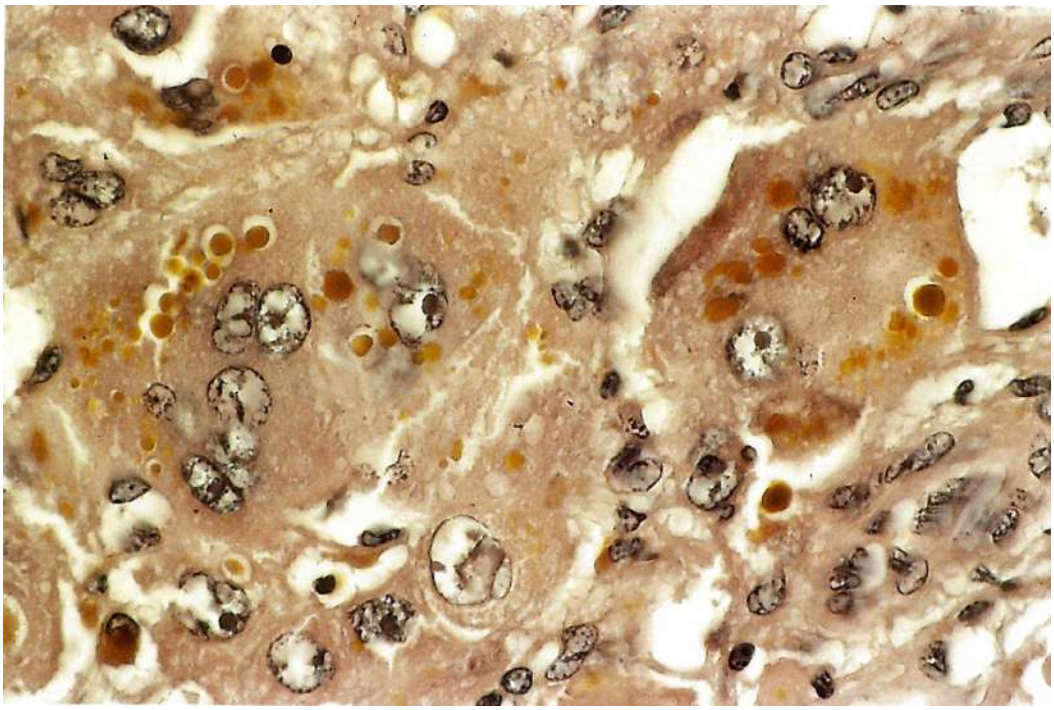
Explanation Why

Hepatic angiosarcomas are the third most common type of primary hepatic malignancy, and their occurrence is associated with exposure to vinyl chloride, which is likely an occupational hazard in this patient, as well as arsenic and thorium dioxide. Hepatic angiosarcomas have a poor prognosis due to their high recurrence rate and resistance to chemotherapy and radiotherapy. Immunophenotyping of tumor cells in hepatic angiosarcoma will be positive for PECAM-1 (also known as CD31), a vascular antigen that indicates the presence of endothelial cells.

D - Hepatocellular carcinoma

Image



Explanation Why

Hepatocellular carcinoma (HCC) should be suspected patients with liver masses and a history of hepatitis B and/or C, Wilson disease, α_1-antitrypsin deficiency, or alcoholic liver cirrhosis. Exposure to aflatoxin and some synthetic azo dyes also is associated with the development of hepatocellular carcinoma. However, vinyl chloride is not a known risk factor for HCC and a biopsy sample of HCC would not stain positive for PECAM-1.

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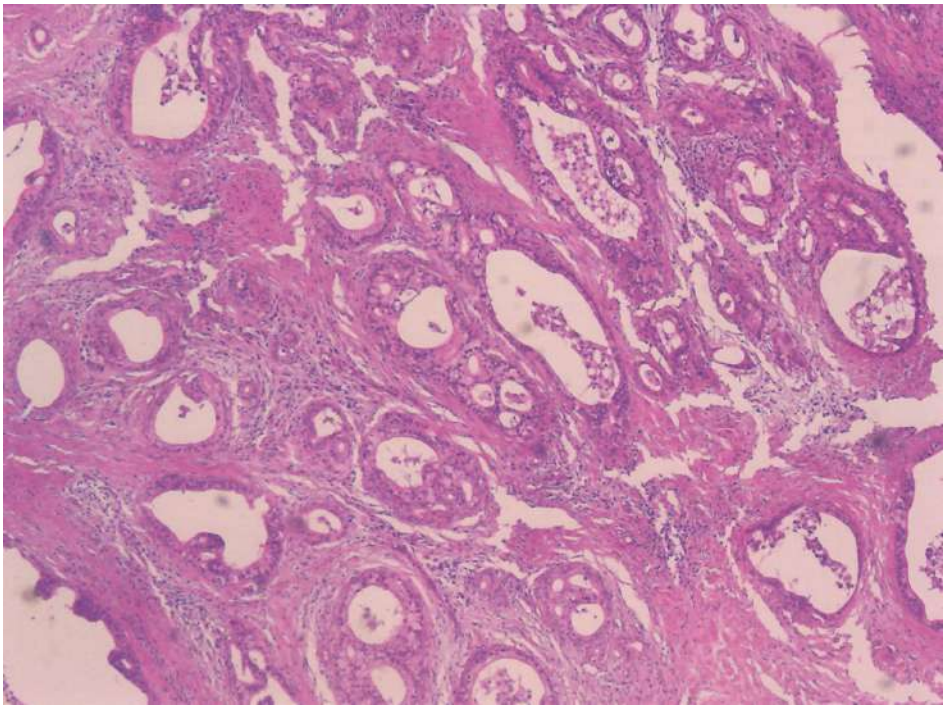
E - Hepatic adenoma

Explanation Why

Hepatic adenoma is a rare, benign liver tumor most commonly associated with increased levels of estrogen. Thus, it usually affects women aged 20–40 on oral contraceptive pills, not elderly men. The use of anabolic steroids and certain diseases, such as glycogen storage disorders and iron overload disorders, are also associated with the development of hepatic adenomas. Vinyl chloride exposure, however, is not a known risk factor for hepatic adenoma, and the presence of PECAM-1 on biopsy suggests a different diagnosis.

F - Cholangiocarcinoma

Image



Explanation Why

Cholangiocarcinoma is a carcinoma of the bile ducts that can occur intrahepatically as well as

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extrahepatically. Classic symptoms of this tumor include cholestasis, a painlessly enlarged gallbladder (Courvoisier sign), and diffuse abdominal discomfort, none of which this patient has. Furthermore, this patient lacks any primary risk factors for this disease (e.g., primary sclerosing cholangitis, choledochal cyst), and the presence of PECAM-1 on biopsy suggests a different diagnosis.

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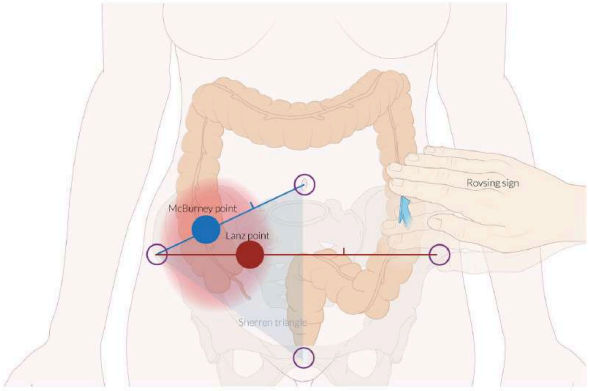
Question # 34

A 15-year-old girl is brought to the physician by her mother for a 2-day history of abdominal pain, nausea, vomiting, diarrhea, and decreased appetite. Her last menstrual period was 3 weeks ago. Her temperature is 37.6°C (99.7°F). Abdominal examination shows tenderness to palpation with guarding in the right lower quadrant. Laboratory studies show a leukocyte count of 12,600/mm^3. Which of the following is the most likely underlying cause of this patient's condition?

	Answer	Image
A	Bacterial mesenteric lymphadenitis	
B	Pseudomembranous plaque formation in the colon	
C	Diverticular inflammation	
D	Congenital anomaly of the omphalomesenteric duct	
E	Lymphatic tissue hyperplasia	
F	Gestation in the fallopian tube	

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Hint

The incidence of this patient's condition peaks between 10–19 years of age.

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Correct Answer

A - Bacterial mesenteric lymphadenitis

Explanation Why

Bacterial mesenteric lymphadenitis is the underlying etiology of pseudoappendicitis. The disease manifests with right lower quadrant pain, fever, vomiting, and leukocytosis, identical to the findings observed in this patient. However, pseudoappendicitis primarily affects children under 5 years of age.

B - Pseudomembranous plaque formation in the colon

Explanation Why

Pseudomembranous plaque formation in the colon is a distinctive feature of *Clostridioides difficile* colitis. The disease manifests with diarrhea, fever, abdominal pain, and leukocytosis, similar to the symptoms seen in this patient. However, *C. difficile* colitis is predominantly an antibiotic-associated diarrhea, and this patient has no history of antibiotic intake. Moreover, *Clostridioides difficile* colitis primarily occurs in patients older than 65 years (often after recent hospitalization) and would be unlikely in this 15-year-old patient.

C - Diverticular inflammation

Explanation Why

Diverticular inflammation (diverticulitis) can manifest with low-grade fevers, loss of appetite, diarrhea, vomiting, and abdominal pain (typically left lower quadrant pain). However, diverticulitis primarily occurs in patients older than 60 years and would be unlikely in this 15-year-old patient.

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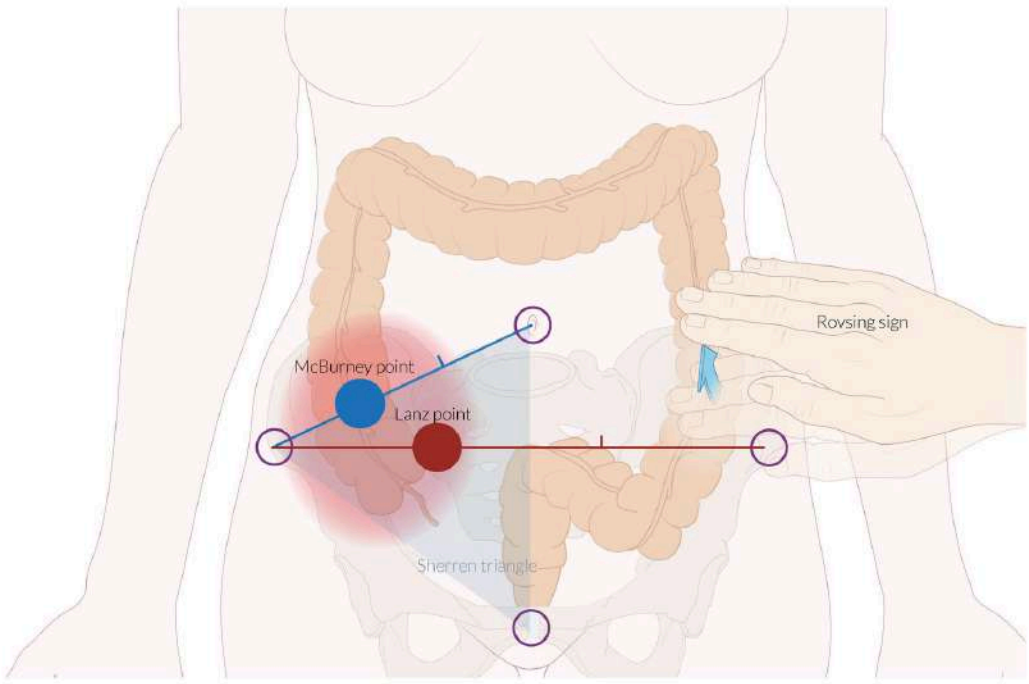
D - Congenital anomaly of the omphalomesenteric duct

Explanation Why

A congenital anomaly of the omphalomesenteric duct is the underlying cause of Meckel diverticulum. This true diverticulum may contain gastric and/or pancreatic tissue. The ectopic activity of these tissues can result in abdominal pain, nausea and vomiting, and loss of appetite. However, most cases of Meckel diverticula remain asymptomatic. Symptomatic Meckel diverticula most commonly present with painless gastrointestinal bleeding, which this patient does not have. Moreover, patients with Meckel diverticula are most likely to present with symptoms in the first two years of life.

E - Lymphatic tissue hyperplasia

Image



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Explanation But

Less common etiologies of appendicitis include obstruction due to foreign bodies, worm infestations, and tumors (e.g., carcinoid tumor).

Explanation Why

This patient most likely presents with acute appendicitis. Lymphatic tissue hyperplasia is the primary etiology of appendicitis in children; fecalith obstruction is the most common etiology in adults. Obstruction within the appendix results in mucus and fluids stasis, allowing bacterial overgrowth and ultimately causing inflammation of the organ. Patients with appendicitis typically present with abdominal pain (dull migratory periumbilical pain that progresses to sharp right lower quadrant pain), fever, loss of appetite, nausea, and leukocytosis, as seen in this patient.

F - Gestation in the fallopian tube

Explanation Why

Gestation in the fallopian tube results in ectopic pregnancy. Patients with ectopic pregnancy often experience lower unilateral abdominal pain resulting in guarding, vomiting, and a loss of appetite. However, ectopic pregnancies usually become symptomatic about 7–8 weeks after the last menses, and this patient had her last menses only 3 weeks ago.

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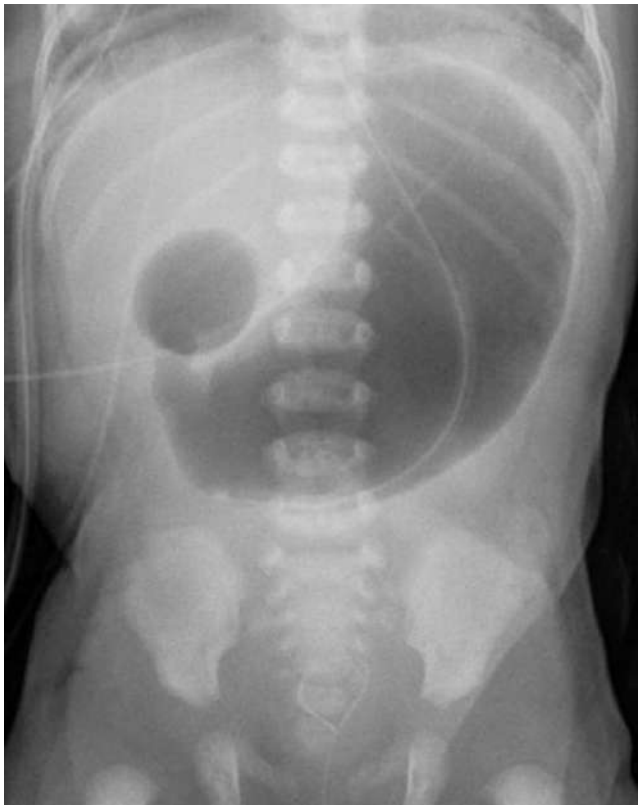
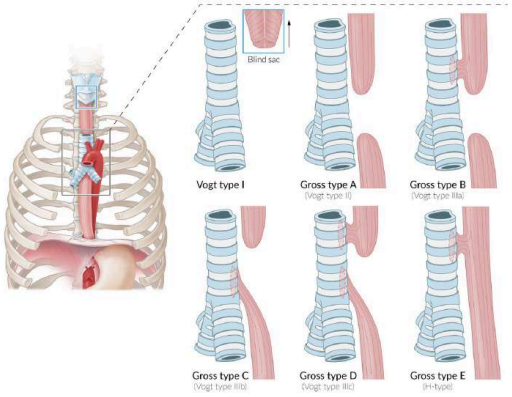
Question # 35

A female newborn delivered at 38 weeks' gestation is evaluated for abdominal distention and bilious vomiting 24 hours after delivery. The pregnancy and delivery were uncomplicated. She appears lethargic and her fontanelles are sunken. An x-ray of the abdomen is shown. This infant most likely has a congenital obstruction affecting which of the following anatomic structures?



	Answer	Image
A	Esophagus	

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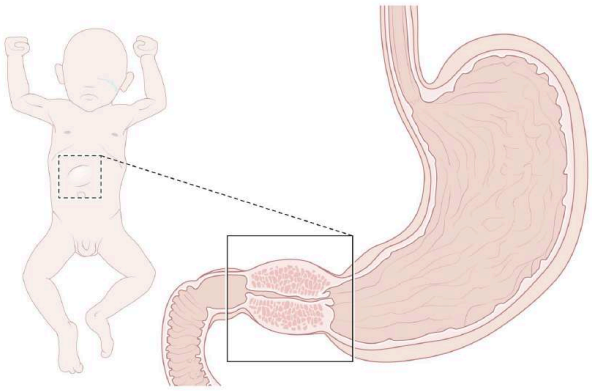
	Answer	Image
B	Common bile duct	
C	Ileum	
D	Pylorus	
E	Duodenum	

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Hint

This condition is strongly associated with trisomy 21.

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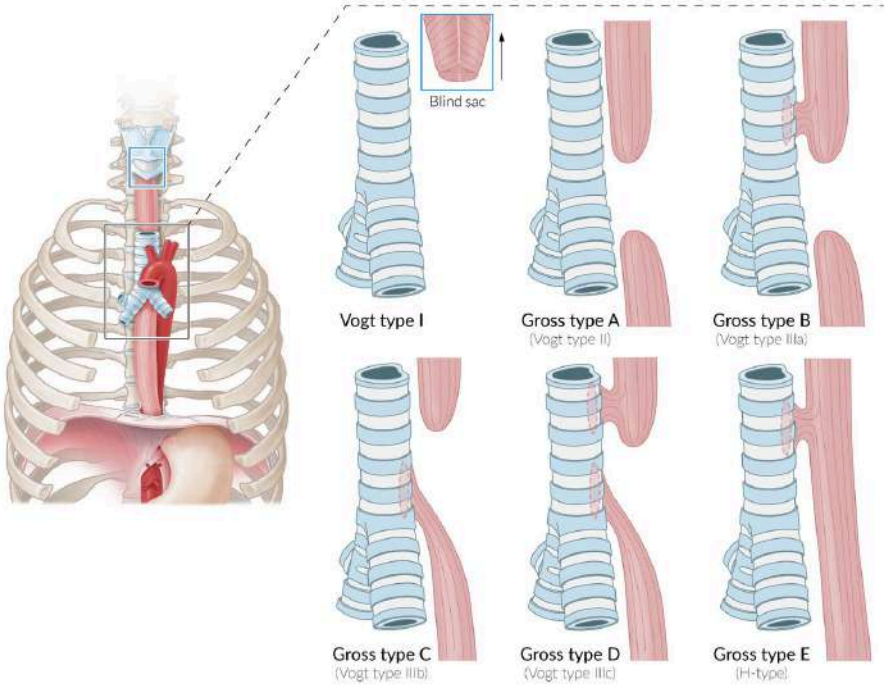
Correct Answer

A - Esophagus

Image



Explanation Why

Congenital obstruction of the esophagus most commonly occurs concurrently with a tracheoesophageal fistula. Although there may be vomiting from esophageal obstruction and gastric distension from air passing from the trachea into the distal esophageal segment as seen in this case, the condition would manifest immediately after birth and the vomitus would be non-bilious.

B - Common bile duct

Explanation Why

Obstruction of the common bile duct, as seen in biliary atresia, causes cholestatic jaundice. This

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patient has bowel obstruction, as evidenced by her abdominal distension, vomiting, dehydration, and dilated bowel on x-ray, but no features of biliary obstruction.

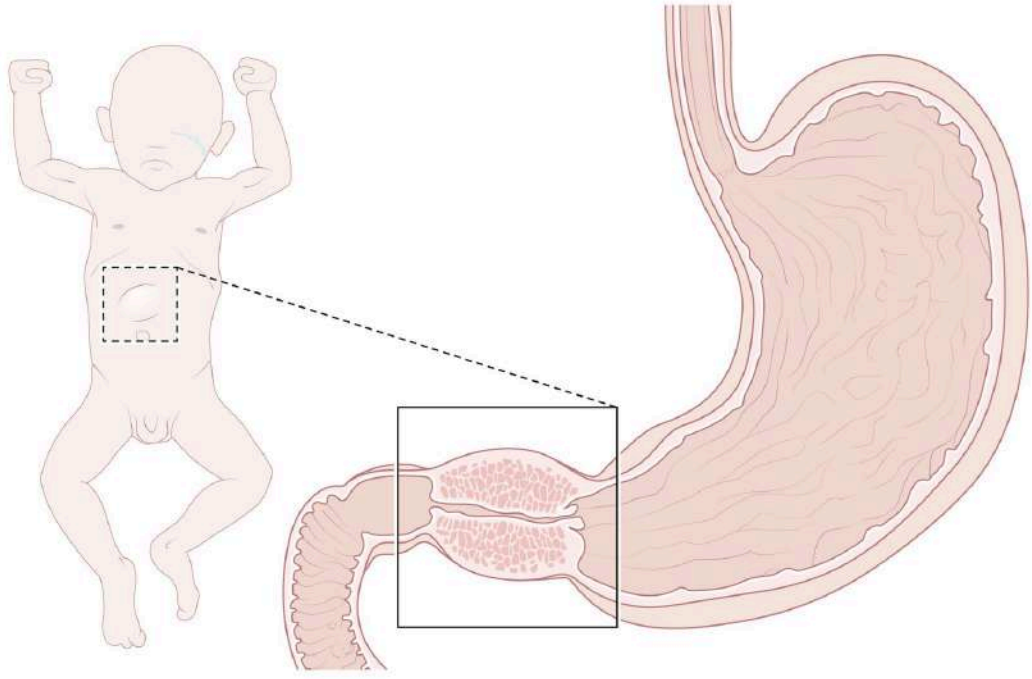
C - Ileum

Explanation Why

Congenital atresia of the ileum would manifest with abdominal distension and vomiting in the first few days of life, as seen in this case. However, an x-ray would show dilated loops of small bowel extending to the level of the obstruction. The x-ray here shows only a very short section of dilated small bowel.

D - Pylorus

Image



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Explanation Why

Obstruction at the pylorus, which is seen in hypertrophic pyloric stenosis, results in vomiting and gastric distension, but the vomitus would be non-bilious since the obstruction is proximal to the major duodenal ampulla. An x-ray would show a stomach distended with air, but not air in the duodenum as seen in this patient. Furthermore, hypertrophic pyloric stenosis becomes symptomatic later, 3–5 weeks after birth.

E - Duodenum

Explanation Why

This patient has congenital duodenal atresia, which causes bowel obstruction just distal to the major duodenal ampulla leading to abdominal distension, bilious vomiting, and features of dehydration (e.g., sunken anterior fontanelle). Her x-ray shows the classic "double bubble sign" of air in a distended stomach and proximal duodenum, which are separated by the pylorus, with no gas in the more distal bowel. Approximately 25% of cases are associated with trisomy 21.

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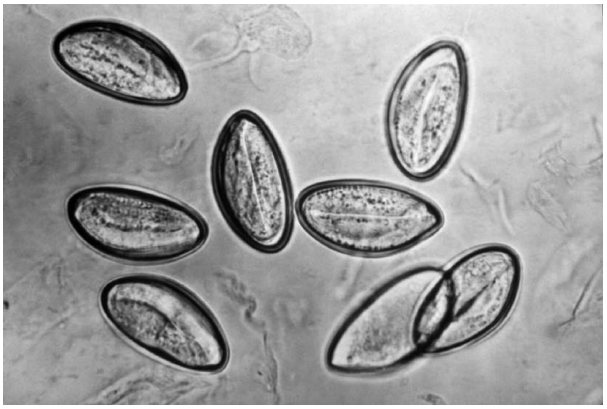
Question # 36

A 38-year-old man comes to the physician because of a 2-week history of abdominal pain and an itchy rash on his buttocks. He also has fever, nausea, and diarrhea with mucoid stools. One week ago, the patient returned from Indonesia, where he went for vacation. Physical examination shows erythematous, serpiginous lesions located in the perianal region and the posterior thighs. His leukocyte count is 9,000/ mm^3 with 25% eosinophils. Further evaluation is most likely to show which of the following findings?

	Answer	Image
A	Rhabditiform larvae on stool microscopy	
B	Eggs on tape test	
C	Oocysts on acid-fast stool stain	
D	Giardia lamblia antibodies on stool immunoassay	
E	Branching septate hyphae on KOH preparation	
F	Entamoaeba histolytica antibodies on stool immunoassay	

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Hint

This patient's fever, gastrointestinal symptoms (abdominal pain, nausea, and diarrhea), serpiginous rash, eosinophilia, and recent travel to a tropical area are highly suggestive of strongyloidiasis.

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Correct Answer

A - Rhabditiform larvae on stool microscopy

Explanation Why

Detection of rhabditiform larvae on stool microscopy is diagnostic of strongyloidiasis. *Strongyloides stercoralis* is transmitted by larval penetration of intact skin (usually when bare feet come into contact with contaminated soil). Larvae travel to the alveoli through the bloodstream, where they ascend the pulmonary system to the pharynx before being coughed up and swallowed. Once in the GI tract, they develop into adult female worms and reproduce via parthenogenesis, with the eggs hatching as rhabditiform larvae. Rhabditiform larvae then develop into infective filariform larvae, penetrating intestinal mucosa or the skin of the perianal region, which completes the process of autoinfection. This patient's serpiginous rash and gastrointestinal symptoms are manifestations of the cutaneous and intestinal phases of infection.

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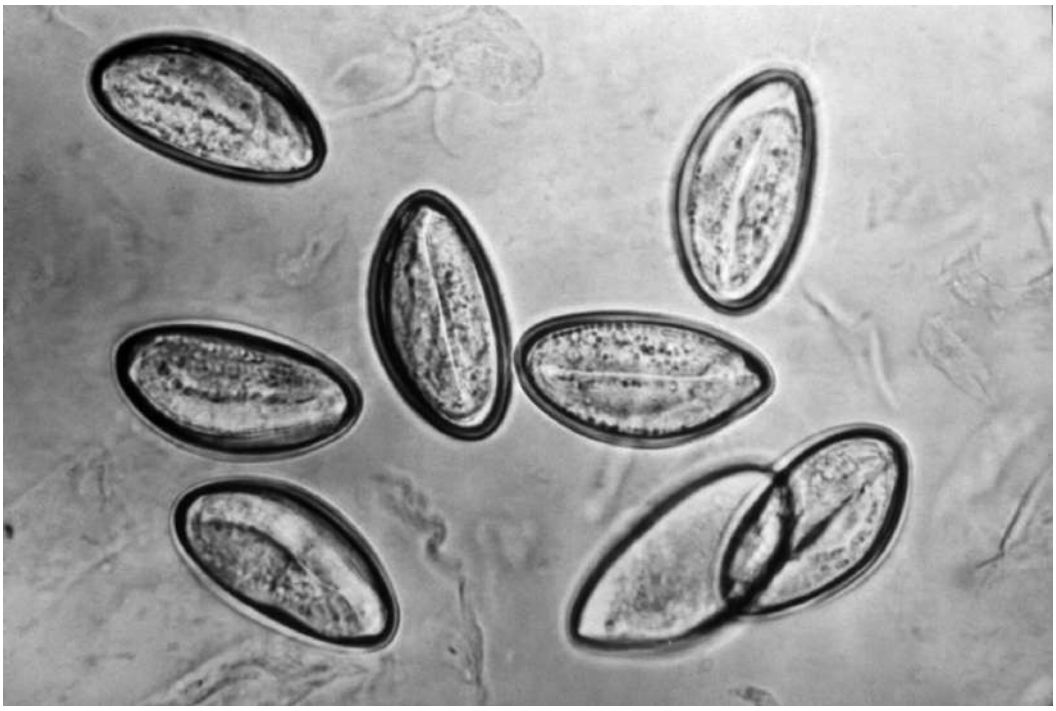
B - Eggs on tape test

Image



Explanation Why

Detection of eggs on a tape test is diagnostic of enterobiasis, which causes nausea, abdominal pain, and pruritus. However, pruritus in enterobiasis is typically limited to the perianal region and is not associated with an erythematous, serpiginous rash extending onto the buttocks and thighs. Furthermore, this condition is most commonly seen in pediatric patients.

C - Oocysts on acid-fast stool stain

Explanation Why

Detection of oocysts on acid-fast stain is diagnostic of cryptosporidiosis. Abdominal pain, nausea, and persistent diarrhea are features of cryptosporidiosis and outbreaks occur worldwide, including Indonesia, especially among travelers. However, cryptosporidiosis would not explain this patient's

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eosinophilia and erythematous, serpiginous rash on his thighs and buttocks.

D - Giardia lamblia antibodies on stool immunoassay

Explanation Why

Detection of *Giardia lamblia* antibodies in the stool is diagnostic of giardiasis. Abdominal pain and diarrhea are features of giardiasis and infection is more likely after travel to a tropical region (e.g., Indonesia). However, giardiasis would not explain this patient's eosinophilia or erythematous, serpiginous rash on his thighs and buttocks.

E - Branching septate hyphae on KOH preparation

Explanation Why

Detection of branching septate hyphae on a KOH preparation is diagnostic of a dermatophyte infection (i.e., tinea), which typically manifests as a pruritic rash. However, the rash seen in tinea is characterized by pruritic plaques with central clearing and raised borders, in contrast to the erythematous, serpiginous rash seen in this patient. Furthermore, tinea infection does not typically cause systemic symptoms such as fever or intestinal symptoms such as abdominal pain, nausea, or diarrhea.

F - Entamoaeba histolytica antibodies on stool immunoassay

Explanation Why

Detection of *Entamoeba histolytica* antibodies on stool immunoassay is diagnostic of amebiasis, which causes fever, abdominal pain, and diarrhea. While the diarrhea has a mucoid component, it is also associated with bright red blood, which is not seen in this patient. Furthermore, amebiasis would not explain this patient's erythematous, serpiginous rash over the thighs and buttocks.

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Question # 37

A 44-year-old man comes to the physician because of fatigue and increased straining during defecation for 3 months. During this time, he has lost 5 kg (12 lb) despite no change in appetite. He has a family history of colon cancer in his maternal uncle and maternal grandfather. His mother died of ovarian cancer at the age of 46. Physical examination shows conjunctival pallor. His hemoglobin concentration is 11.2 g/dL, hematocrit is 34%, and mean corpuscular volume is 76 μm^3. Colonoscopy shows an exophytic mass in the ascending colon. Pathologic examination of the resected mass shows a poorly differentiated adenocarcinoma. Genetic analysis shows a mutation in the *MSH2* gene. Which of the following is the most likely diagnosis?

	Answer	Image
A	Familial adenomatous polyposis	
B	Li-Fraumeni syndrome	
C	Turcot syndrome	
D	Peutz-Jeghers syndrome	
E	Gardner syndrome	
F	Lynch syndrome	

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Hint

Mutations in the *MSH2* DNA mismatch repair gene lead to microsatellite instability. In addition to having an increased risk of colorectal cancer, individuals with this mutation are more likely to develop other cancers such as endometrial, ovarian, and gastric carcinomas.

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Correct Answer

A - Familial adenomatous polyposis

Explanation Why

Familial adenomatous polyposis (FAP) is an autosomal dominant condition caused by a mutation in the tumor suppressor gene *APC*. Affected individuals have hundreds of colonic polyps that typically develop in the second and third decades of life. The lifetime risk of colorectal cancer is 100% by 45 years of age. This patient's *MSH2* gene mutation and lack of polyps on colonoscopy are inconsistent with FAP.

B - Li-Fraumeni syndrome

Explanation Why

Li-Fraumeni syndrome is an autosomal dominant condition caused by a mutation in the *p53* tumor suppressor gene. Subsequent loss of heterozygosity results in the development of multiple malignancies (e.g., sarcomas, adrenal gland and breast cancer, leukemia) at an early age. This patient's *MSH2* gene mutation is consistent with a different condition.

C - Turcot syndrome

Explanation Why

Turcot syndrome is a variant of either familial adenomatous polyposis (FAP) or Lynch syndrome. It is associated with an increased risk for colorectal cancer as well as malignant CNS tumors (e.g., medulloblastoma with FAP, glioma with Lynch syndrome). Although *MSH2* mutations can be found in patients with Turcot syndrome, lack of evidence of a CNS tumor in this patient makes this diagnosis unlikely.

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D - Peutz-Jeghers syndrome

Explanation Why

Peutz-Jeghers syndrome (PJS) is an autosomal dominant condition associated with a mutation in the *STK11* gene. PJS manifests with multiple hamartomatous polyps throughout the gastrointestinal tract (predominantly in the jejunum) and mucocutaneous hyperpigmentation of the lips, buccal mucosas, palms, and soles. Individuals with PJS have an increased risk for colorectal cancer (~ 40% lifetime risk) as well as for extraintestinal cancers (e.g., ovarian, breast, pancreatic cancer). This patient's *MSH2* gene mutation, lack of polyps on colonoscopy, and absence of mucocutaneous hyperpigmentation are inconsistent with PJS.

E - Gardner syndrome

Explanation Why

Gardner syndrome is a subtype of familial adenomatous polyposis (FAP) caused by an autosomal dominant mutation in the tumor suppressor gene *APC*. Gardner syndrome is characterized by the presence of hundreds of colonic polyps together with bony and/or soft tissue tumors (e.g., osteomas, desmoid tumors, lipomas, fibromas). The lifetime risk of developing colorectal cancer is 100%. This patient's *MSH2* gene mutation, lack of polyps on colonoscopy, and absence of extracolonic bony and/or soft tissue tumors are inconsistent with Gardner syndrome.

F - Lynch syndrome

Explanation Why

Lynch syndrome is a familial cancer syndrome caused by autosomal dominant mutations in DNA mismatch repair genes (e.g., *MSH2, MLH1*). Individuals with this syndrome have an ~ 80% lifetime risk of developing colorectal cancer (typically in the proximal colon). While genetic testing is the test of choice to confirm the diagnosis, the family history-based Amsterdam II criteria can be used to identify individuals who are likely to be affected ("3-2-1 rule": Lynch syndrome-associated cancer in ≥ 3 family members, within 2 generations, and in 1 relative under 50 years of age). This patient

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fulfills the Amsterdam II criteria.

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Question # 38

A 34-year-old woman, gravida 3, para 2, at 16 weeks' gestation comes to the physician because of nausea and recurrent burning epigastric discomfort for 1 month. Her symptoms are worse after heavy meals. She does not smoke or drink alcohol. Examination shows a uterus consistent in size with a 16-week gestation. Palpation of the abdomen elicits mild epigastric tenderness. The physician prescribes her medication to alleviate her symptoms. Treatment with which of the following drugs should be avoided in this patient?

	Answer	Image
A	Pantoprazole	
B	Misoprostol	
C	Magnesium hydroxide	
D	Cimetidine	
E	Sucralfate	

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Hint

The medication that should be avoided for treatment of this patient's dyspepsia is sometimes used off-label to induce labor by ripening the cervix.

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Correct Answer

A - Pantoprazole

Explanation Why

Pantoprazole and other commonly used proton pump inhibitors (PPIs) are safe to use throughout pregnancy and are a preferred treatment option for dyspepsia in pregnant women.

B - Misoprostol

Explanation Why

Misoprostol is contraindicated during pregnancy because it is associated with an increased risk of abortion and congenital malformations. Misoprostol is a prostaglandin (PGE_1) analog that can prevent NSAID-induced peptic ulcer formation by increasing the production of the gastric mucus barrier and decreasing gastric acid secretion. In pregnancy, misoprostol can be used off-label for cervical ripening in labor induction and in combination with a progesterone antagonist for medical abortion.

C - Magnesium hydroxide

Explanation Why

Magnesium hydroxide neutralizes gastric acid in the stomach and also acts as an osmotic laxative. Taken orally, a small amount of magnesium is absorbed systemically into the maternal serum and is able to cross the placenta. However, no adverse fetal side effects associated with the oral intake of magnesium hydroxide have been reported, making it safe to use during pregnancy for the treatment of dyspepsia and/or constipation.

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D - Cimetidine

Explanation Why

Cimetidine is an H2-blocker that reduces gastric acid production. Although it crosses the placenta, no adverse fetal effects associated with the use of this drug have been reported. H2-blockers are a preferred treatment option for dyspepsia in pregnant women.

E - Sucralfate

Explanation Why

Sucralfate acts by forming a protective barrier over the gastric/duodenal mucosa. Only a very small portion is absorbed and sucralfate can be used to treat dyspepsia throughout pregnancy.

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Question # 39

A 6-year-old boy is brought to the physician by his mother because of a 6-month history of mild episodic abdominal pain. The episodes occur every 1–2 months and last for a few hours. The pain is located in the epigastrium, radiates to his back, and is occasionally associated with mild nausea. His mother is concerned that his condition might be hereditary because his older sister was diagnosed with congenital heart disease. He is otherwise healthy and has met all developmental milestones. He is at the 75^{th} percentile for height and the 65^{th} percentile for weight. Physical examination shows no abdominal distention, guarding, or rebound tenderness. Which of the following congenital conditions would best explain this patient's symptoms?

	Answer	Image
A	Duodenal atresia	
B	Hypertrophic pyloric stenosis	
C	Biliary cyst	
D	Tracheoesophageal fistula	
E	Intestinal malrotation	

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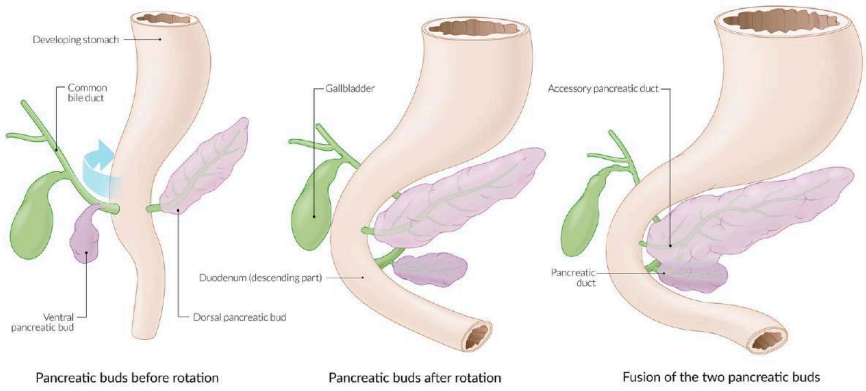
	Answer	Image
F	Pancreas divisum	

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Hint

This patient's episodic nausea with epigastric pain that radiates to the back suggests recurrent acute pancreatitis.

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Correct Answer

A - Duodenal atresia

Explanation Why

Duodenal atresia manifests within the first 1–2 days of life with delayed meconium passage, vomiting, epigastric distention, and a scaphoid lower abdomen. Recurrent epigastric pain in a 6-year-old patient is not consistent with this diagnosis.

B - Hypertrophic pyloric stenosis

Explanation Why

Hypertrophic pyloric stenosis typically manifests with postprandial, nonbilious projectile vomiting, visible epigastric peristaltic waves, and a palpable olive-shaped structure in the epigastrium within the first few weeks of life. Recurrent epigastric pain in a 6-year-old patient is not consistent with this diagnosis.

C - Biliary cyst

Explanation Why

A biliary cyst can cause recurrent acute pancreatitis during childhood as a result of pancreatic duct obstruction and pancreaticobiliary reflux. However, patients with pancreatitis due to a biliary cyst would also have obstructive jaundice and a palpable right hypochondrial mass, which are not present here. A different diagnosis is more likely in this patient.

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D - Tracheoesophageal fistula

Explanation Why

A tracheoesophageal fistula typically manifests immediately after birth (following the first feeding) with features of aspiration (e.g., choking, coughing, cyanosis). Recurrent epigastric pain in a 6-year-old boy is not consistent with this diagnosis.

E - Intestinal malrotation

Explanation Why

Intestinal malrotation can manifest in young children with recurrent episodes of abdominal pain as a result of chronic midgut volvulus or chronic duodenal obstruction. However, patients with chronic midgut volvulus would have clinical features of malabsorption syndrome (e.g., diarrhea, failure to thrive) and patients with chronic duodenal obstruction would have episodes of bilious vomiting; the absence of these features and the presence of epigastric pain with radiation to the back suggest a different diagnosis.

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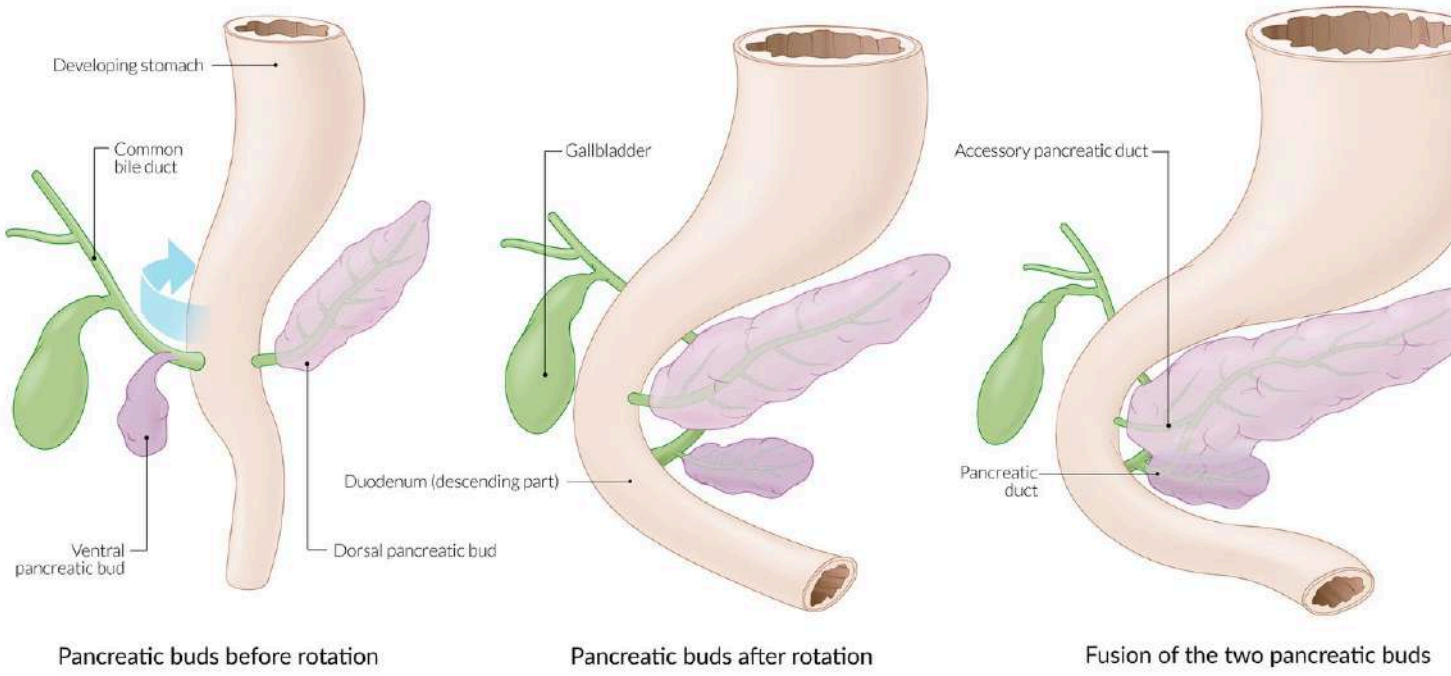
F - Pancreas divisum

Image



Explanation Why

Pancreas divisum is a congenital malformation that is caused by a failure of fusion of the ventral and dorsal pancreatic ducts, which normally join at 8 weeks of gestation. Pancreas divisum is present in about 10% of the population and is usually asymptomatic, but a minority of cases can develop chronic abdominal pain or recurrent episodes of acute pancreatitis, as seen here. Pancreas divisum can be diagnosed by endoscopic ultrasonography or MRCP, which would show a ventral pancreatic duct that drains along with the common bile duct into the major duodenal papilla and a dorsal pancreatic duct that drains separately into the duodenum via the minor duodenal papilla.

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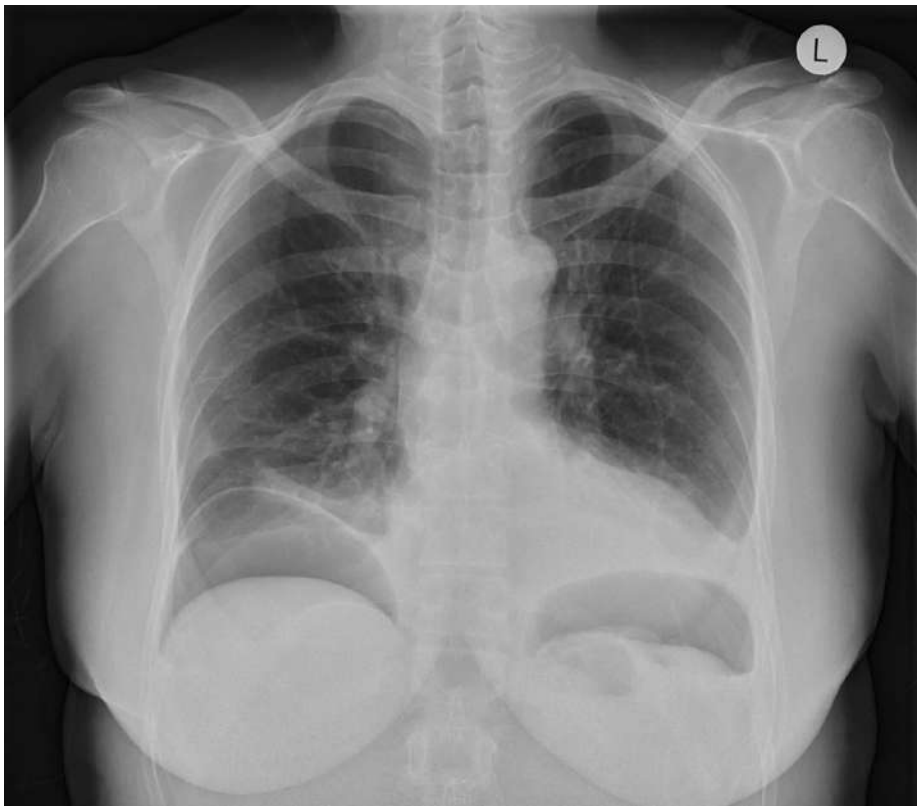
Question # 40

A 54-year-old woman comes to the emergency department because of a 5-hour history of diffuse, severe abdominal pain, nausea, and vomiting. She reports that there is no blood or bile in the vomitus. Two weeks ago, she started having mild aching epigastric pain, which improved with eating. Since then, she has gained 1.4 kg (3 lb). She has a 2-year history of osteoarthritis of both knees, for which she takes ibuprofen. She drinks 1–2 glasses of wine daily. She is lying supine with her knees drawn up and avoids any movement. Her temperature is 38.5°C (101.3°F), pulse is 112/min, respirations are 20/min, and blood pressure is 115/70 mm Hg. Physical examination shows abdominal tenderness and guarding; bowel sounds are decreased. An x-ray of the chest is shown. Which of the following is the most likely cause of this patient's current symptoms?



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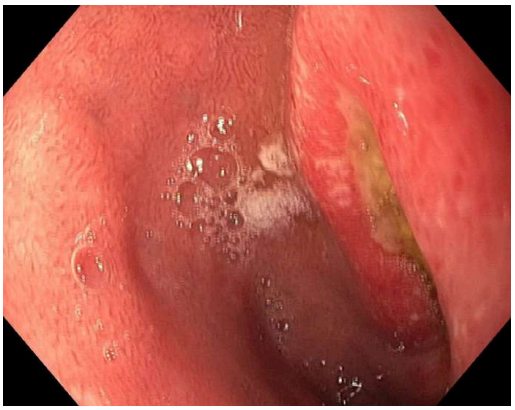
	Answer	Image
A	Perforated peptic ulcer	
B	Acute pancreatitis	
C	Acute mesenteric ischemia	
D	Gastric cancer	
E	Gastroesophageal reflux disease	
F	Cholecystolithiasis	

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Hint

The chest x-ray shows free air below the diaphragm.

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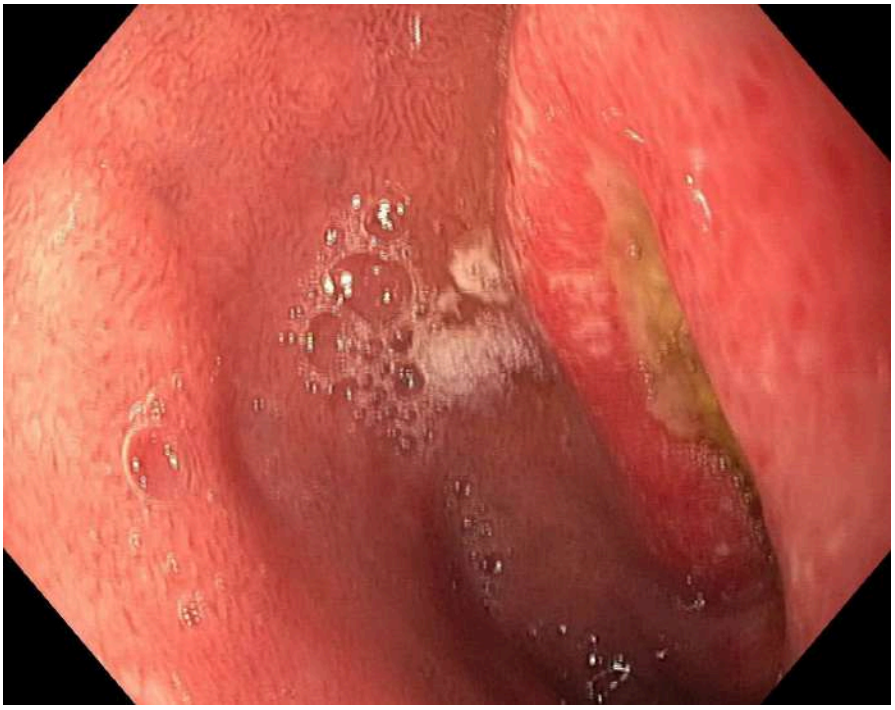
Correct Answer

A - Perforated peptic ulcer

Image



Explanation Why

Perforation of a peptic ulcer can manifest with acute, diffuse abdominal pain, nausea, vomiting, fever, and tachycardia, all of which are seen in this patient. The chest x-ray finding of pneumoperitoneum further supports this diagnosis. Examination findings are typical for secondary peritonitis (abdominal guarding) and developing paralytic ileus (decreased bowel sounds). This patient's recent history of epigastric pain relieved by food intake in combination with regular alcohol consumption and ibuprofen use indicates an underlying duodenal ulcer. Perforation is the second most common complication of peptic ulcer disease (after gastrointestinal bleeding) and most often occurs in duodenal ulcers of the anterior wall, which are less protected than other types of ulcers by surrounding anatomical structures.

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B - Acute pancreatitis

Explanation Why

Acute pancreatitis typically manifests with severe abdominal pain (usually radiating to the back), nausea, and vomiting, and it can be triggered by alcohol use. Examination findings may include fever, tachycardia, abdominal tenderness, signs of peritonitis (abdominal guarding), and reduced bowel sounds (indicating ileus), as seen here. This patient's chest x-ray findings of free intraabdominal gas, however, are not sufficiently explained by acute pancreatitis. Moreover, this patient has a history of epigastric pain that is relieved with food intake whereas pain in pancreatitis usually worsens after meals.

C - Acute mesenteric ischemia

Explanation Why

Acute mesenteric ischemia may manifest with diffuse abdominal pain, nausea, and vomiting, all of which are seen here. Examination findings may show fever, tachycardia, and abdominal tenderness. However, chest x-ray findings of free gas in the abdominal cavity are not a typical feature of this condition. Instead, abdominal x-ray findings in acute mesenteric ischemia would more likely be normal in early stages, with distended intestinal loops and small gas enclosures inside the wall of the intestine (indicating transmural ischemia) appearing in later stages.

D - Gastric cancer

Explanation Why

Gastric cancer may manifest with abdominal pain, nausea, and vomiting, all of which are seen here. However, the acute worsening of this patient's symptoms, as well as the chest x-ray findings of free gas in the abdominal cavity make gastric cancer less likely than another condition. Furthermore, patients with gastric cancer present with weight loss rather than weight gain.

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E - Gastroesophageal reflux disease

Explanation Why

Gastroesophageal reflux disease (GERD) may manifest with abdominal pain, nausea, and vomiting, all of which are seen here. In addition, alcohol consumption is a common trigger of this condition. Patients typically present with chronic epigastric pain that worsens after eating. This patient, however, has a history of epigastric pain that is relieved with food intake. Furthermore, the chest x-ray findings of free gas in the abdominal cavity are not explained by GERD.

F - Cholecystolithiasis

Explanation Why

Cholecystolithiasis is a condition that is typically asymptomatic. A minority of patients may develop biliary colic, which can manifest with right upper quadrant/epigastric pain, nausea, and vomiting. The pain from biliary colic is triggered by eating. This patient, however, has a history of epigastric pain that is relieved with food intake. Moreover, cholecystolithiasis and biliary colic do not sufficiently explain the chest x-ray findings of free intraabdominal gas.

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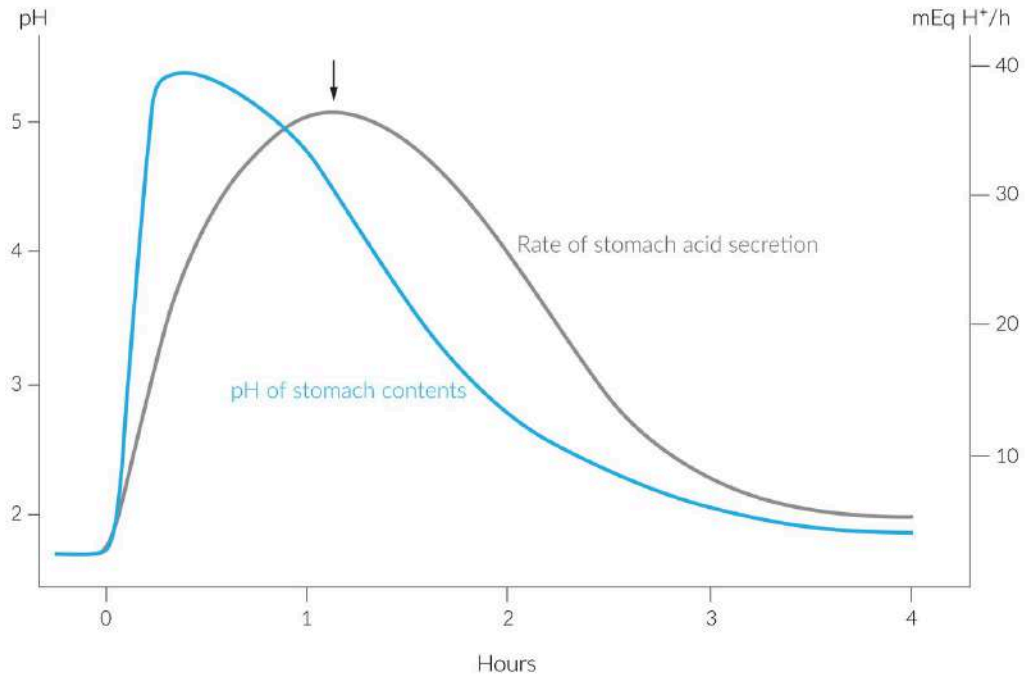
Question # 1

An investigator is studying the effects of different gastrointestinal regulatory substances. A healthy subject is asked to eat a meal at hour 0, and the pH of the stomach contents and the rate of stomach acid secretions are measured over the next 4 hours. The results of the study are shown. Which of the following mechanism most likely contributes to the change in trajectory of the graph at the point marked by the arrow?



	Answer	Image
A	Increased vagal stimulation	

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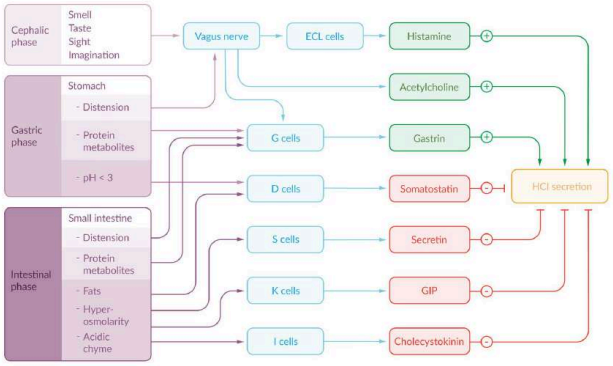
	Answer	Image
B	Increased activity of D cells	
C	Increased activation of H_2 receptors	
D	Increased activity of enterochromaffin-like cells	
E	Increased activity of I cells	

Hint

At the point of the graph marked by an arrow, the rate of stomach acid secretion decreases.

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Correct Answer

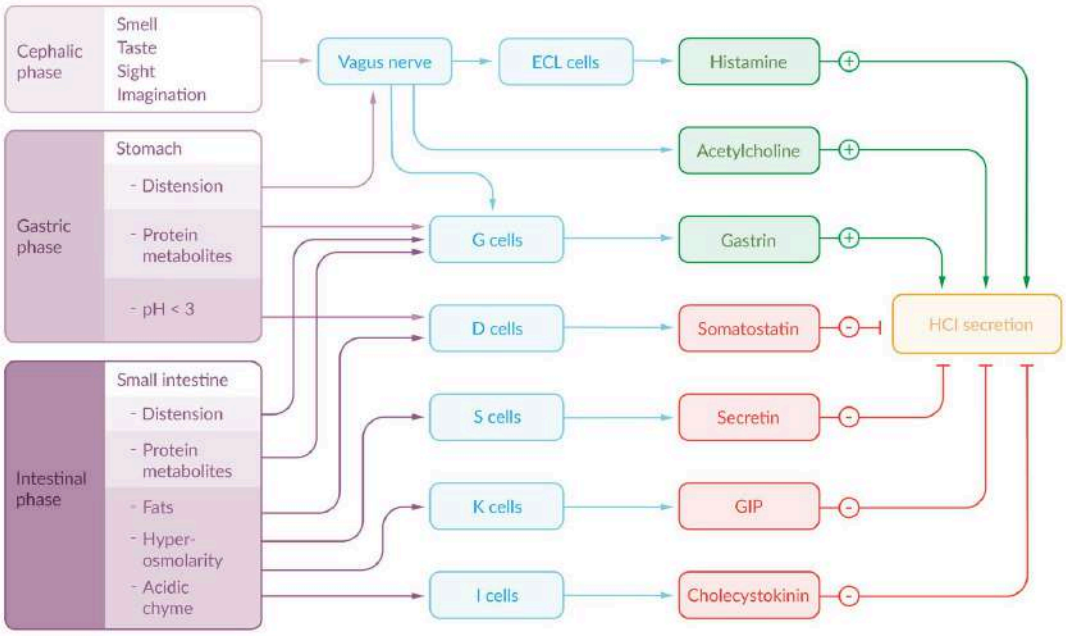
A - Increased vagal stimulation

Explanation Why

Vagal stimulation, which is elicited by the thought, smell, and taste of food, activates muscarinic receptors and increases gastric acid secretion by stimulating parietal cells. This stimulation results in an increased gastrin release and inhibited somatostatin secretion. Prior to the increase in gastric acid secretion, the pH of stomach contents rapidly turns more alkaline due to the buffering effect of food arriving in the stomach. As gastric acid secretion increases, the pH slowly becomes more acidic. The initial increasing slope of gastric acid secretion is consistent with vagal stimulation; the decrease after the arrow is not.

B - Increased activity of D cells

Image



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Explanation Why

D cells secrete somatostatin in response to increased gastrin concentration and/or decreased stomach pH, thereby decreasing gastric acid secretion. Somatostatin release inhibits histamine and, to a lesser extent, also inhibits gastrin release, which corresponds with the change in trajectory marked by the arrow in the graph. The changes to gastric acid secretion are classically categorized into three phases: cephalic, gastric, and intestinal. While gastric acid secretion is increased during the cephalic phase (in response to the thought, sight, and smell of food) and the gastric phase (due to the entry of food into the stomach), the predominant effect during the intestinal phase is inhibitory (due to the release of somatostatin, secretin, GIP, and cholecystokinin).

C - Increased activation of H_2 receptors

Explanation Why

Activation of histaminergic H_2 receptors on parietal cells increases gastric acid secretion and occurs during the gastric phase, which is represented in the graph by the initial increasing slope of gastric acid secretion. The arrow marks a point in the graph where gastric acid secretion decreases, which is not consistent with activation of histaminergic receptors.

D - Increased activity of enterochromaffin-like cells

Explanation Why

Enterochromaffin-like cells secrete histamine in response to stimulation by gastrin, thereby activating histaminergic H2 receptors on parietal cells and increasing gastric acid secretion. This occurs during the gastric phase, which is represented by the initial increasing slope of gastric acid secretion in the graph. The arrow marks a point on the graph where the rate of gastric acid secretion begins to decrease.

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E - Increased activity of I cells

Explanation Why

I cells located in the duodenum and jejunum secrete cholecystokinin (CCK) in response to fatty acids and amino acids. CCK stimulates pancreatic exocrine secretion, gallbladder contraction, and sphincter of Oddi relaxation. CCK can increase or decrease gastric acid secretion based on the type of receptor it acts on, but CCK would not have had as pronounced of an effect on pH so soon after the ingestion of food as that seen in this graph. Another mechanism has a much stronger impact on gastric pH regulation.

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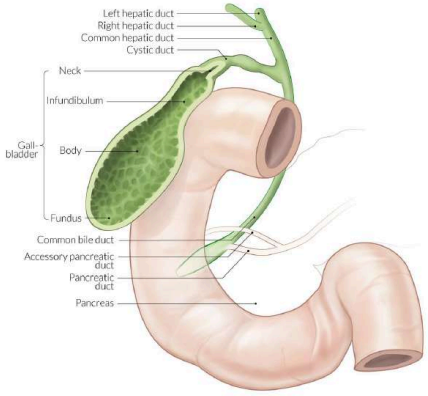
Question # 2

A 41-year-old woman comes to the physician because of an 8-hour history of colicky abdominal pain and nausea. The pain worsened after she ate a sandwich, and she has vomited once. She has no history of serious medical illness. Her temperature is 37.2°C (99.1°F), pulse is 80/min, and blood pressure is 134/83 mm Hg. Physical examination shows scleral icterus and diffuse tenderness in the upper abdomen. Serum studies show:

Total bilirubin	2.7 mg/dL
AST	35 U/L
ALT	38 U/L
Alkaline phosphatase	180 U/L
γ-Glutamyltransferase	90 U/L (N = 5–50)

Ultrasonography is most likely to show a stone located in which of the following structures?

	Answer	Image
A	Common bile duct	
B	Common hepatic duct	

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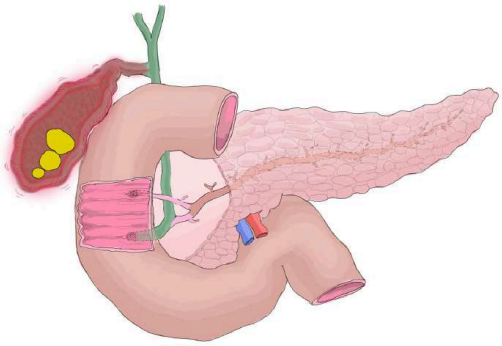
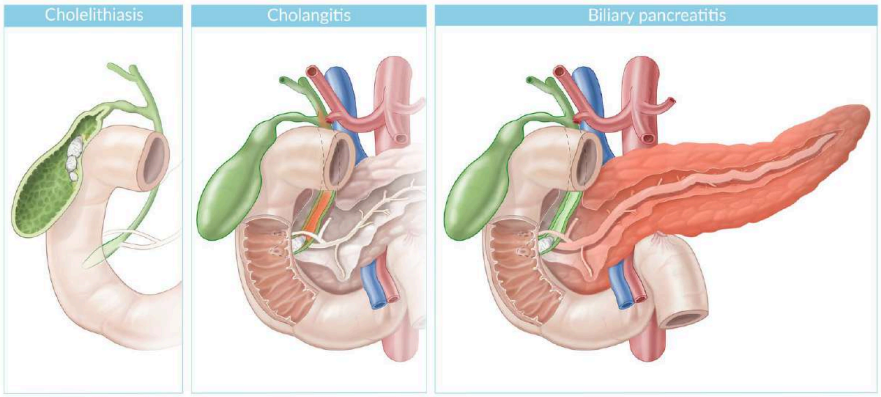
	Answer	Image
C	Cystic duct	
D	Gallbladder neck	
E	Gallbladder fundus	
F	Pancreatic duct	

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Hint

This patient presents with biliary colic (postprandial, colicky abdominal pain, nausea, vomiting). The prolonged episode of pain, signs of extrahepatic cholestasis (scleral icterus, elevated parameters of cholestasis), and absence of fever indicate choledocholithiasis.

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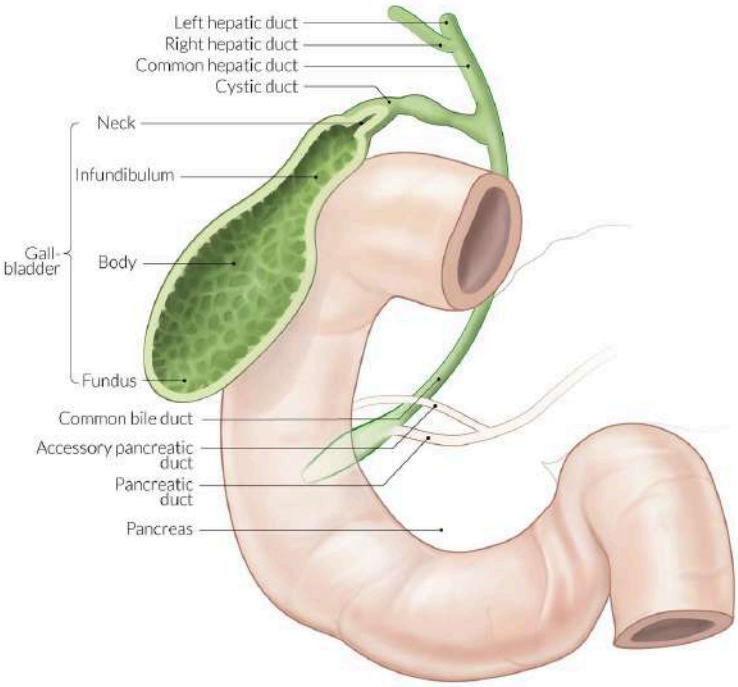
Correct Answer

A - Common bile duct

Image



Explanation But

Choledocholithiasis is treated with spasmolytics, analgesia, and removal of the stone, usually via endoscopic retrograde cholangiopancreatography. An elective laparoscopic cholecystectomy is commonly indicated to prevent a recurrence.

Explanation Why

Choledocholithiasis is the presence of gallstones in the common bile duct and is most commonly a result of the passage of gallstones from the gallbladder. This patient's signs and symptoms are due to common bile duct obstruction (leading to elevated parameters of cholestasis such as γ-glutamyltransferase, alkaline phosphatase, and direct bilirubin) and consequent biliary tract spasms. In addition to the occluding gallstone, ultrasonography typically shows a dilated common bile duct with possible intrahepatic biliary dilatation.

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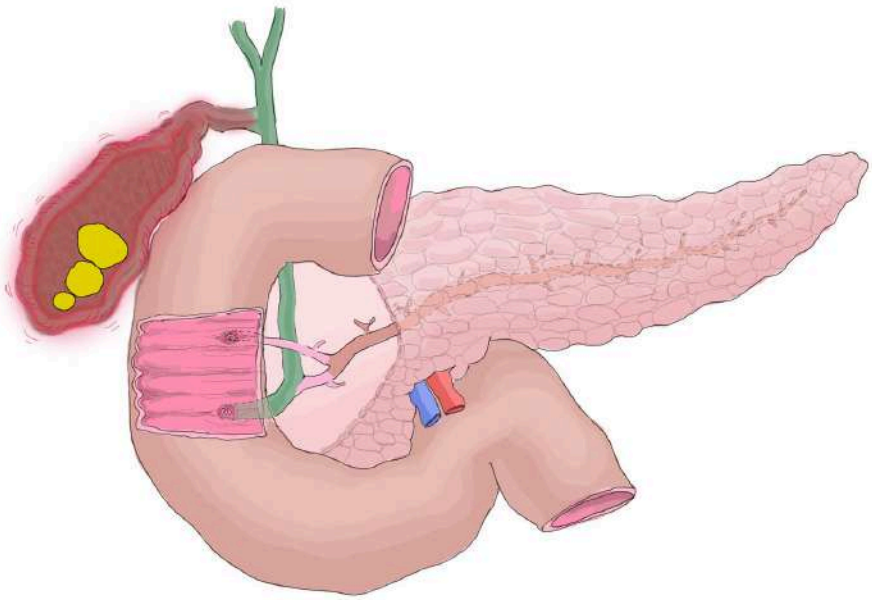
B - Common hepatic duct

Explanation Why

Obstruction of the common hepatic duct can manifest with abdominal pain, scleral icterus, and elevated parameters of cholestasis, all of which are seen here. However, common hepatic duct obstruction is rarely due to intraluminal gallstones; rather, it is caused by extrinsic compression by a gallstone impacted in the cystic duct or gallbladder neck (i.e., Mirizzi syndrome).

C - Cystic duct

Image



Explanation Why

A gallstone obstructing the cystic duct can cause acute cholecystitis, which typically manifests with postprandial abdominal pain, nausea, and vomiting, all of which are seen here. This patient, however, does not present with classic features of acute cholecystitis, such as fever and a positive Murphy

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sign. In addition, scleral icterus, and elevated parameters of cholestasis are uncommon in uncomplicated acute cholecystitis because the flow of bile from the liver into the duodenum is usually not obstructed.

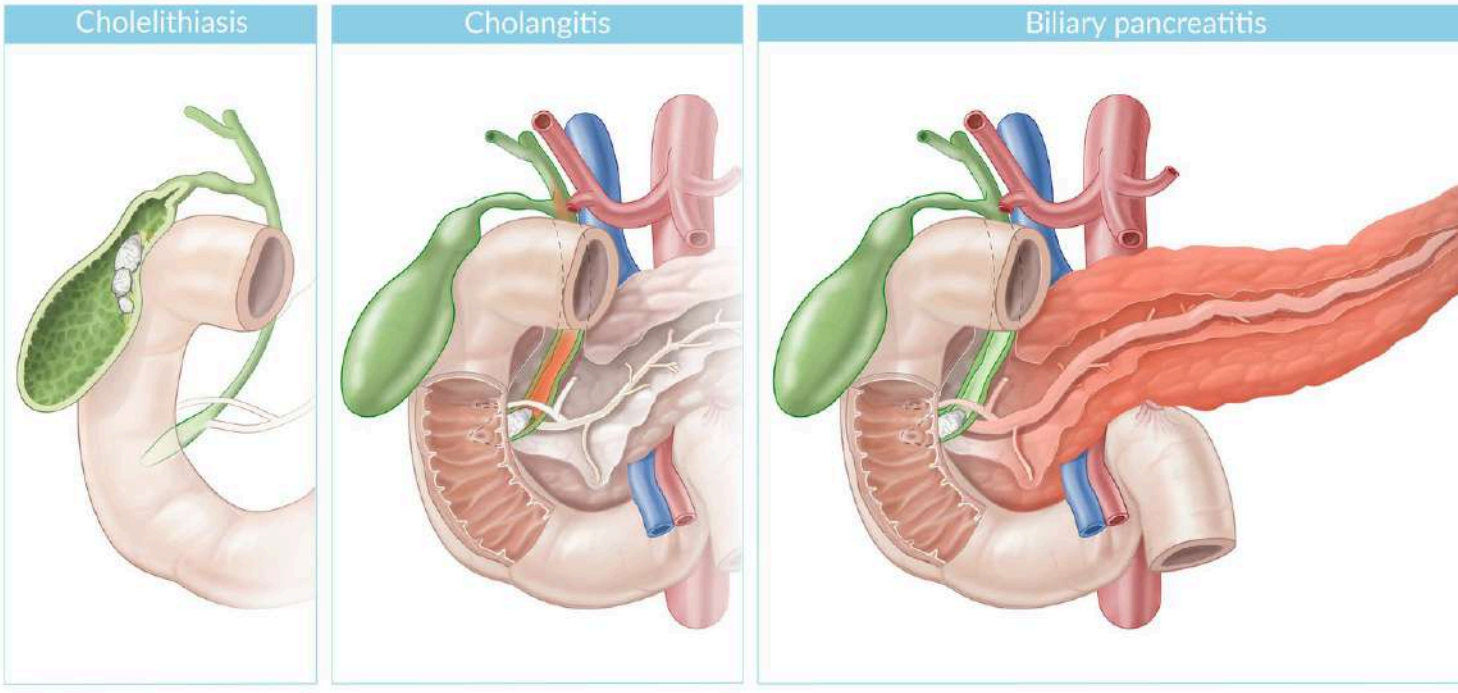
D - Gallbladder neck

Explanation Why

A gallstone obstructing the gallbladder neck can cause acute cholecystitis, which typically manifests with postprandial abdominal pain, nausea, and vomiting, all of which are seen here. This patient, however, does not present with classic features of acute cholecystitis, such as fever and a positive Murphy sign. In addition, scleral icterus, and elevated parameters of cholestasis are uncommon in uncomplicated acute cholecystitis because the flow of bile from the liver into the duodenum is usually not obstructed.

E - Gallbladder fundus

Image



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Explanation Why

Cholelithiasis is the presence of gallstones in the gallbladder (e.g., the fundus). Cholelithiasis is usually asymptomatic but can manifest with postprandial abdominal pain, nausea, and vomiting, all of which are seen here. However, pain lasting for more than 6 hours, scleral icterus, and elevated parameters of cholestasis are inconsistent with cholelithiasis.

F - Pancreatic duct

Explanation Why

Obstruction of the pancreatic duct can cause acute pancreatitis, which can manifest with postprandial abdominal pain, nausea, vomiting, and, in the case of concomitant biliary obstruction, scleral icterus and elevated parameters of cholestasis. However, when pancreatitis is caused by a gallstone, the gallstone is stuck in the common bile duct just past the ampulla of Vater, not inside the pancreatic duct.

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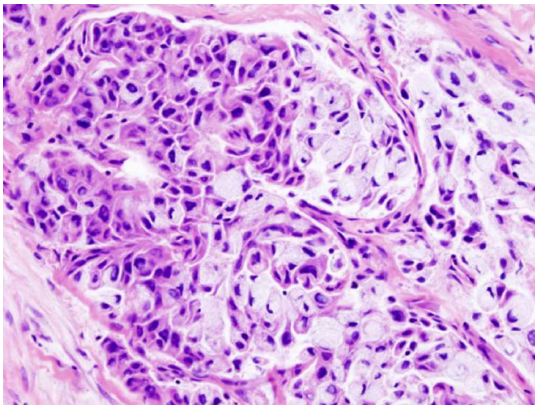
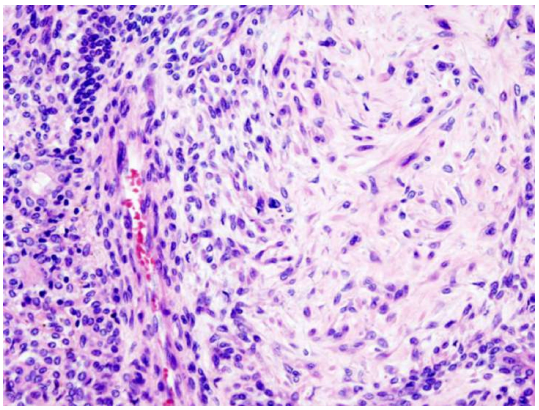
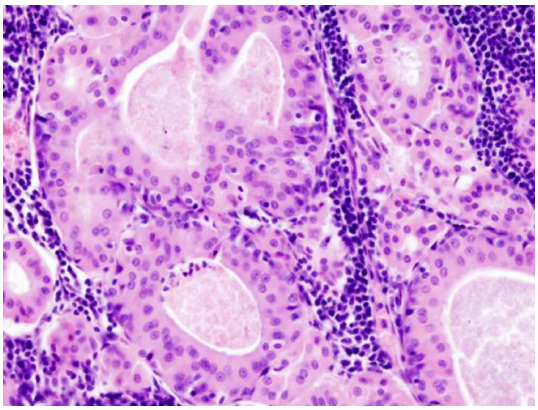
Question # 3

A 58-year-old woman comes to the physician for a 3-month history of gradual swelling on the right side of her face. She has smoked 1 pack of cigarettes daily for the past 18 years. Physical examination shows a right-sided, movable facial mass that is nontender to palpation. There is a visible protrusion of the right lateral wall of the oropharynx. The patient is able to fully open her mouth. There is no cervical lymphadenopathy. Cranial nerves are intact. An MRI shows a 3.3-cm sharply demarcated, lobulated hyperintense mass arising from the right parotid gland. The lesion is surrounded by a hypointense capsule. A biopsy of the mass shows nests of epithelial cells mixed with a chondromyxoid stroma. Which of the following is the most likely diagnosis?

	Answer	Image
A	Mucoepidermoid carcinoma	
B	Pleomorphic adenoma	

	Answer	Image
C	Papillary cystadenoma lymphomatosum	
D	Adenoid cystic carcinoma	
E	Granulomatous sialadenitis	

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Hint

A well-encapsulated mass, in the absence of signs of tumor invasion into the surrounding tissues (e.g., facial nerve palsy, trismus) or lymphatic spread, suggests a benign lesion of the parotid gland.

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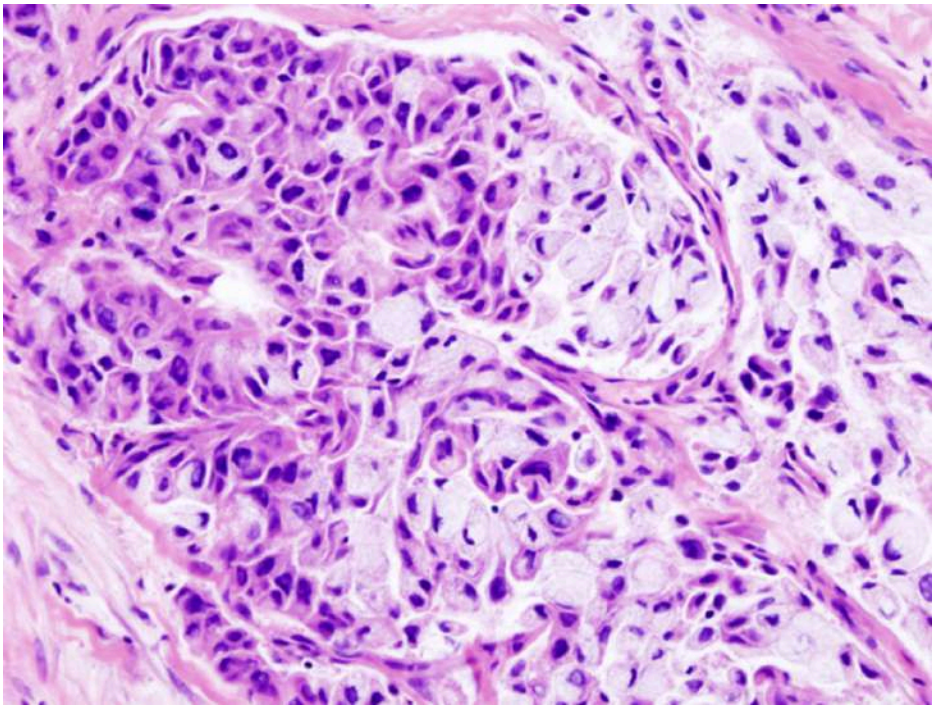
Correct Answer

A - Mucoepidermoid carcinoma

Image



Explanation Why

Mucoepidermoid carcinoma is the most common malignant salivary gland tumor and can manifest as a gradually growing, painless unilateral mass arising from the parotid gland. However, malignant salivary gland tumors usually invade into the surrounding tissues and present as a fixed and nonmobile mass, along with cervical lymphadenopathy, facial nerve palsy, and/or trismus, unlike this patient's presentation. Moreover, a biopsy of a mucoepidermoid carcinoma would show an admixture of mucin-producing columnar cells and epidermoid cells, which are not seen here.

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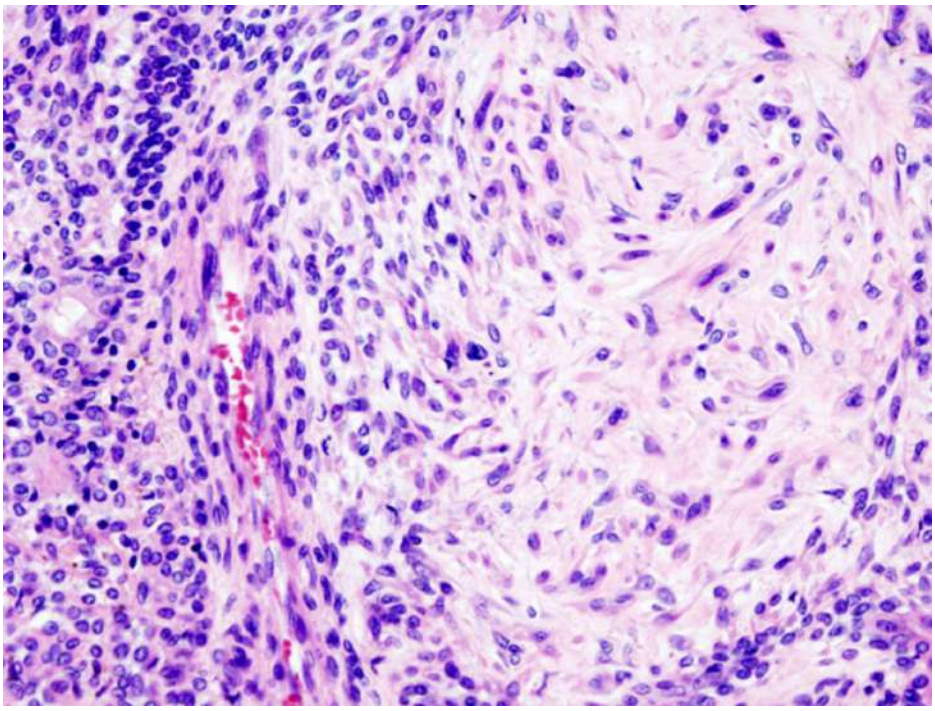
B - Pleomorphic adenoma

Image



Explanation But

A pleomorphic adenoma can recur if incompletely resected. In a patient with pleomorphic adenoma, rapid enlargement of the mass or the development of facial nerve palsy should raise concern for malignant transformation.

Explanation Why

A gradually growing, painless, mobile, and well-encapsulated unilateral mass arising from the parotid gland without facial nerve palsy should raise suspicion for a pleomorphic adenoma, the most common benign tumor of the salivary glands. An admixture of epithelial components and chondromyxoid stroma are pathognomonic for pleomorphic adenomas. Because these benign growths have the potential to undergo malignant transformation, complete resection is recommended.

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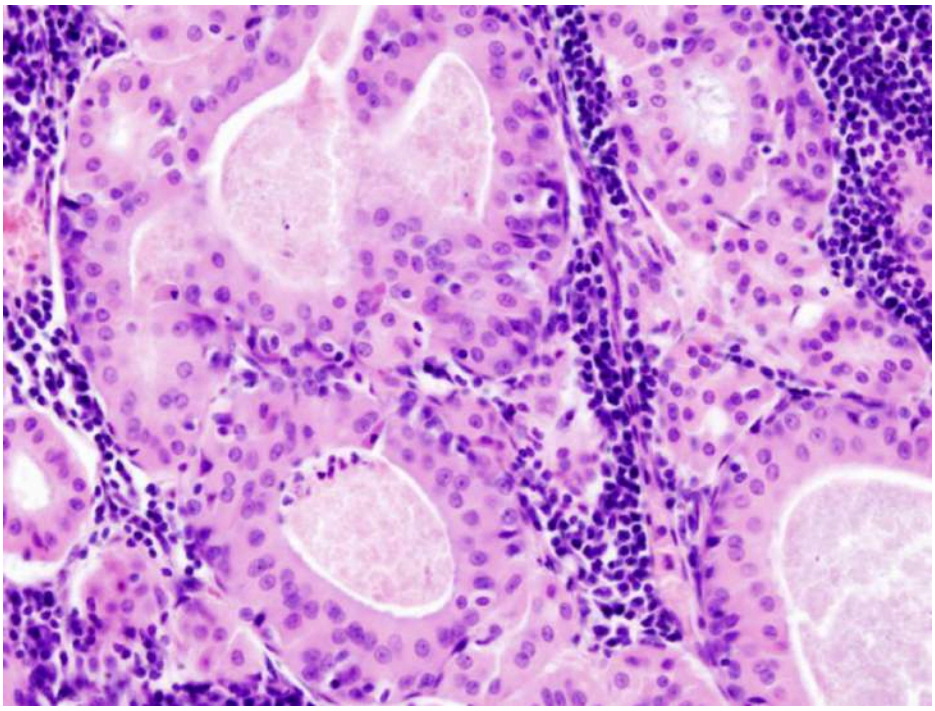
C - Papillary cystadenoma lymphomatosum

Image



Explanation Why

Papillary cystadenoma lymphomatosum (Warthin tumor) most commonly occurs among smokers and would present as a gradually growing, painless, mobile, and well-encapsulated mass arising from the parotid gland without facial nerve palsy, which is consistent with this patient's presentation. However, a biopsy of a Warthin tumor would reveal cystic components, abundant lymphocytes, germinal centers, and lymph node-like stroma, which are not seen here.

D - Adenoid cystic carcinoma

Explanation Why

Adenoid cystic carcinoma (ACC) can manifest as a gradually growing, painless unilateral mass arising from the parotid gland. However, malignant salivary gland tumors usually invade into the

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surrounding tissues and present as a fixed and nonmobile mass, along with cervical lymphadenopathy, facial nerve palsy, and/or trismus, unlike this patient's presentation. Moreover, a biopsy of ACC would show an admixture of ductal and myoepithelial cells displaying cribriform, tubular, or solid growth patterns, which are not seen here.

E - Granulomatous sialadenitis

Explanation Why

A painless and mobile parotid swelling without facial nerve palsy, as seen here, is consistent with granulomatous sialadenitis. However, this condition is characterized by noncaseating granulomatous inflammation (i.e., macrophages, epitheloid cells, and multinucleated giant cells surrounded by lymphocytes), which is not present in this patient.

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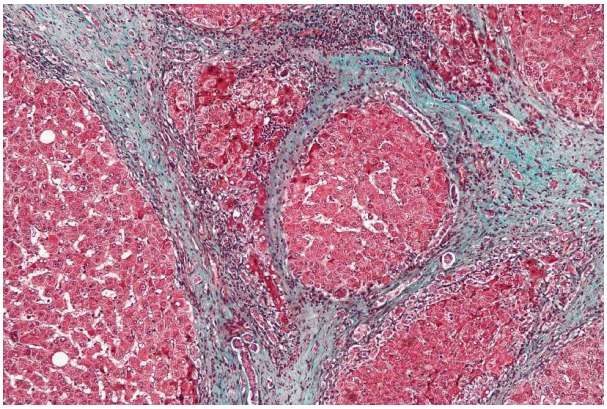
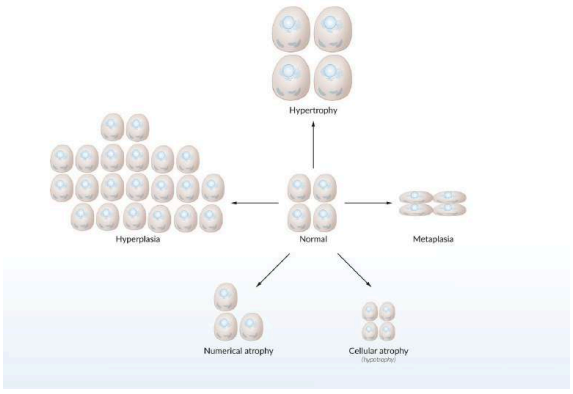
Question # 4

A 44-year-old man is brought to the emergency department 30 minutes after being involved in a high-speed motor vehicle accident as a restrained driver. His pulse is 145/min and blood pressure is 102/63 mm Hg. Physical examination shows dark bruising and discoloration over the right upper quadrant of his abdomen and right flank. The abdomen is guarded and markedly tender to palpation. A CT scan of the chest and abdomen shows lacerations and compression injuries in the right lobe of the liver. An emergency partial hepatectomy is performed. Ultrasonography on follow-up examination 6 months later shows that the liver has grown back to almost the original size. Microscopic examination of the newly formed liver tissue is most likely to show which of the following findings?

	Answer	Image
A	Regenerative nodules	
B	Hypertrophic hepatocytes	

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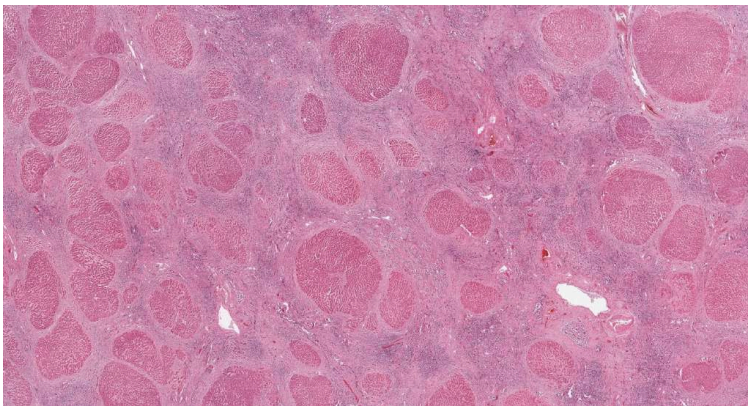
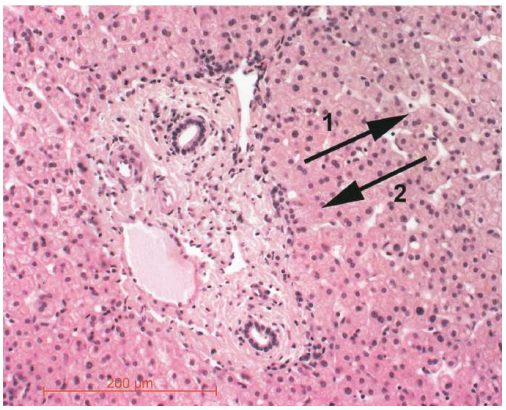
	Answer	Image
C	Proliferating fibroblasts	
D	Normal hepatic tissue	
E	Inflammatory infiltrate	

Hint

Hepatocytes, like the cells of many other glands, are stable cells that are capable of multiplying after becoming damaged.

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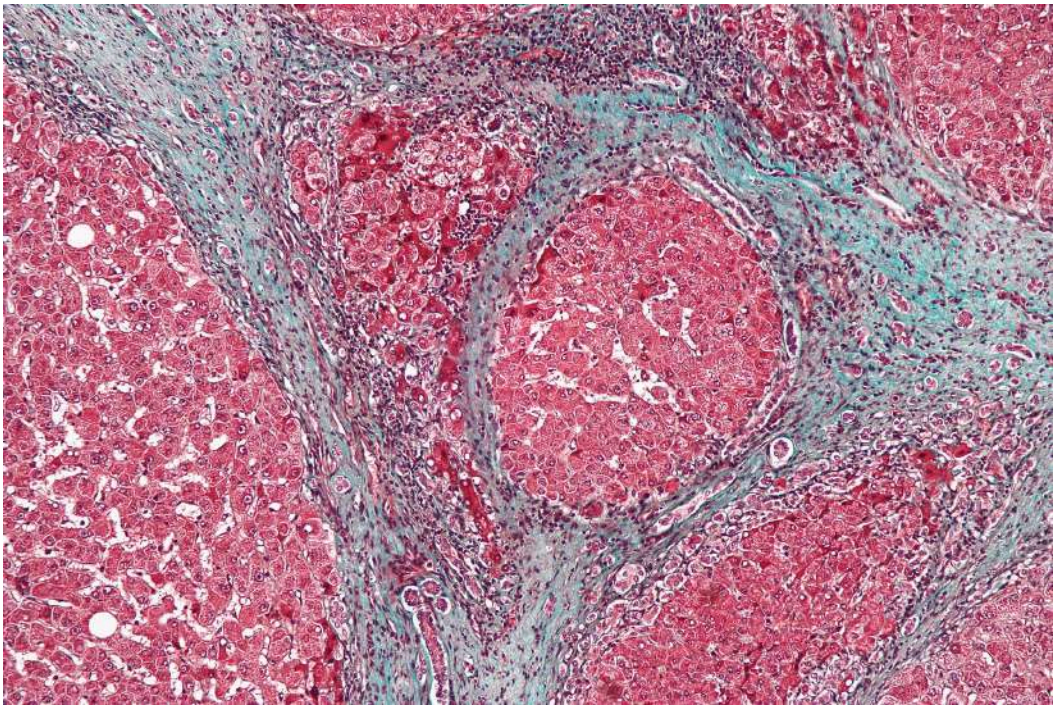
Correct Answer

A - Regenerative nodules

Image



Explanation Why

Regenerative nodules are an irreversible response to chronic liver injury (e.g., due to hepatitis C or alcohol use disorder). The nodules are formed by bridging fibrosis, which occurs via stellate cells; continued fibrosis leads to cirrhosis of the liver if the stimulus is not removed. The development of regenerative nodules inhibits hepatic function and leads to shrinkage of the liver, not regrowth.

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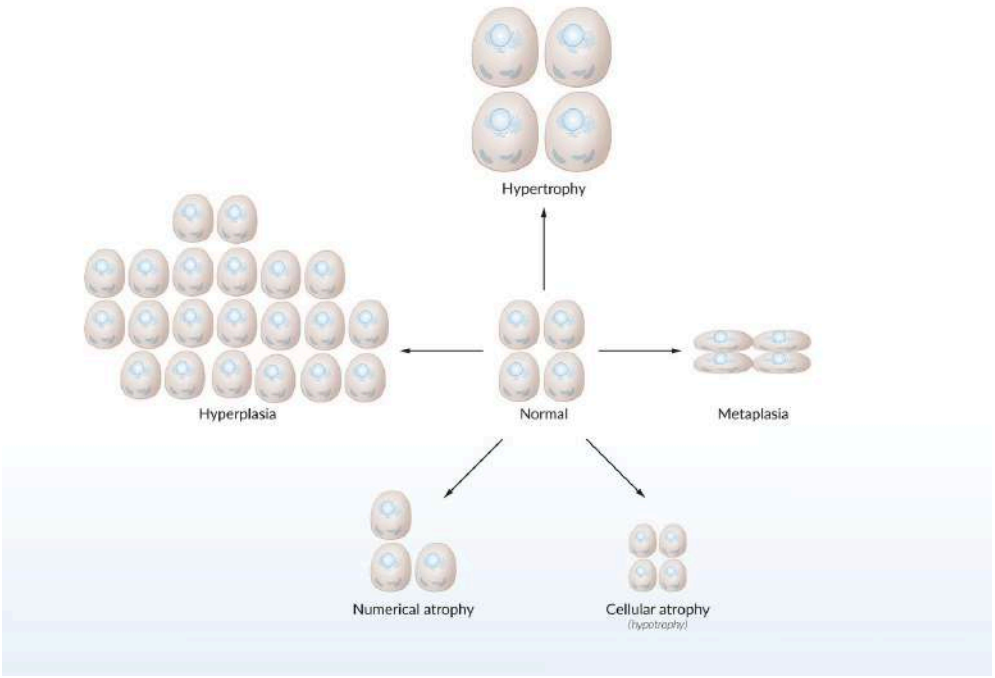
B - Hypertrophic hepatocytes

Image



Explanation Why

Hypertrophy of hepatocytes is a cellular response usually caused by drugs or toxins. Although hepatocyte hypertrophy can also sometimes be seen in remnant tissue after liver resection, newly-formed liver tissue does not typically show increased cell size. Additionally, hypertrophy alone would not be sufficient to achieve full regeneration of the liver.

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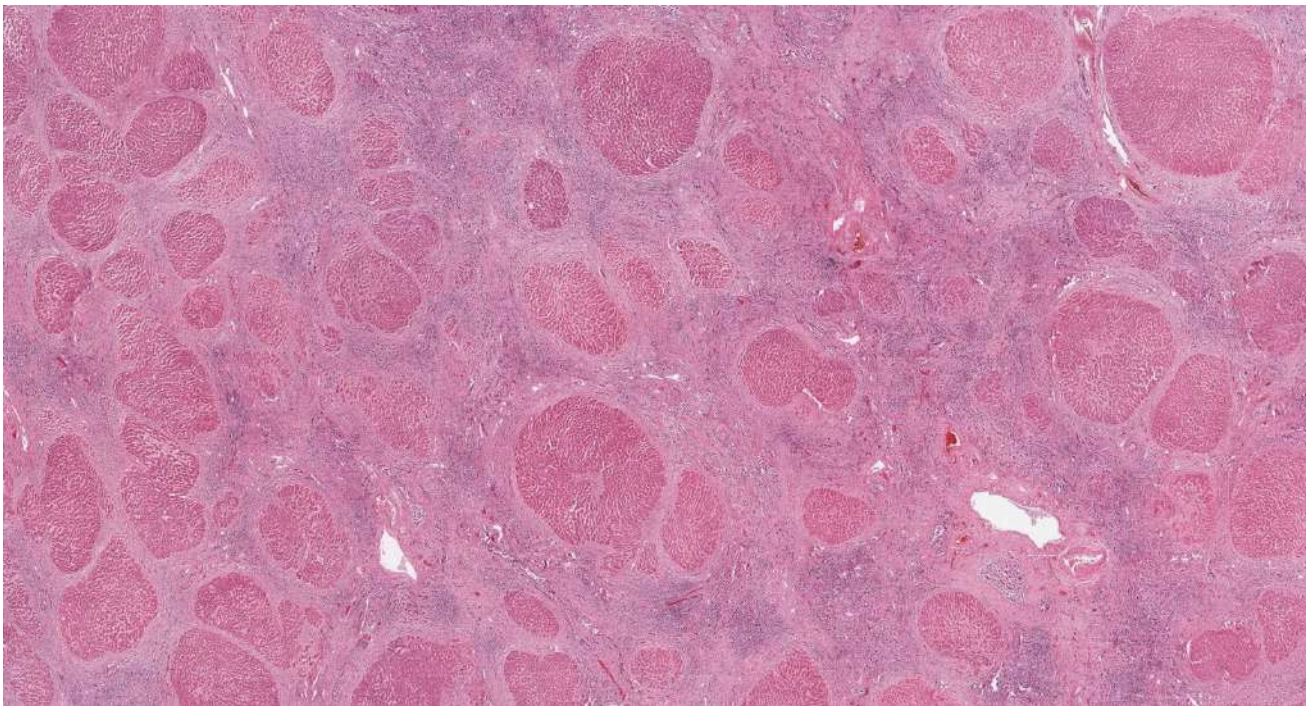
C - Proliferating fibroblasts

Image



Explanation Why

Excessive proliferation of fibroblasts is seen in liver cirrhosis (e.g., due to infection or alcohol use disorder). The presence of cytokines and other metabolites causes hepatic cells (e.g., stellate cells) to transform into myofibroblasts. The resulting remodeling of liver tissue leads to increased stiffness (due to excessive synthesis of collagenous fibers) and shrinkage of the liver, not regrowth. Partial liver resection would not lead to excessive fibroblast proliferation.

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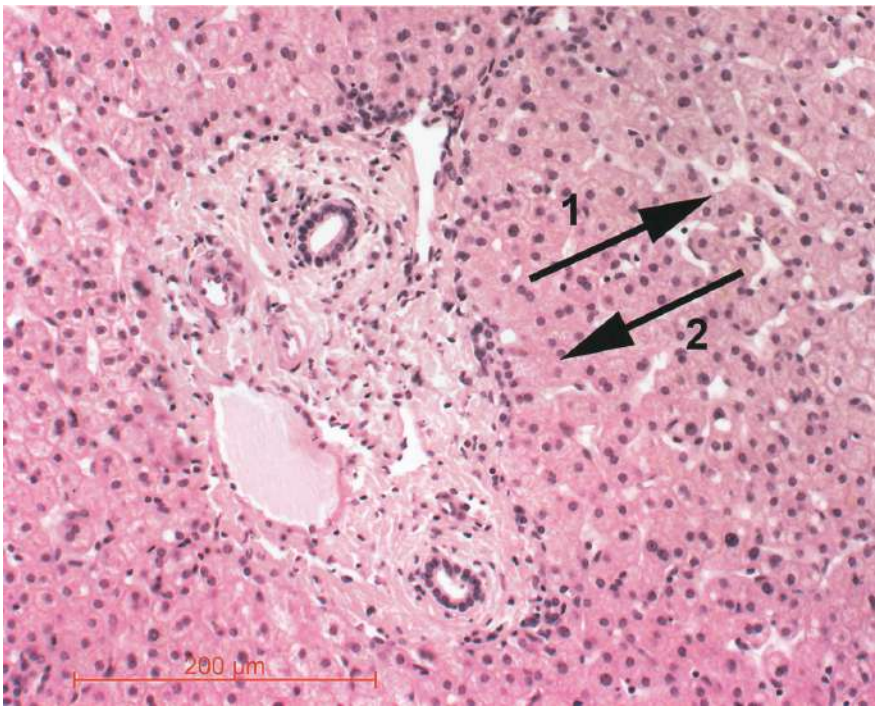
D - Normal hepatic tissue

Image



Explanation Why

Liver tissue has the unique ability to regenerate after resection or trauma through replication of remaining hepatocytes and repopulation from progenitor cells, such that regenerated areas will show normal hepatic tissue on microscopic examination. Stimulation of stable cells (e.g., injured hepatocytes) results in the transition from the G_0 to G_1 phase. Regeneration begins at the periportal zone, advances to the mid-zonal hepatocytes, then to the centrilobular zone, and ends at the central veins. After regeneration, biliary epithelial and endothelial cells proliferate and an extracellular matrix is produced by stellate cells. Through this process, the liver can restore itself to its full mass and preserve its essential metabolic functions.

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E - Inflammatory infiltrate

Explanation Why

An inflammatory infiltrate develops in response to infections or toxins. Although liver resections can cause inflammation (e.g., due to entry of infectious agents during surgery), this would manifest earlier in the post-surgical course (days to weeks rather than months), and fever would be expected. Inflammatory cells may be chronically present in response to toxins (e.g., in chronic alcohol use). However, chronic inflammation would lead to an increase of myofibroblasts in liver tissue, causing fibrosis and shrinkage rather than regrowth.

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Question # 5

A 56-year-old woman comes to the physician because of profuse watery diarrhea for the last 3 days. She reports having up to 6 loose stools per day. She has not had any fever, nausea, or vomiting. She is otherwise healthy and takes no medications. Her temperature is 37.1°C (98.8°F), pulse is 104/min, respirations are 26/min, and blood pressure is 102/65 mm Hg. Physical examination shows poor skin turgor, a capillary refill time of 5 seconds, and dry mucous membranes. Arterial blood gas analysis on room air shows a pH of 7.31. This patient is most likely to have which of the following additional laboratory findings?

	Answer	Image
A	Decreased serum Mg^{2+}	
B	Decreased serum Na^{+}	
C	Increased arterial pCO_2	
D	Decreased serum HCO_3^{-}	
E	Decreased serum Cl^{-}	

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Hint

This patient has a metabolic acidosis caused by her diarrhea.

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Correct Answer

A - Decreased serum Mg^{2+}

Explanation Why

Diarrhea can cause decreased serum Mg^{2+} concentrations. However, these findings are more common for conditions of chronic diarrhea associated with steatorrhea because Mg^{2+} ions in the intestinal lumen combine with fatty acids to form insoluble soaps, which are excreted with the stool. This patient has acute diarrhea, which is less likely to affect the serum Mg^{2+} concentration. In addition, acidosis and dehydration, which are also seen in this patient, do not usually have a significant impact on serum Mg^{2+} concentration.

B - Decreased serum Na^{+}

Explanation Why

Fluid losses from diarrhea can lead to ADH release to facilitate reabsorption of water in the kidneys. If sodium intake is concurrently decreased, this scenario can result in hypoosmolar hyponatremia. However, it is much more common for diarrhea to result in hypernatremia because water is typically lost in excess of Na^{+} ions.

C - Increased arterial pCO_2

Explanation Why

Increased arterial pCO_2 can cause a decrease in pH (respiratory acidosis). However, this patient's history and clinical manifestations do not suggest an underlying cause of respiratory acidosis (e.g., chronic obstructive pulmonary disease, medications that cause respiratory depression). Her respiratory rate is increased, which indicates a degree of respiratory compensation (via hyperventilation) for underlying metabolic acidosis, which leads to a decreased, not increased, arterial pCO_2.

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D - Decreased serum HCO_3^-

Explanation But

Acute, severe watery diarrhea is associated with a significant loss of K^+ ions through the stool. At the same time, acidosis can cause hyperkalemia through a shift of K^+ ions into the extracellular space in exchange for H^+ ions, which are buffered intracellularly. The net balance of serum K^+ concentrations in patients with metabolic acidosis and diarrhea is difficult to predict, but most commonly, serum K^+ concentrations are decreased.

Explanation Why

Severe diarrhea typically causes metabolic acidosis through a loss of HCO_3^- ions with the stool. Physiologically, HCO_3^- ions are secreted into the small intestine to neutralize acidic chyme and are later reabsorbed in the form of organic anion salts in the enterohepatic circulation. In patients with diarrhea, reabsorption is decreased due to increased motility of the intestines (decreased colon transit time) while secretion remains constant. Serum HCO_3^- concentrations subsequently decrease, which causes an increase in serum Cl^- concentrations (hyperchloremic metabolic acidosis) in order to maintain blood electroneutrality.

E - Decreased serum Cl^-

Explanation Why

Decreased serum Cl^- concentrations, in association with metabolic alkalosis, can occur in the setting of severe vomiting. However, this patient has a metabolic acidosis from diarrhea, which is typically associated with increased serum Cl^- concentrations. When anions are lost through the stool and serum concentrations decrease, Cl^- ions shift into the extracellular space in order to maintain net blood electroneutrality. In addition, volume contraction and Cl^- retention by the kidney in the setting of dehydration further contribute to an increased serum Cl^- concentration.

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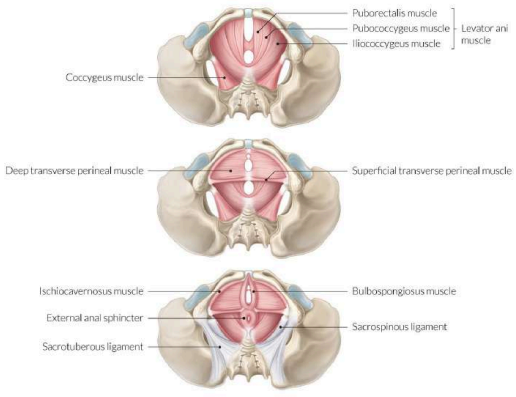
Question # 6

A 70-year-old man with a 1-year history of constipation comes to the physician for a follow-up examination. He has bowel movements 1–2 times a week and sometimes has to use his fingers for stool evacuation. Defecation is painful and preceded by a sense of bowel obstruction. Flexible sigmoidoscopy two months prior showed normal results. His current medication is a laxative. Abdominal examination shows no abnormalities. Digital examination of the rectum shows an increased resting and squeezing tone of the anal sphincter. This patient's symptoms are most likely caused by dysfunction of which of the following processes?

	Answer	Image
A	Involuntary relaxation of the external anal sphincter	
B	Involuntary relaxation of the iliococcygeus muscle	
C	Involuntary relaxation of the pubococcygeus muscle	
D	Voluntary relaxation of the internal anal sphincter	
E	Voluntary relaxation of the puborectalis muscle	

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	Answer	Image
F	Voluntary relaxation of the coccygeus muscle	

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Hint

This patient most likely has primary constipation due to an inability to coordinate relaxation of the pelvic muscles that are involved in defecation.

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Correct Answer

A - Involuntary relaxation of the external anal sphincter

Explanation Why

Relaxation of the external anal sphincter allows expulsion of stool into the anal canal during the defecation process. Dysfunction in relaxation of the external anal sphincter also leads to increased tonus during digital rectal examination and can cause constipation, both of which are seen in this patient. However, the external anal sphincter is a voluntary, not an involuntary, muscle.

B - Involuntary relaxation of the iliococcygeus muscle

Explanation Why

The iliococcygeus muscle is part of the levator ani, a muscle group that is important for maintaining continence and providing stability of the abdominal and pelvic organs. The iliococcygeus muscle is voluntary, not involuntary, and has no role in the defecation process, making it an unlikely cause of this patient's increased rectal tonus and constipation.

C - Involuntary relaxation of the pubococcygeus muscle

Explanation Why

The pubococcygeus muscle is part of the levator ani, a muscle group that is important for maintaining continence and providing stability of the abdominal and pelvic organs. Pubococcygeus muscle dysfunction (failure to relax) can lead to increased tonus on digital rectal examination. However, the pubococcygeal muscle is not directly involved in defecation and is, therefore, unlikely to be responsible for this patient's chronic constipation. Additionally, the pubococcygeus is a voluntary, not an involuntary muscle.

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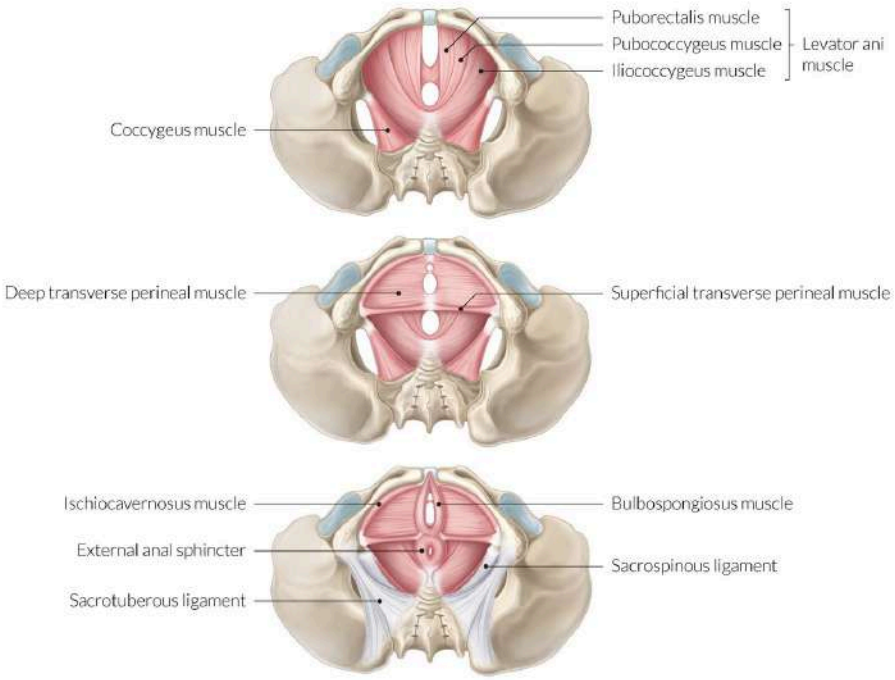
D - Voluntary relaxation of the internal anal sphincter

Explanation Why

Relaxation of the internal anal sphincter occurs once intestinal contents have reached the rectum. At this stage, a small amount of rectal content is expelled into the anal canal for anal sampling. Dysfunction in relaxation of the internal anal sphincter would also lead to increased tonus on digital rectal examination and constipation. However, the internal anal sphincter is an involuntary, not a voluntary muscle.

E - Voluntary relaxation of the puborectalis muscle

Image



Explanation But

Weakening of the puborectalis muscle is associated with fecal incontinence.

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Explanation Why

The puborectalis muscle, part of the levator ani muscle group, must be voluntarily relaxed to facilitate defecation. This patient most likely has pelvic dyssynergia, which leads to increased sphincter tonus and inability to empty the anal canal. Normally, defecation is enabled by simultaneous voluntary contraction of abdominal muscles and relaxation of the external anal sphincter and puborectalis muscle.

F - Voluntary relaxation of the coccygeus muscle

Explanation Why

The coccygeus muscle is part of the pelvic floor, supports and stabilizes intraabdominal organs, and pulls the coccyx forward after defecation. Because this muscle is not directly involved in the defecation process, it is unlikely to be the cause of this patient's increased rectal tonus and constipation.

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Question # 7

A 54-year-old man comes to the physician because of a 4-month history of yellow discoloration of the skin. He reports a loss of appetite. He lives with his wife and three children in a rural town where he works as a safety inspector at the local nuclear power plant. He is not physically active and his diet consists mostly of donuts and highly caloric processed food. He does not smoke but drinks 5 cans of beer daily. He is 182 cm (6 ft) tall and weighs 101 kg (222 lb); BMI is 30 kg/m^2. His vital signs are within normal limits. Physical examination shows jaundice of the skin and scleral icterus. There is a palpable, nontender mass below the right costal margin. Scratch marks are seen on the extremities. Which of the following is the most likely cause of this patient's symptoms?

	Answer	Image
A	Infection	
B	Lithiasis	
C	Hemolysis	
D	Steatosis	
E	Neoplasia	
F	Autoimmune disease	

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Hint

The Springfield Shopper reports that Duff Adequate beer may have been contaminated with uranium for years.

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Correct Answer

A - Infection

Explanation Why

This patient's loss of appetite and jaundice may result from hepatobiliary infection (e.g., viral hepatitis, acute cholangitis, acute cholecystitis). Hepatitis can also cause pruritus, a feature also seen in this patient. However, none of these infections would explain the positive Courvoisier sign (palpable, nontender gall bladder, and painless jaundice). Rather, acute cholecystitis causes a positive Murphy sign, acute cholangitis causes RUQ tenderness, and hepatitis typically causes tender hepatomegaly. Furthermore, this patient lacks other features of infection, including fever, nausea, vomiting, and abdominal pain.

B - Lithiasis

Explanation Why

Cholecystolithiasis is the presence of gallstones in the gallbladder. Although this condition is typically asymptomatic, some individuals may present with symptoms of biliary colic, which are absent here. Choledocholithiasis is characterized by stones in the common bile duct and can manifest with jaundice and pruritus, both of which are seen here. However, choledocholithiasis would not explain this patient's positive Courvoisier sign. In addition, other typical features of choledocholithiasis (e.g., RUQ pain, nausea, vomiting, pale stool, dark urine) are absent in this patient.

C - Hemolysis

Explanation Why

Hemolysis, the breakdown of RBCs, is the cause of hemolytic anemia, which can manifest with jaundice. However, hemolytic anemia would not explain this patient's loss of appetite and positive Courvoisier sign (palpable, nontender gall bladder, and painless jaundice). Moreover, this patient lacks other features of anemia, including fatigue, weakness, and pallor.

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D - Steatosis

Explanation Why

Hepatic steatosis can occur secondary to alcohol use (i.e., alcoholic fatty liver) or body habitus (i.e., nonalcoholic fatty liver), and may cause jaundice. However, patients with hepatic steatosis are generally asymptomatic, unlike this man who presents with loss of appetite, pruritus, and a palpable gall bladder.

E - Neoplasia

Explanation Why

This patient most likely has neoplasia of the gastrointestinal tract that has resulted in biliary system obstruction, as evidenced by his pruritus, loss of appetite, and Courvoisier sign (enlarged gallbladder and painless jaundice). Possible etiologies include pancreatic head carcinoma, cholangiocarcinoma, and hepatocellular carcinoma (HCC). Exposure to ionizing radiation (e.g., from working at a power plant) increases the risk of malignancy. Heavy alcohol consumption is a risk factor for HCC and pancreatic cancer, whereas obesity is a risk factor for pancreatic adenocarcinoma. Diagnostic evaluation should include liver function tests, parameters of cholestasis, and tumor markers (e.g., alpha-fetoprotein, CA 19-9, CEA).

F - Autoimmune disease

Explanation Why

This patient has jaundice, scleral icterus, and pruritus, which may be indicative of an autoimmune disease such as autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), or primary sclerosing cholangitis (PSC). Although AIH and PBC are more common in women, PSC is more common in men. A positive Courvoisier sign (palpable, nontender gall bladder, and painless jaundice), however, is not consistent with an autoimmune condition. Moreover, AIH, PBC, and PSC typically cause fatigue and abdominal pain (worst in the RUQ), which are not present in this patient.

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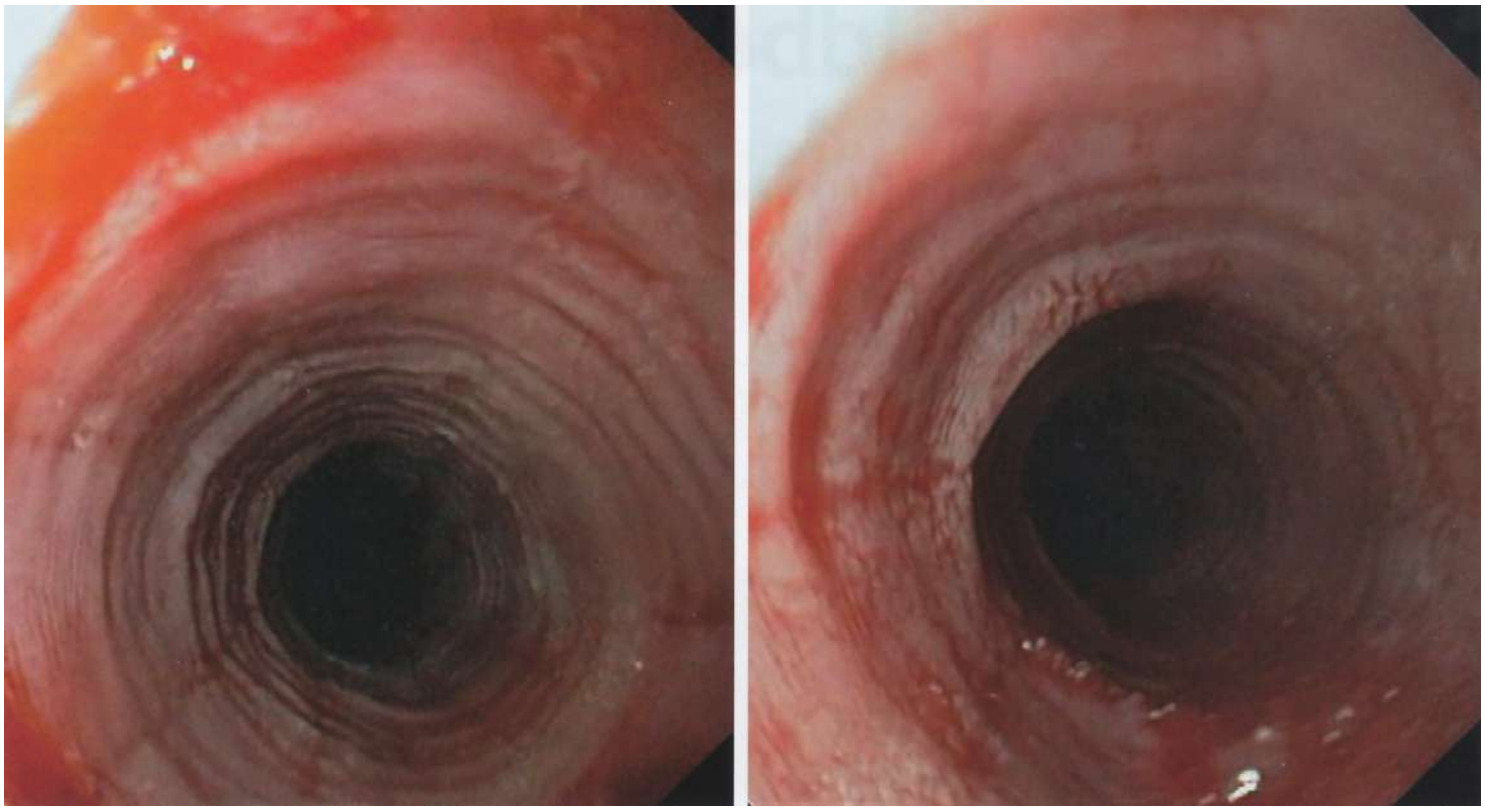
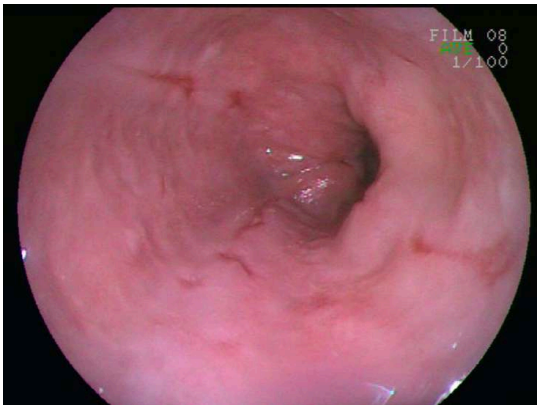
Question # 8

A 36-year-old woman comes to the physician for difficulty swallowing and a burning sensation in her chest for the past 2 years. She has increased her fluid consumption to help with swallowing when eating. She reports having used both over-the-counter antacids and pantoprazole for 2 months without any relief of symptoms. She uses a daily low-dose inhaled corticosteroid and an albuterol inhaler as needed for allergic asthma. She is 170 cm (5 ft 6 in) tall and weighs 75 kg (165 lbs); her BMI is 26 kg/m^2. Her vital signs are within normal limits. Physical examination shows no abnormalities. Findings of an upper endoscopy are shown. Which of the following is the most likely diagnosis?



	Answer	Image
A	Gastroesophageal reflux disease	

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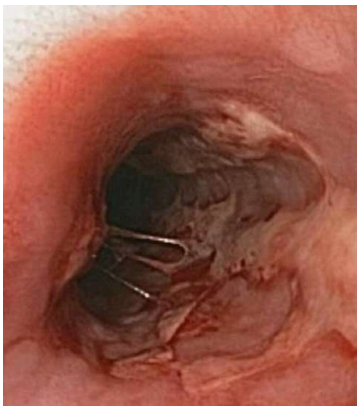
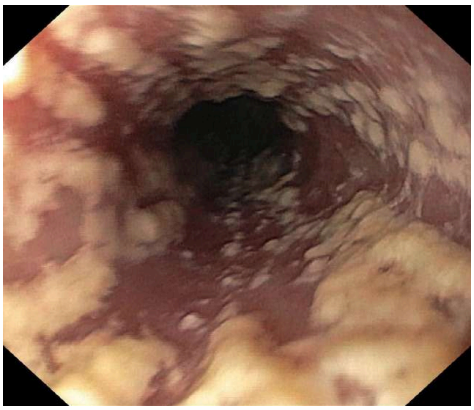
	Answer	Image
B	Herpes esophagitis	
C	Candida esophagitis	
D	Drug-induced esophagitis	
E	Eosinophilic esophagitis	
F	Cytomegalovirus esophagitis	

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Hint

This patient's upper endoscopy shows white, circumferential mucosal lesions (trachealization of the esophagus), mucosa fragility, and linear, longitudinal furrows.

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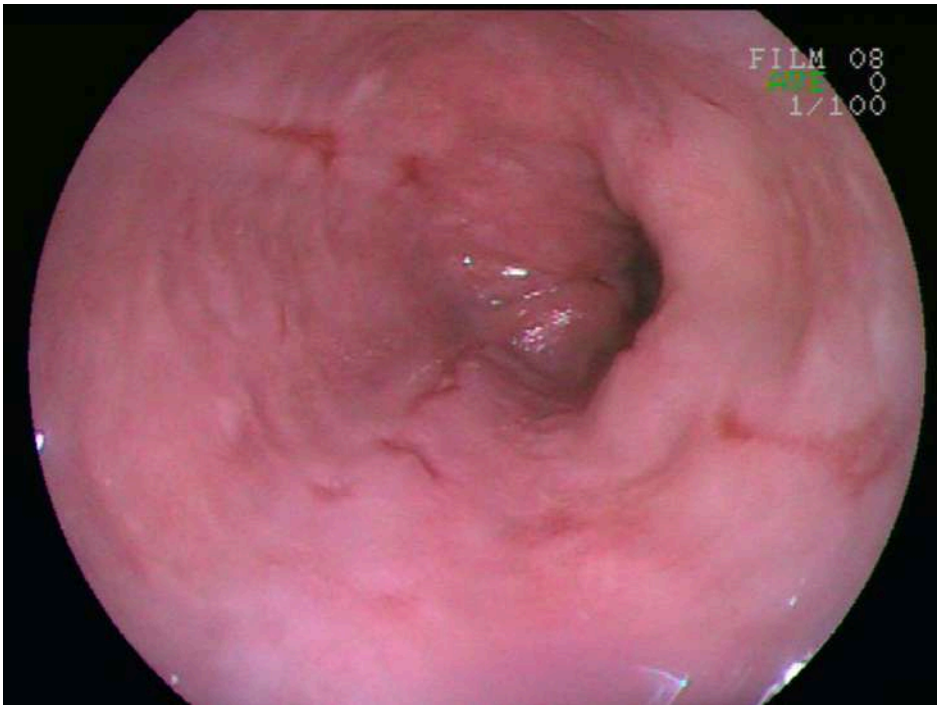
Correct Answer

A - Gastroesophageal reflux disease

Image



Explanation Why

The presence of heartburn and dysphagia raises suspicion for gastroesophageal reflux disease (GERD). However, symptoms of GERD usually improve with proton pump inhibitor (PPI) therapy. GERD commonly affects the distal esophagus, which may be normal or show evidence of esophagitis; endoscopic evaluation of the upper esophagus will often be normal. Other endoscopic findings in individuals with longstanding GERD may reveal esophageal ulcers, strictures, Barrett esophagus, and/or esophageal adenocarcinoma, none of which are present in this patient.

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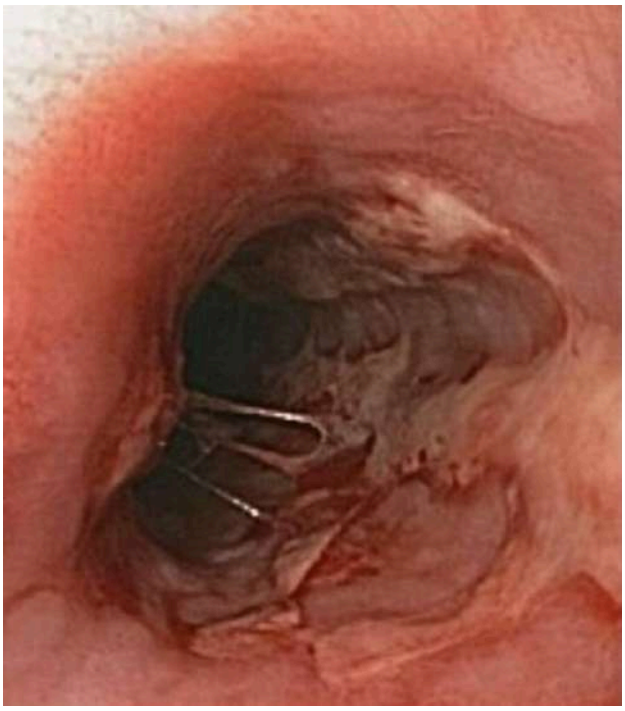
B - Herpes esophagitis

Image



Explanation Why

Dysphagia and heartburn refractory to proton pump inhibitors may raise suspicion for herpes (HSV) esophagitis. However, HSV esophagitis is usually present in individuals who are immunocompromised (e.g., AIDS, immunosuppressant medication use). Moreover, endoscopic evaluation of HSV esophagitis would show vesicles and multiple small superficial round/ovoid ulcers in the mid esophagus that may coalesce to form diffuse superficial ulcers, which are not seen here.

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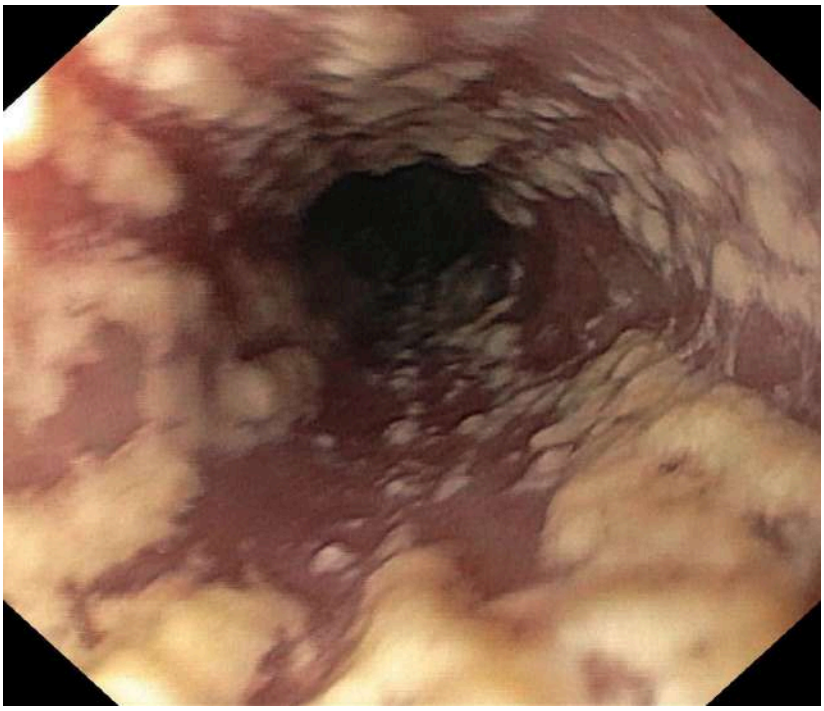
C - Candida esophagitis

Image



Explanation Why

Dysphagia and heartburn refractory to proton pump inhibitors may raise suspicion for candida esophagitis. However, candida esophagitis is typically present in individuals who are immunocompromised (e.g., AIDS, immunosuppressant medication use). Although this patient's inhaled corticosteroid increases the risk of oropharyngeal candidiasis, it is only rarely associated with esophageal candidiasis. Moreover, endoscopic evaluation of candida esophagitis would reveal white mucosal plaque-like lesions, which are not seen here.

D - Drug-induced esophagitis

Explanation Why

The presence of dysphagia and heartburn refractory to proton pump inhibitors raises suspicion for

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drug-induced esophagitis. However, endoscopic evaluation of drug-induced esophagitis would reveal a discrete punched-out ulcer surrounded by relatively normal mucosa that may be mildly inflamed. Moreover, common causes of drug-induced esophagitis include NSAIDs, bisphosphonates, tetracyclines, potassium chloride, and iron, none of which this patient is taking.

E - Eosinophilic esophagitis

Explanation But

EoE is managed initially by avoidance of food triggers, topical glucocorticoids (e.g., PO fluticasone or PO budesonide), and mechanical dilation in the setting of esophageal stricture.

Explanation Why

Dysphagia and heartburn refractory to proton pump inhibitors in an individual with a history of atopy are indicative of eosinophilic esophagitis (EoE). A diagnosis of EoE is further supported by the findings on this patient's endoscopy (trachealization of the esophagus, longitudinal furrows, friable mucosa). Individuals with EoE may also present with food impaction, reflux, and vomiting. An endoscopic esophageal biopsy will typically show an eosinophilic infiltrate.

F - Cytomegalovirus esophagitis

Explanation Why

Dysphagia and heartburn refractory to proton pump inhibitors may raise suspicion for cytomegalovirus (CMV) esophagitis. However, CMV esophagitis usually manifests in immunocompromised individuals (e.g., AIDS, immunosuppressant medication use). Moreover, endoscopic evaluation of CMV esophagitis would show large linear ulcerations in the distal esophagus that are typically shallow, which are not seen here.

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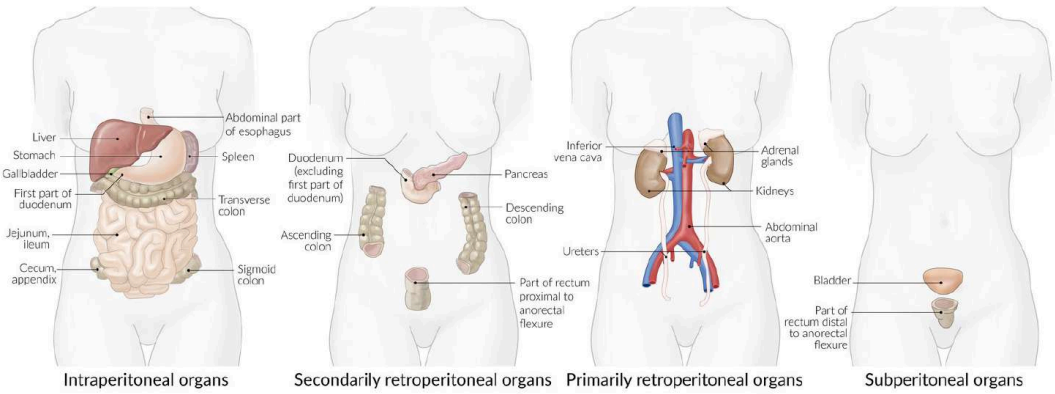
Question # 9

A 32-year-old man with Crohn disease is admitted to the hospital to undergo intestinal resection. Microscopic examination of a cross-sectional microtome slice of a resected intestinal segment shows squamous mesothelial cells surrounding the entire slice. The microtome slice was most likely obtained from which of the following parts of the intestine?

	Answer	Image
A	Proximal rectum	
B	Ascending colon	
C	Transverse colon	
D	Third part of the duodenum	
E	Second part of the duodenum	

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Hint

The serosa layer of the intestine is composed of squamous mesothelial cells. Retroperitoneal organs are not completely covered by serosa.

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Correct Answer

A - Proximal rectum

Explanation Why

The proximal rectum is a retroperitoneal organ. Although its anterior surface is covered by serosa (parietal peritoneum), its posterior surface is covered by adventitia, which is composed of fibrous connective tissue rather than squamous mesothelial cells.

B - Ascending colon

Explanation Why

The ascending colon is a retroperitoneal organ. Although its anterior surface is covered by serosa (parietal peritoneum), its posterior surface is covered by adventitia, which is composed of fibrous connective tissue rather than squamous mesothelial cells.

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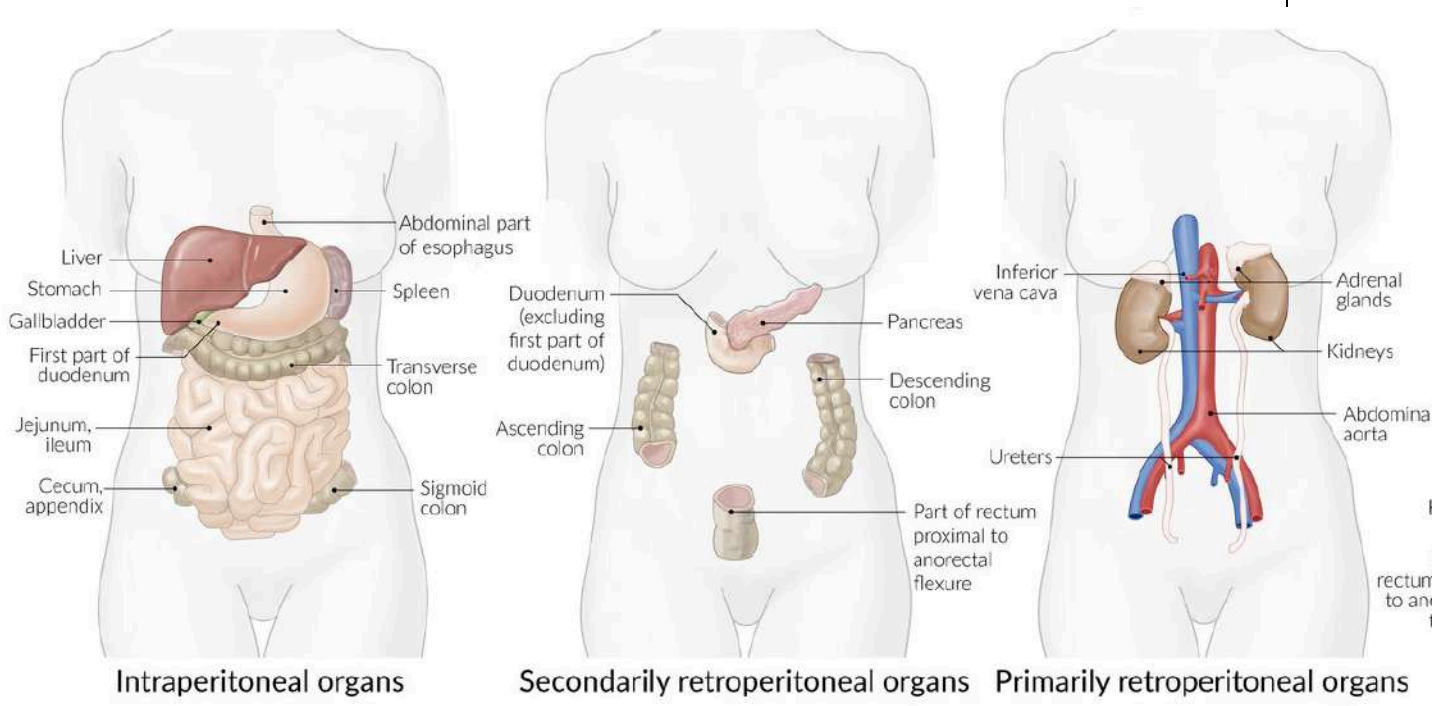
C - Transverse colon

Image



Explanation Why

The transverse colon is an intraperitoneal organ, which by definition is completely covered by visceral peritoneum. Visceral peritoneum forms the serosa layer of the intraperitoneal organs. Other intraperitoneal structures include the stomach, 1st part of the duodenum, jejunum, ileum, cecum, sigmoid colon, liver, gall bladder, spleen, and tail of the pancreas.

D - Third part of the duodenum

Explanation Why

The 3rd part of the duodenum is a retroperitoneal organ. Although its anterior surface is covered by serosa (parietal peritoneum), its posterior surface is covered by adventitia, which is composed of

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fibrous connective tissue rather than squamous mesothelial cells.

E - Second part of the duodenum

Explanation Why

The 2nd part of the duodenum is a retroperitoneal organ. Although its anterior surface is covered by serosa (parietal peritoneum), its posterior surface is covered by adventitia, which is composed of fibrous connective tissue rather than squamous mesothelial cells.

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Question # 10

A 42-year-old woman with metabolic syndrome comes to the physician for a 1-week history of intermittent diarrhea, abdominal distention, and flatulence. Two weeks ago, she was prescribed a medication for weight loss. She is 162 cm (5 ft 4 in) tall and weighs 102 kg (225 lb); BMI is 39 kg/m^2. Fecal analysis shows increased triglyceride concentration. Which of the following medications was most likely prescribed to this patient?

	Answer	Image
A	Sevelamer	
B	Ezetimibe	
C	Miglitol	
D	Orlistat	
E	Colesevelam	

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Hint

This patient was most likely prescribed a lipase inhibitor, which decreases the breakdown of dietary triglycerides to fatty acids.

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Correct Answer

A - Sevelamer

Explanation Why

Sevelamer can cause osmotic diarrhea and abdominal discomfort. This drug binds to phosphate in the intestinal lumen, which decreases phosphate absorption. However, because it does not affect lipase activity, fecal triglyceride excretion is not increased in patients who take sevelamer. Moreover, sevelamer is not used for weight loss; it is used to treat hyperphosphatemia.

B - Ezetimibe

Explanation Why

Ezetimibe can cause diarrhea and abdominal discomfort. This drug inhibits cholesterol reabsorption at the brush border of enterocytes, which leads to increased fecal cholesterol excretion. However, because it does not affect lipase activity, fecal triglyceride excretion is not increased in patients who take ezetimibe. Moreover, ezetimibe is not used for weight loss; it is a second-line lipid-lowering agent.

C - Miglitol

Explanation Why

Miglitol can cause osmotic diarrhea and abdominal discomfort. This drug inhibits α-glucosidase, which leads to decreased intestinal absorption of monosaccharides (e.g., glucose) and increased excretion of oligosaccharides and disaccharides. However, because it does not affect lipase activity, fecal triglyceride excretion is not increased in patients who take miglitol. Moreover, miglitol is not used for weight loss; it is used to decrease postprandial hyperglycemia.

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D - Orlistat

Explanation Why

Orlistat is a gastric and pancreatic lipase inhibitor that prevents complete hydrolyzation of dietary triglycerides into monoglycerides and fatty acids. As a result, triglycerides are not absorbed in the gastrointestinal tract, which leads to increased fecal triglyceride excretion and weight loss. Common adverse effects include diarrhea, abdominal distention, and flatulence, as seen in this patient.

E - Colesevelam

Explanation Why

Colesevelam can cause gastrointestinal symptoms but causes constipation more commonly than diarrhea. This drug binds to bile acids in the intestine and forms an insoluble complex that is then excreted in feces. Because it does not affect lipase activity, fecal triglyceride excretion is not increased in patients who take colesevelam. Moreover, colesevelam is not used for weight loss; it is a second-line lipid-lowering agent.

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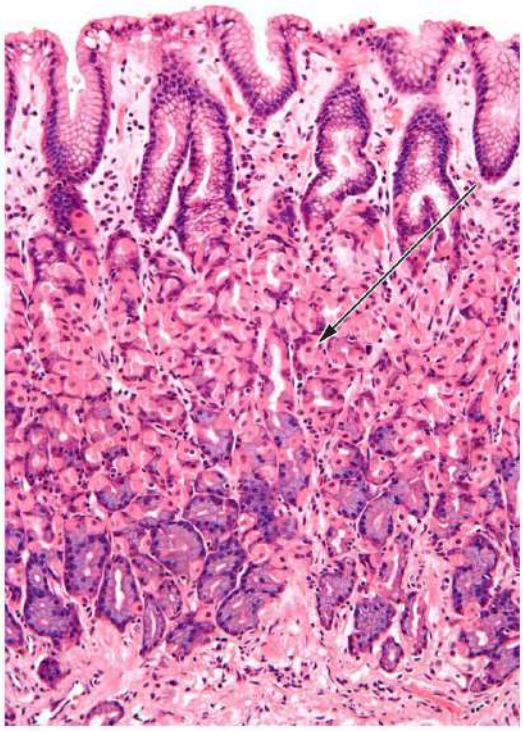
Question # 11

During an experimental study on the mucosa of the gastrointestinal tract, an investigator finds that vagal stimulation regulates the activity of a cell type that is mainly found in the fundus and body of the stomach. A photomicrograph of a normal gastric mucosa is shown; the cell type under investigation is indicated by the arrow. Stimulation of the labeled cell is most likely to cause increased secretion of which of the following substances?



	Answer	Image
A	Bicarbonate	
B	Gastrin	

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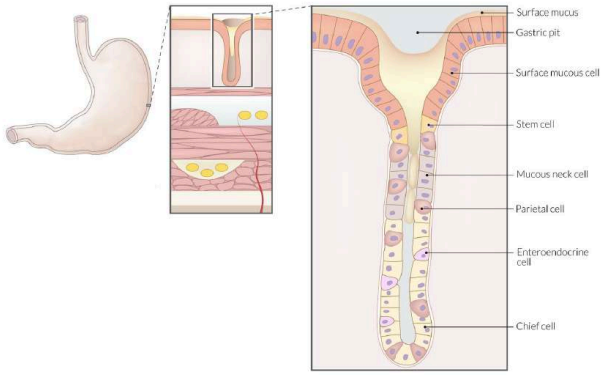
	Answer	Image
C	Intrinsic factor	
D	Somatostatin	
E	Histamine	
F	Pepsinogen	

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Hint

The photomicrograph shows a large eosinophilic cell with a circular nucleus (fried egg appearance), which is characteristic of parietal cells. These cells are typically located in the middle of the gastric glands.

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Correct Answer

A - Bicarbonate

Explanation Why

Bicarbonate is secreted by mucosal cells, which can be located in the body and fundus of the stomach. However, their activity is regulated by secretin rather than vagal stimulation. Moreover, the labeled cell is not a mucosal cell, which is located at the surface of the gland and usually has a clearer cytoplasm.

B - Gastrin

Explanation Why

Gastrin is secreted by G cells, whose activity is stimulated by vagal stimulation. However, these cells are typically located in the antrum of the stomach rather than the body and fundus. Moreover, the labeled cell is not a G cell, which typically has a clearer cytoplasm.

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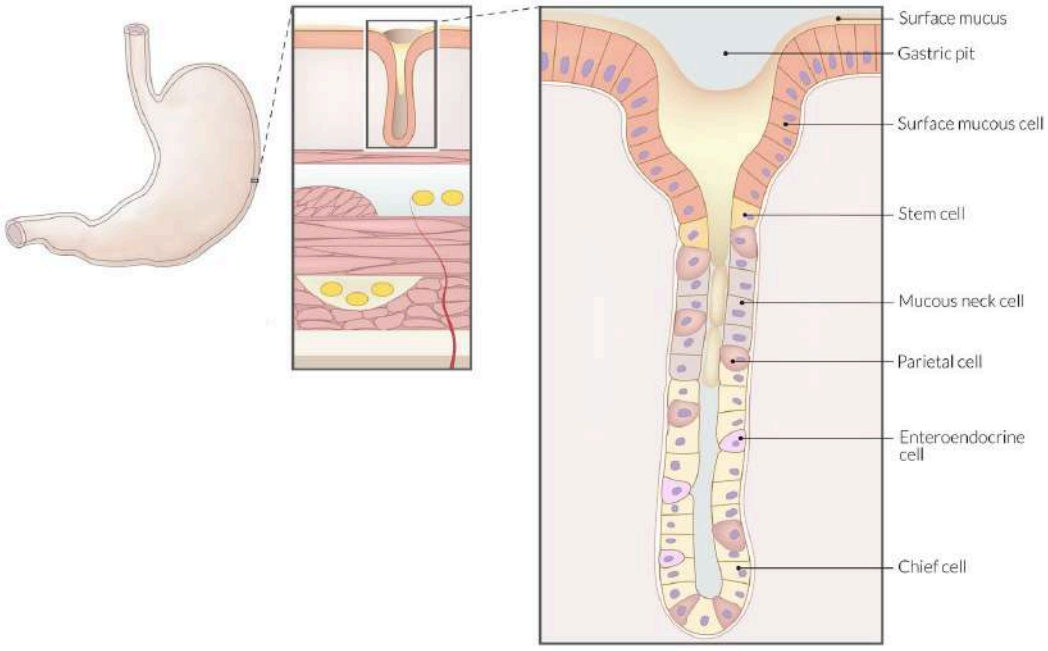
C - Intrinsic factor

Image



Explanation But

Autoimmune destruction of parietal cells leads to pernicious anemia and chronic gastritis.

Explanation Why

Parietal cells are responsible for the secretion of intrinsic factor, which facilitates vitamin B12 transportation and absorption in the terminal ileum. Parietal cells also secrete HCl, which maintains the acidic environment of the stomach necessary for digestion. In addition, these cells play an important role in the homeostasis of gastric mucosa by secreting multiple growth factors. The activity of parietal cells is stimulated by acetylcholine (via vagal stimulation), histamine, and gastrin, and is inhibited by somatostatin, secretin, prostaglandins, CCK, and GIP.

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D - Somatostatin

Explanation Why

Somatostatin is secreted by D cells, whose activity is inhibited by vagal stimulation. However, these cells are mainly located in the antrum and pylorus of the stomach rather than the fundus and body. Moreover, the labeled cell is not a D cell, which typically has clear cytoplasm.

E - Histamine

Explanation Why

Histamine is secreted by enterochromaffin-like cells, which are mainly located in the fundus and body of the stomach. However, their activity is regulated by gastrin rather than directly through vagal stimulation (vagal stimulation does affect gastrin release though). Moreover, the labeled cell is not an enterochromaffin-like cell, which is usually smaller, located in the deeper parts of the gland, and has a clearer cytoplasm.

F - Pepsinogen

Explanation Why

Pepsinogen is secreted by chief cells, which are mainly located in the fundus and body of the stomach and whose activity is regulated by vagal stimulation. However, the labeled cell is not a chief cell, which is located at the base of the gland, has a granular basophilic cytoplasm due to pepsinogen granules, and is typically pyramid-shaped.

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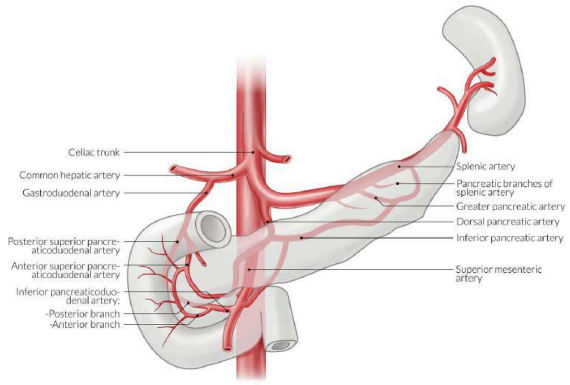
Question # 12

A 54-year-old woman comes to the emergency department because of recurrent episodes of fatigue, nausea, palpitations, and diaphoresis for the past 2 months. Her symptoms usually improve after drinking juice but during the past week, she has also been having symptoms approximately 2 hours after meals. She has no history of serious illness and takes no medication. Abdominal examination shows no abnormalities. Her fasting serum glucose concentration is 46 mg/dL; both serum insulin concentration and serum C-peptide concentrations are increased. A contrast-enhanced CT scan of the abdomen shows a 2-cm, well-demarcated lesion in the pancreatic tail. The patient is scheduled to undergo laparoscopic tumor resection. Which of the following arteries is at greatest risk for injury during the procedure?

	Answer	Image
A	Common hepatic	
B	Splenic	
C	Left gastric	
D	Inferior pancreaticoduodenal	
E	Inferior mesenteric	

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Hint

This is a tortuous artery that arises from the celiac trunk and branches off the greater curvature of the stomach (short gastric artery, left gastroepiploic artery) and pancreas (greater pancreatic artery, dorsal pancreatic artery).

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Correct Answer

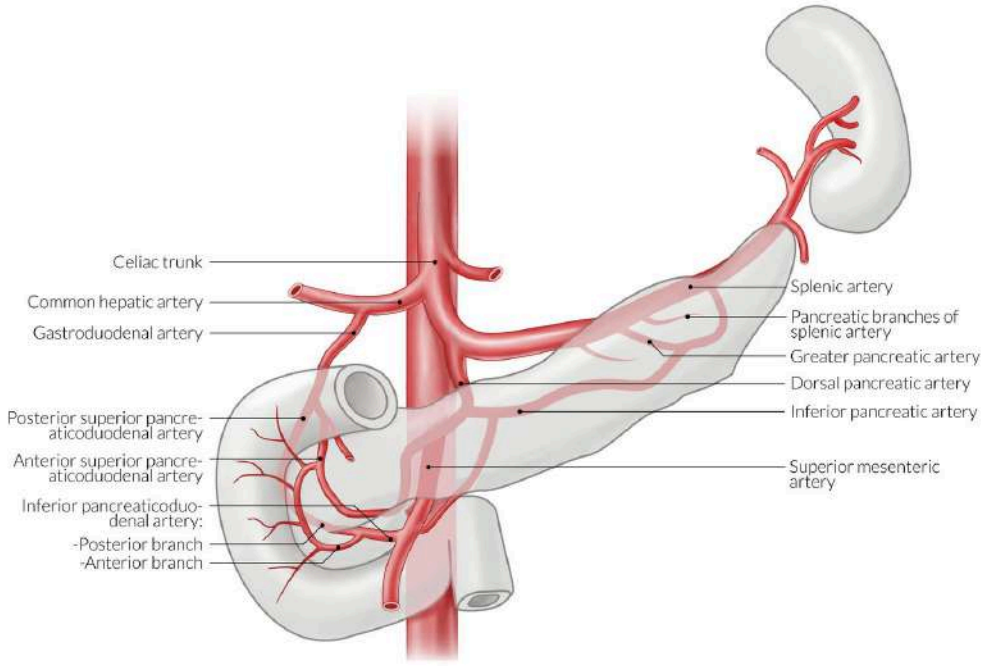
A - Common hepatic

Explanation Why

The common hepatic artery branches off the celiac trunk and lies in close proximity to the first part of the duodenum and the superior border of the pancreatic head. This common hepatic artery is, therefore, at risk for injury during resection of the head of the pancreas or duodenum (e.g., Whipple procedure) but is unlikely to be injured during resection of the tail of the pancreas (distal pancreatectomy), which would be performed in this patient.

B - Splenic

Image



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Explanation Why

The splenic artery runs to the hilum of the spleen through the splenorenal ligament, which also contains the splenic vein and the tail of the pancreas (the only intraperitoneal part of the pancreas). This patient's low fasting glucose levels, increased serum concentration of C-peptide and insulin levels, and a mass in the pancreatic tail on imaging suggests an insulinoma, a neuroendocrine tumor that most commonly arise from pancreatic β-cells. When resecting an insulinoma in the tail of the pancreas (distal pancreatectomy), the surgeon will dissect the splenorenal ligament and possibly the spleen (because of the high risk of splenic metastasis in the case of neuroendocrine tumors). Therefore, the splenic artery and vein are at greatest risk of being damaged during this procedure.

C - Left gastric

Explanation Why

The left gastric artery branches off the celiac trunk, runs upward within the gastrohepatic ligament, and anastomoses with the right gastric artery along the lesser curvature of the stomach. The left gastric artery can be injured during gastrohepatic ligament dissection, which is performed to gain access to the superior recess of the lesser sac. The pancreas is present in the lesser sac's inferior recess, which is accessed by an incision in the gastrocolic ligament rather than the gastrohepatic ligament. The left gastric artery is, therefore, unlikely to be injured during this patient's procedure.

D - Inferior pancreaticoduodenal

Explanation Why

The inferior pancreaticoduodenal artery branches off the superior mesenteric artery and lies in close proximity to the uncinate process, head of the pancreas, as well as the third part of the duodenum. The inferior pancreaticoduodenal artery is, therefore, at risk for injury during resection of the uncinate process, head of the pancreas, or duodenum (e.g., Whipple procedure) but is unlikely to get damaged during resection of the tail of the pancreas (distal pancreatectomy), which would be performed in this patient.

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E - Inferior mesenteric

Explanation Why

The inferior mesenteric artery branches off the abdominal aorta at the level of the L_3 vertebra, while the tail of the pancreas is located further away at the level of the T_{12} vertebra. Therefore, the inferior mesenteric artery is unlikely to get damaged during resection of the tail of the pancreas.

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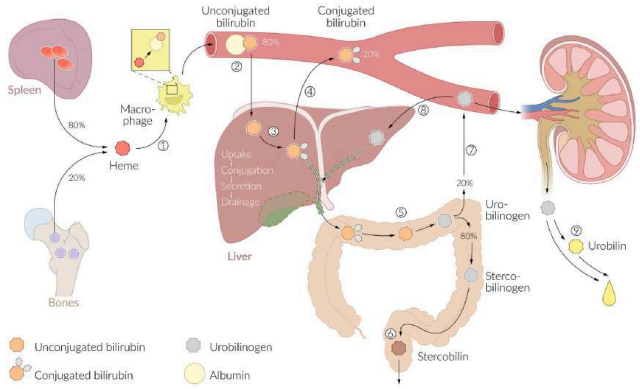
Question # 13

Two days after delivery, a 4500-g (10-lb) male newborn develops poor feeding and irritability. He was born at 38 weeks' gestation. Delivery was complicated by a prolonged second stage of labor and vacuum extraction was performed. He appears lethargic. Physical examination shows yellow discoloration of the skin and mucous membranes. There is a swelling in the occipital region. His total serum bilirubin concentration is 21.5 mg/dL. The newborn is placed in an incubator with a non-UV, blue-green light. Two days later, his total serum bilirubin concentration is within the reference range. Which of the following processes best explains the decrease of this newborn's total bilirubin concentration?

	Answer	Image
A	Oxidation of conjugated bilirubin molecules	
B	Reduction of conjugated bilirubin molecules	
C	Isomerization of unconjugated bilirubin molecules	
D	Photolysis of conjugated bilirubin molecules	
E	Glucuronidation of unconjugated bilirubin molecules	

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Hint

This patient developed neonatal jaundice most likely as a result of a cephalohematoma and was subsequently treated successfully with phototherapy.

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Correct Answer

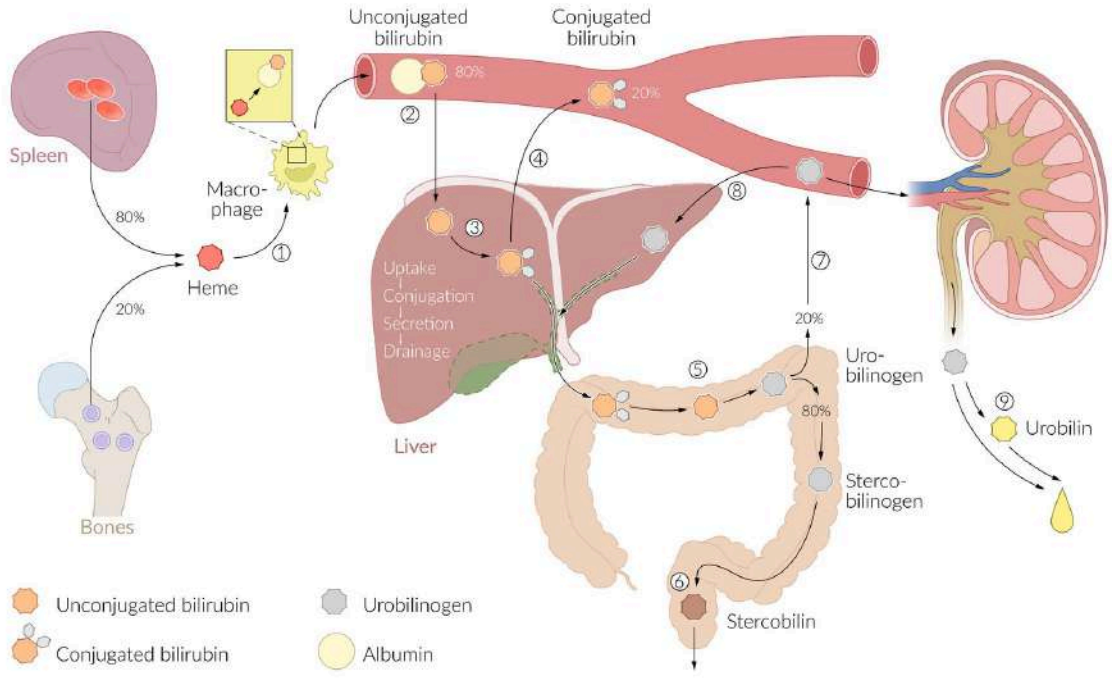
A - Oxidation of conjugated bilirubin molecules

Explanation Why

Oxidation of bilirubin molecules leads to the formation of photooxidation products that can be excreted in the urine and is one of the mechanisms by which phototherapy increases bilirubin elimination. However, this process is slow and contributes minimally to the effect of phototherapy. Moreover, photooxidation induced by phototherapy is a process that occurs with unconjugated rather than conjugated bilirubin.

B - Reduction of conjugated bilirubin molecules

Image



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Explanation Why

The reduction of conjugated bilirubin molecules by bacteria to stercobilinogen and urobilinogen occurs in the GI tract rather than the skin, where phototherapy exerts its effects.

C - Isomerization of unconjugated bilirubin molecules

Explanation But

Photoisomerization is also the mechanism for the conversion of cutaneous 7-dehydrocholesterol by UVB light (280–320 nm) to cholecalciferol (vitamin D_3)

Explanation Why

In the type of phototherapy used to treat neonatal jaundice, 420–480 nm light is utilized to convert unconjugated, water-insoluble bilirubin (4Z,15Z-bilirubin) in the skin to water-soluble isomers (e.g., Z-lumirubin, 4Z,15E-bilirubin), which can be eliminated in urine and/or bile without being conjugated by the liver. Photoisomerization is the primary mechanism for the elimination of unconjugated bilirubin during phototherapy. Phototherapy is indicated for newborns with severe unconjugated bilirubinemia because unconjugated bilirubin is lipophilic and can cross the immature blood-brain barrier of newborns, leading to kernicterus. Newborns undergoing phototherapy must receive eye protection to prevent retinal degeneration from bright light, and adequate fluid supplementation to prevent dehydration.

D - Photolysis of conjugated bilirubin molecules

Explanation Why

Photolysis (photodecomposition) is the breakdown of a molecule by light. It is partially responsible for the effectiveness of radiotherapy and certain phototherapies, such as UVB therapy and PUVA therapy. The type of phototherapy used to treat neonatal jaundice does not use UV light and does not break down bilirubin molecules; instead, it transforms these molecules into more water-soluble products.

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E - Glucuronidation of unconjugated bilirubin molecules

Explanation Why

Glucuronidation of unconjugated to conjugated bilirubin by hepatic UDP-glucuronosyltransferase (UDP-GT) is the physiological process that allows for the protein-mediated transport of bilirubin across the apical hepatocyte membrane into bile canaliculi for excretion. In newborns, UDP-GT activity is low and does not contribute significantly to the elimination of bilirubin. Phototherapy is required to mitigate low UDP-GT activity, as seen here, but it does induce glucuronidation.

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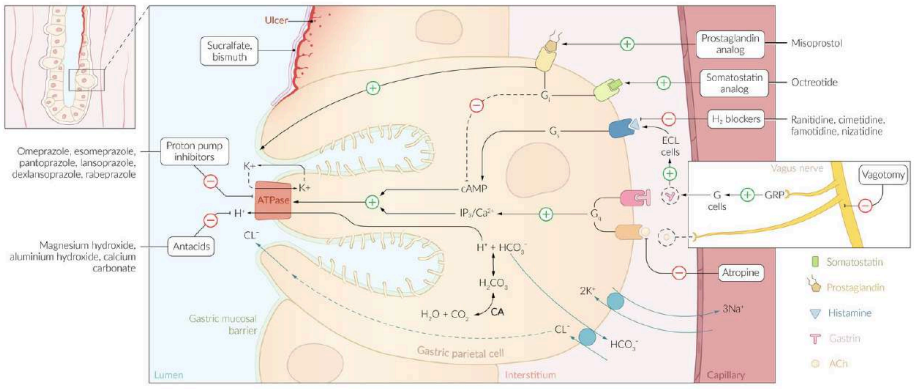
Question # 14

An investigator is studying the effect of a new drug on gastric mucosa cells. She finds that under physiologic conditions, the new drug acts as a competitive antagonist of a G-protein coupled receptor that is located on the cell membrane of parietal cells. Activation of this type of receptor increases the intracellular concentration of cyclic adenosine monophosphate. The mechanism of action of the new drug is most similar to that of which of the following?

	Answer	Image
A	Atropine	
B	Octreotide	
C	Misoprostol	
D	Cimetidine	
E	Dexlansoprazole	

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Hint

Activation of the G_s G-protein coupled receptor subtype causes an increase in cyclic adenosine monophosphate.

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Correct Answer

A - Atropine

Explanation Why

Atropine is an antagonist of muscarinic receptors including the M3 muscarinic isoform, which are also located on parietal cells and are a type of G protein-coupled receptor (GPCR). However, M3 receptors are G_q-coupled receptors. Activation of this receptor increases phospholipase C activity, which, in turn, increases intracellular inositol triphosphate and diacylglycerol production and subsequently increases calcium concentration in the cell and protein phosphorylation via protein kinase C. A change in the intracellular concentration of cyclic adenosine monophosphate would not occur via this signal transduction pathway.

B - Octreotide

Explanation Why

Octreotide is an agonist at somatostatin receptors, which are also located on parietal cells and are G-protein coupled receptors (GPCR). However, somatostatin receptors are G_i-coupled receptors. Activation of these receptors would decrease, not increase, the intracellular concentration of cyclic adenosine monophosphate (cAMP). The drug being studied by the investigator binds to a type of GPCR that increases intracellular cAMP on activation.

C - Misoprostol

Explanation Why

Misoprostol is an agonist of prostaglandin E1 (PGE1) receptors, which are also located on parietal cells and are a type of G protein-coupled receptor (GPCR). However, PGE1 receptors are G_i-coupled receptors. Activation of these receptors would decrease, not increase, the intracellular concentration of cyclic adenosine monophosphate (cAMP). The drug being studied by the investigator binds to a type of GPCR that increases intracellular cAMP on activation.

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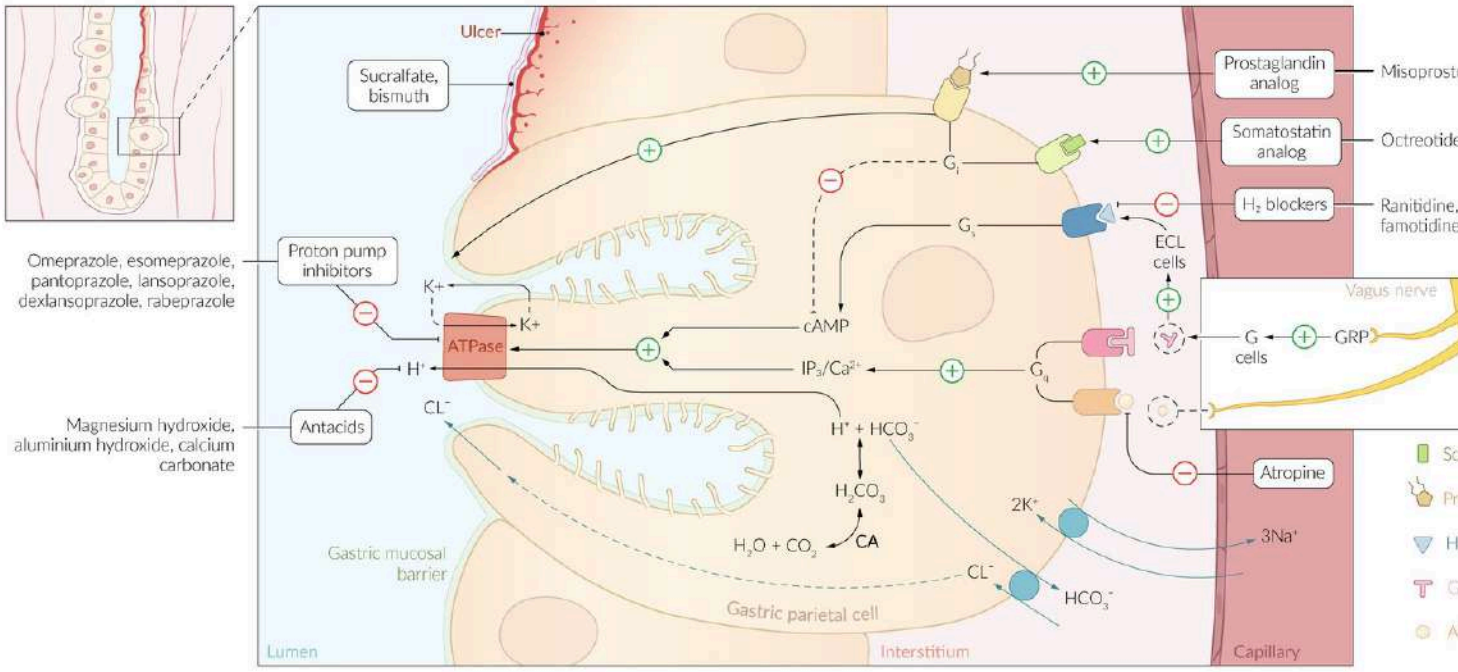
D - Cimetidine

Image



Explanation Why

Cimetidine is a competitive antagonist of histamine-2 (H2) receptors, which are found on parietal cells and are G_s-protein coupled receptors. Activation of these receptors would increase adenylyl cyclase activity, which leads to increased cyclic adenosine monophosphate (cAMP) levels. cAMP activates protein kinase A, which, in turn, phosphorylates and activates the proton pump (H^+/K^+ ATPase). H2 receptor antagonists would, therefore, decrease cAMP levels in parietal cells and decrease gastric acid secretion. The mechanism of action of the drug being studied by the investigator is most similar to this class of drugs.

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E - Dexlansoprazole

Explanation Why

Dexlansoprazole is a proton pump inhibitor (PPI), which directly inhibits H^+/K^+ ATPase found on the luminal part of gastric parietal cells. PPIs do not cause a change in the intracellular concentration of cyclic adenosine monophosphate.

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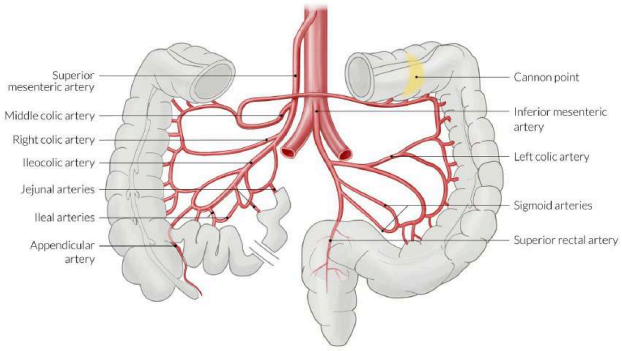
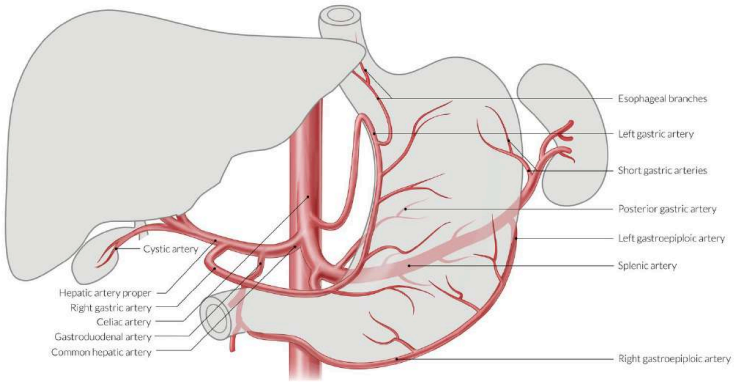
Question # 15

A 67-year-old woman is brought to the emergency department because of severe abdominal pain for 1 hour. She has hypertension and coronary heart disease. She has smoked 2 packs of cigarettes daily for 30 years. Her pulse is 140/min and blood pressure is 89/58 mm Hg. Physical examination shows a pulsatile abdominal mass. A CT scan of the abdomen shows a ruptured abdominal aortic aneurysm. The patient is taken to the operating room for emergency open surgery. During the procedure, an artery that branches off from the aorta, just below the renal arteries, at the level of the L2 vertebra is damaged. The arterial supply to which of the following structures is most likely to be impaired by the intraoperative vascular damage?

	Answer	Image
A	Ascending colon	
B	Liver	

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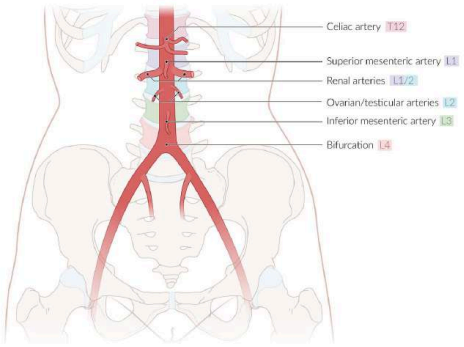
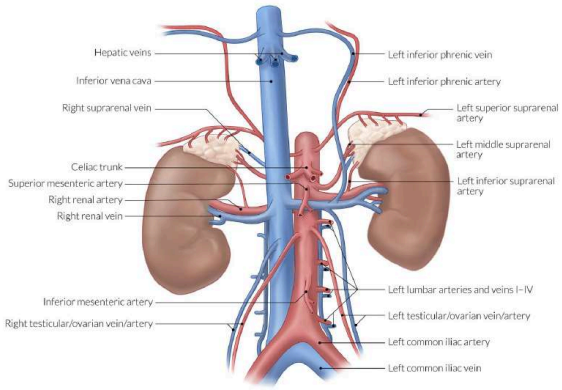
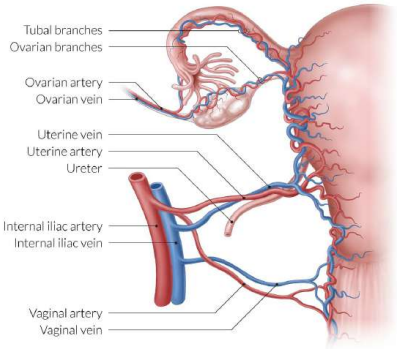
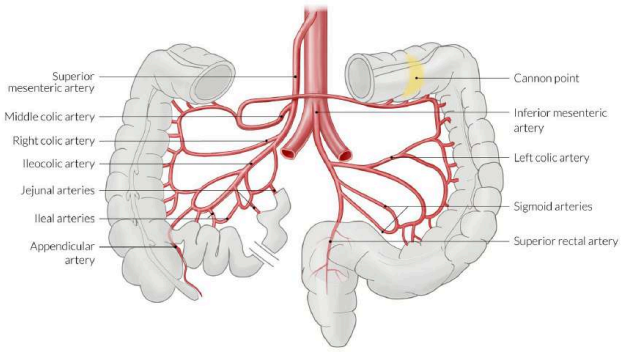
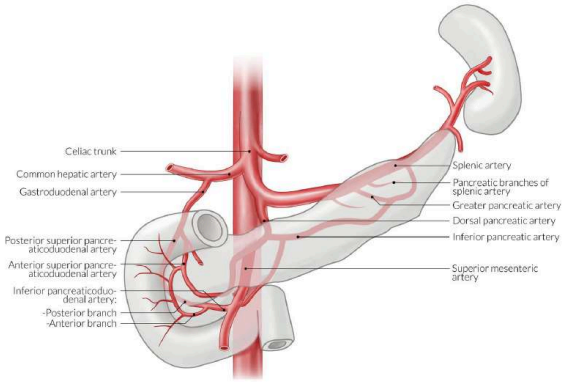
	Answer	Image
C	Ovary	
D	Adrenal gland	
E	Cervix	

https://t.me/USMLEAmboss

	Answer	Image
F	Descending colon	
G	Spleen	

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Hint

The damaged artery passes through the infundibulopelvic ligament.

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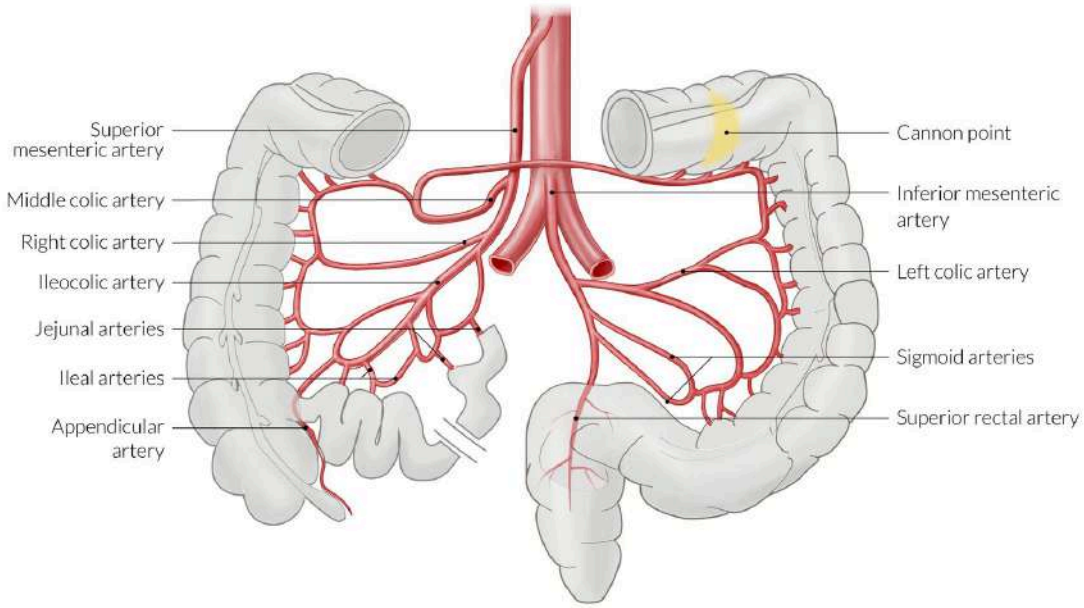
Correct Answer

A - Ascending colon

Image



Explanation Why

The ascending colon is supplied mostly by the right colic artery, which branches off from the superior mesenteric artery. The superior mesenteric artery is a direct branch of the abdominal aorta and arises suprarenally at the level of the T12 vertebra. The artery in question, however, is located at the level of the L2 vertebra.

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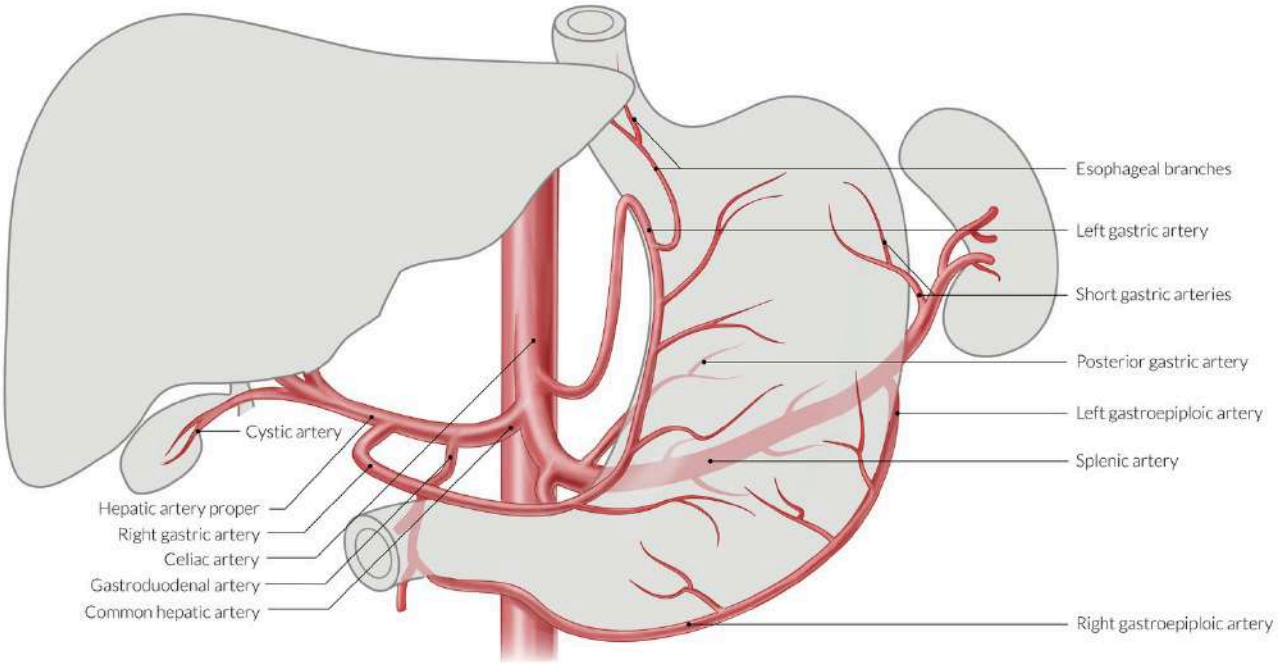
B - Liver

Image



Explanation Why

The liver receives 40% of its blood supply from the hepatic artery proper, a branch of the common hepatic artery, which is, in turn, a branch of the celiac trunk of the abdominal aorta. The celiac trunk arises suprarenally at the level of the T12 vertebra. The injured artery in this patient, however, arises at the level of the L2 vertebra.

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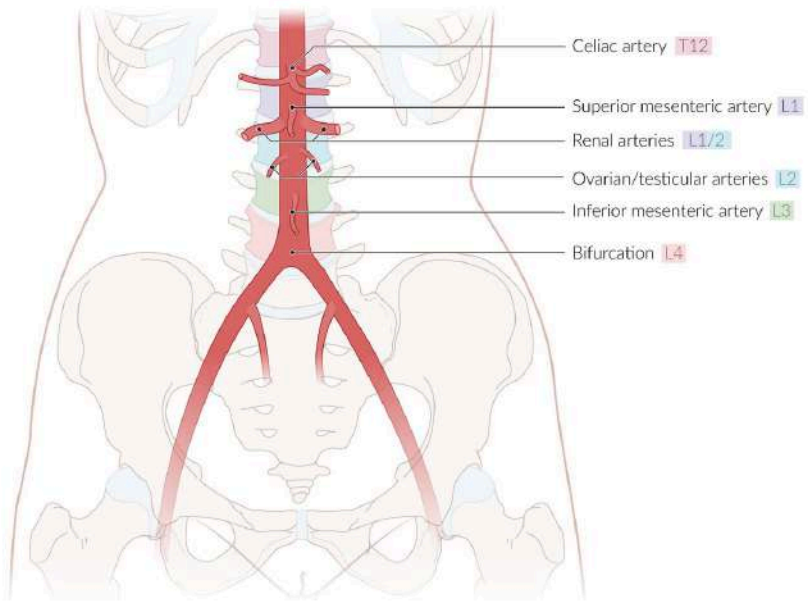
C - Ovary

Image



Explanation Why

Both ovarian arteries branch off directly from the abdominal aorta just below the renal arteries at the level of the L2 vertebra. An injury to one of the ovarian arteries, as seen here, would significantly deprive the respective ovary of its arterial blood supply. The ovarian artery, which forms an anastomosis with the uterine artery, also supplies the lateral two-thirds of the fallopian tube as well as the proximal part of the uterus.

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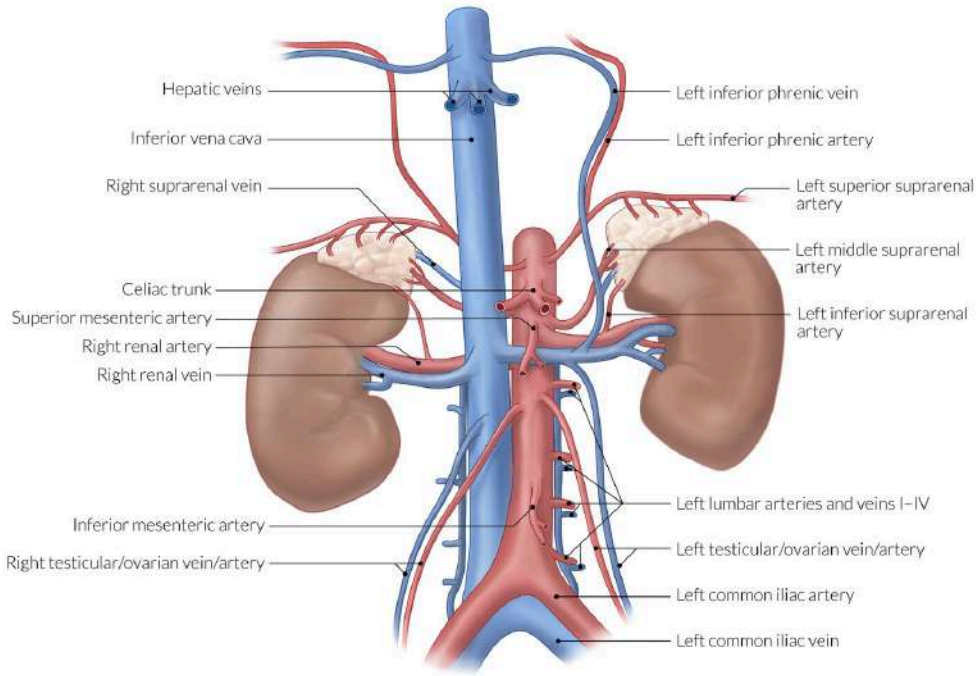
D - Adrenal gland

Image



Explanation Why

The adrenal glands are supplied by three arteries: the superior suprarenal artery (from the inferior phrenic artery), middle suprarenal artery (from the abdominal aorta), and inferior suprarenal artery (from the renal artery). All of these arteries arise between the T12 and the lower border of the L1 vertebrae. The injured artery in this patient, however, arises at the level of the L2 vertebra.

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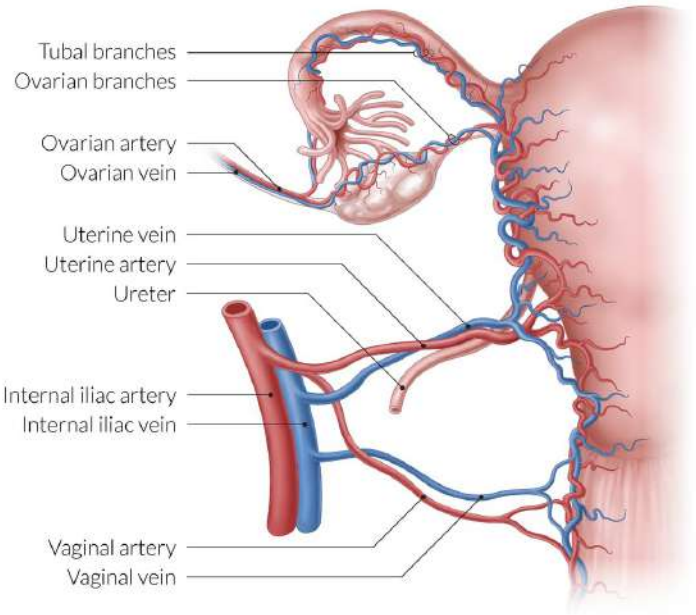
E - Cervix

Image



Explanation Why

The cervix is supplied by the uterine artery, which is a branch of the internal iliac artery. The internal iliac artery branches off in the pelvic region from the common iliac artery, which arises from the abdominal aorta at the level of the L4 vertebra. The artery injured in this patient, however, arises at the level of the L2 vertebra.

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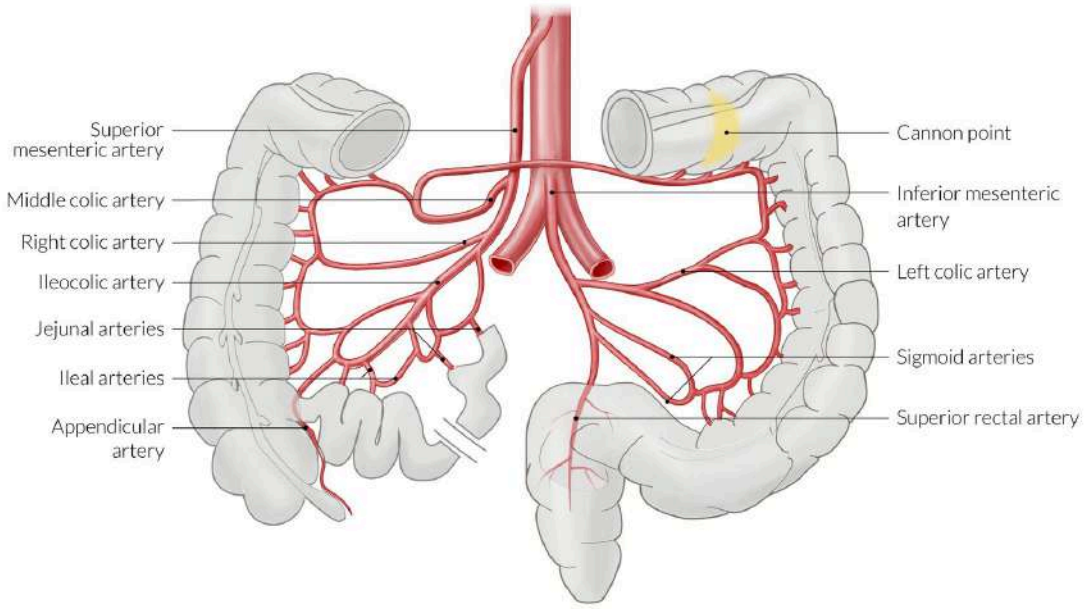
F - Descending colon

Image



Explanation Why

The descending colon is supplied mostly by the left colic artery, which branches off from the inferior mesenteric artery. The inferior mesenteric artery is a direct branch of the abdominal aorta and arises at the level of the L3 vertebra. The artery in question, however, is located at the level of the L2 vertebra.

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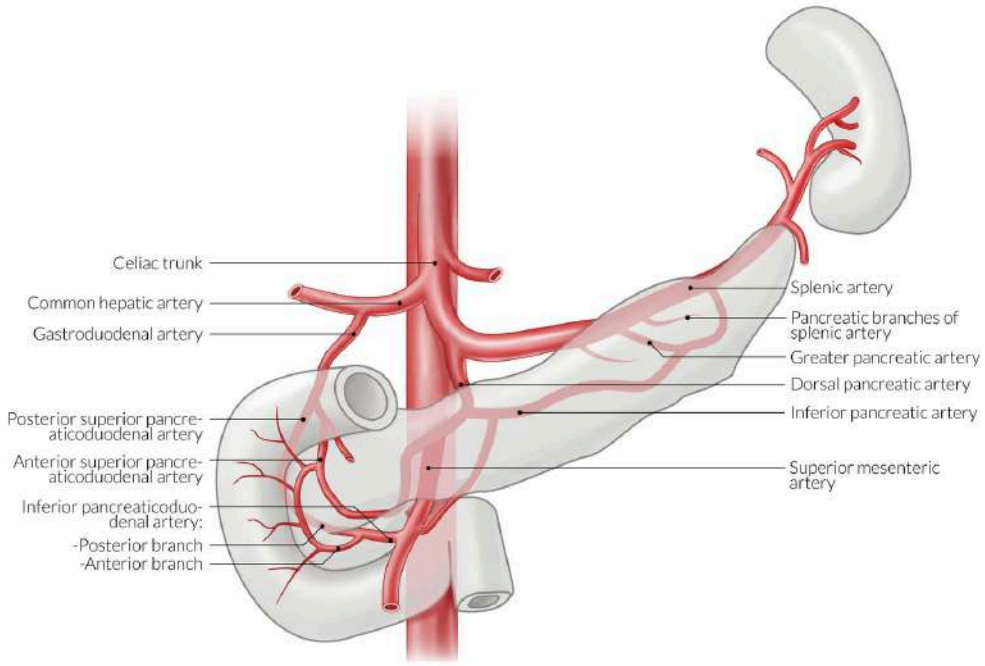
G - Spleen

Image



Explanation Why

The spleen receives its arterial blood supply from the splenic artery, which branches off from the celiac trunk. The celiac trunk, in turn, branches off from the aorta suprarenally at the superior border of the T12 vertebra. The artery in question, however, is located at the level of the L2 vertebra.

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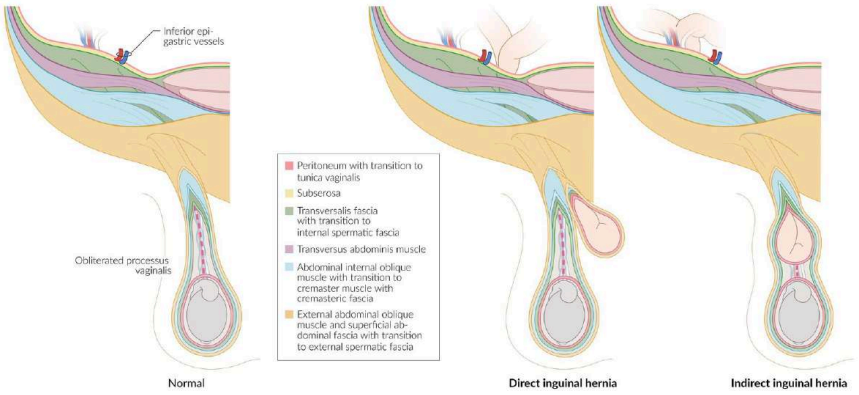
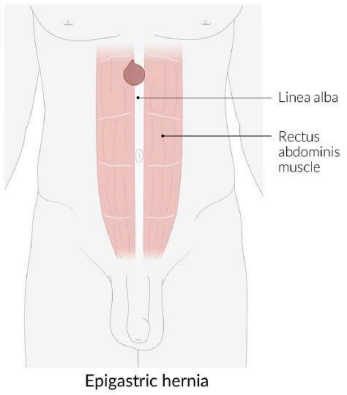
Question # 16

A 79-year-old man is brought to the emergency department because of a 1-hour history of severe groin pain, nausea, and vomiting. He reports that he has had a groin swelling that worsens with standing, coughing, and straining for the past 3 months, but he has not sought medical attention for it. Examination shows a nonreducible bulging mass of the left groin that is severely tender to palpation; the overlying skin is erythematous. Abdominal ultrasound shows protrusion of abdominal contents through a defect medial to the inferior epigastric vessels. Which of the following is the most likely site of protrusion of the patient's groin mass?

	Answer	Image
A	Inguinal triangle	
B	Linea alba	
C	Rectus abdominis muscle	

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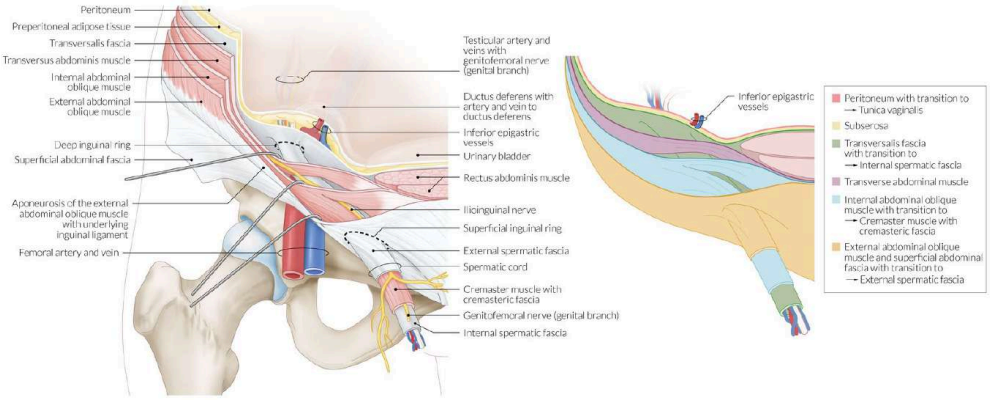
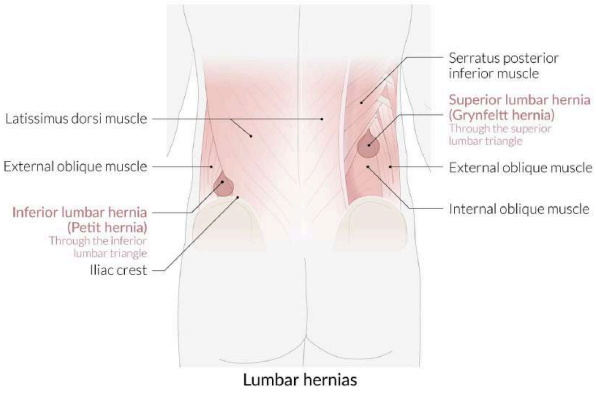
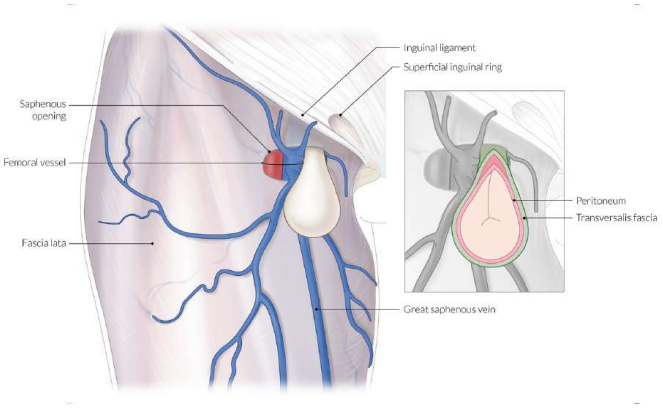
	Answer	Image
D	Deep inguinal ring	
E	Inferior lumbar triangle	 Lumbar hernias
F	Femoral ring	

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Hint

A groin swelling that worsens with standing, coughing, and straining is suggestive of a hernia, and severe pain with features of bowel obstruction (e.g., nausea, vomiting) indicates strangulation of this hernia. The type of hernia seen here typically occurs as a result of weakening of the transversalis fascia.

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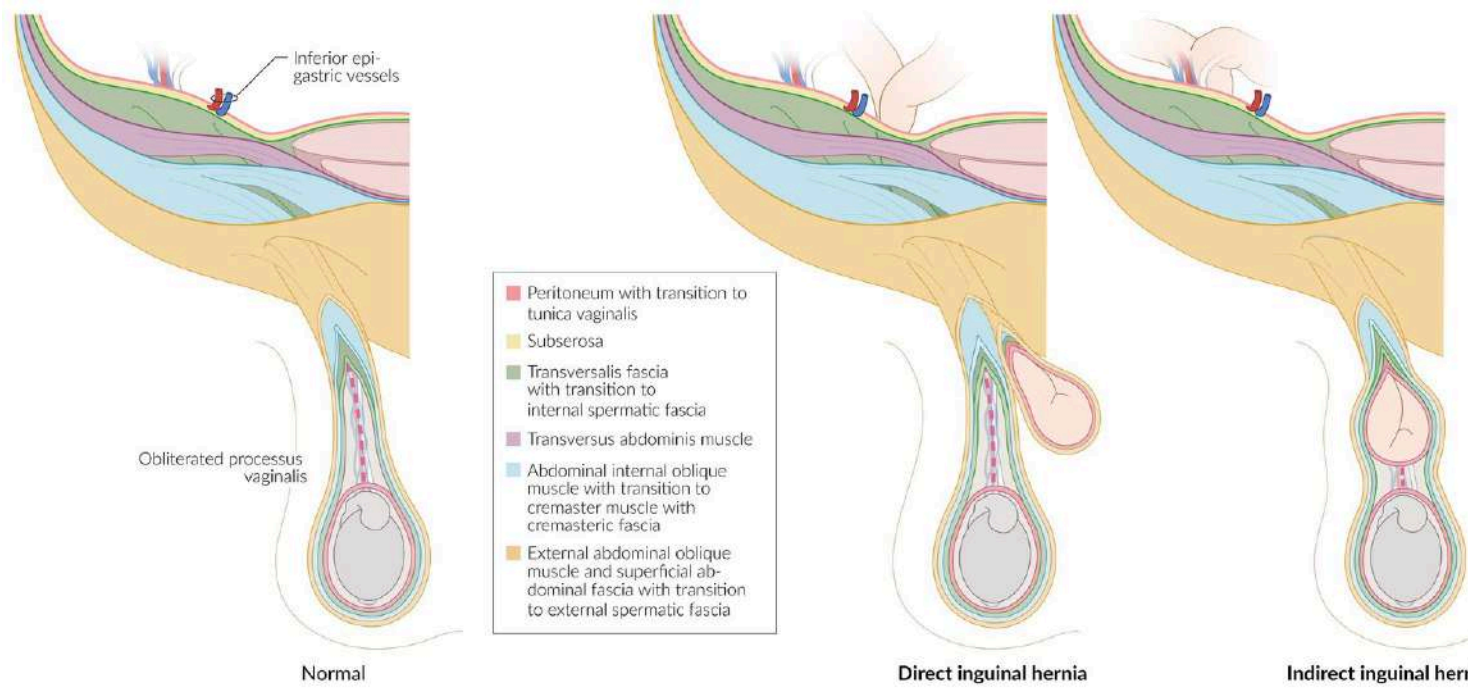
Correct Answer

A - Inguinal triangle

Image



Explanation Why

The inguinal triangle (Hesselbach triangle) is the site of protrusion of direct inguinal hernias, as seen here. This triangle is bordered laterally by the inferior epigastric vessels, medially by the lateral edge of the rectus abdominis sheath, and inferiorly by the inguinal ligament, and covered anteriorly by the transversalis fascia, conjoined tendon, and the aponeurosis of the external oblique muscle. Unlike indirect inguinal hernias, which pass through both the superficial and deep inguinal rings and are, therefore, covered by all layers of the spermatic cord, direct inguinal hernias pass only through the superficial inguinal ring and, at this point, are only covered by the external spermatic fascia.

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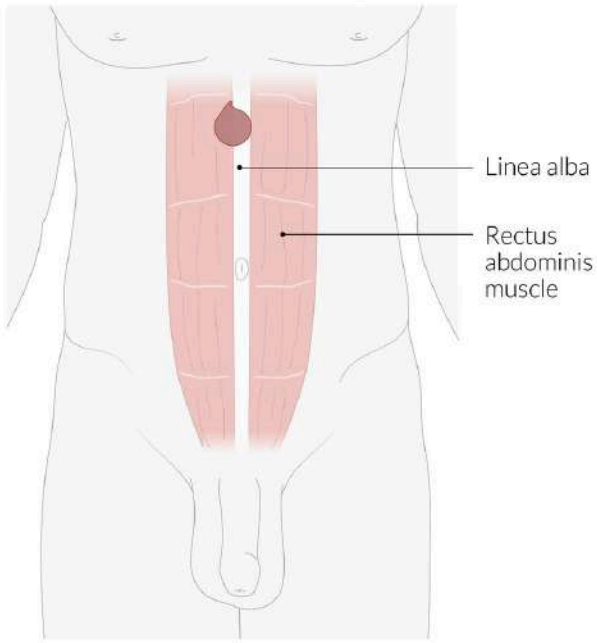
B - Linea alba

Image



Epigastric hernia

Explanation Why

The segment of the linea alba between the xiphoid process and the umbilicus is the site of protrusion of epigastric hernias, which cause swelling in the epigastric area rather than the groin.

C - Rectus abdominis muscle

Explanation Why

The hernia in this patient protrudes at a site that is lateral to the rectus abdominis muscle and covered by the transversalis fascia, conjoined tendon, and the aponeurosis of the external oblique muscle; it does not protrude through the rectus abdominis.

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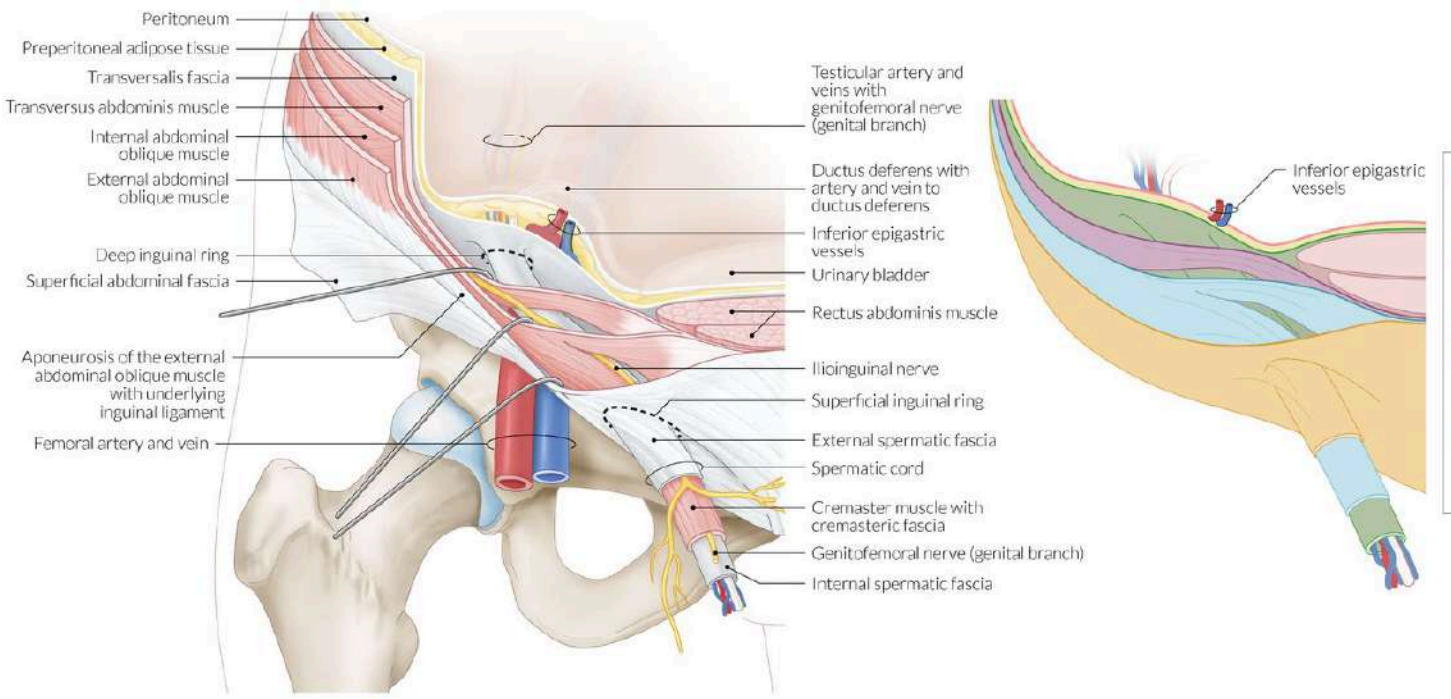
D - Deep inguinal ring

Image



Explanation Why

The deep inguinal ring is the site of protrusion of indirect inguinal hernias, which manifest as a groin mass, like the one seen here. However, the deep inguinal ring is located lateral to the inferior epigastric vessels; this patient, however, has a hernia that protrudes medial to these vessels and does not pass through the deep inguinal ring.

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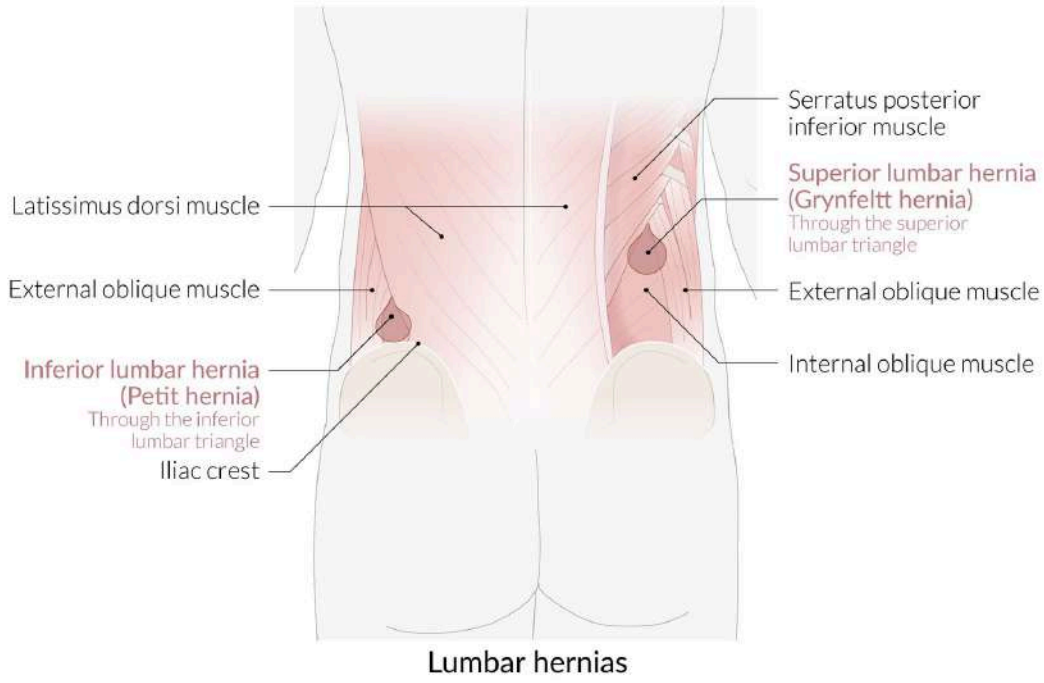
E - Inferior lumbar triangle

Image



Lumbar hernias

Explanation Why

The inferior lumbar triangle is the site of protrusion of inferior lumbar hernias, which cause swelling in the lumbar region rather than the groin.

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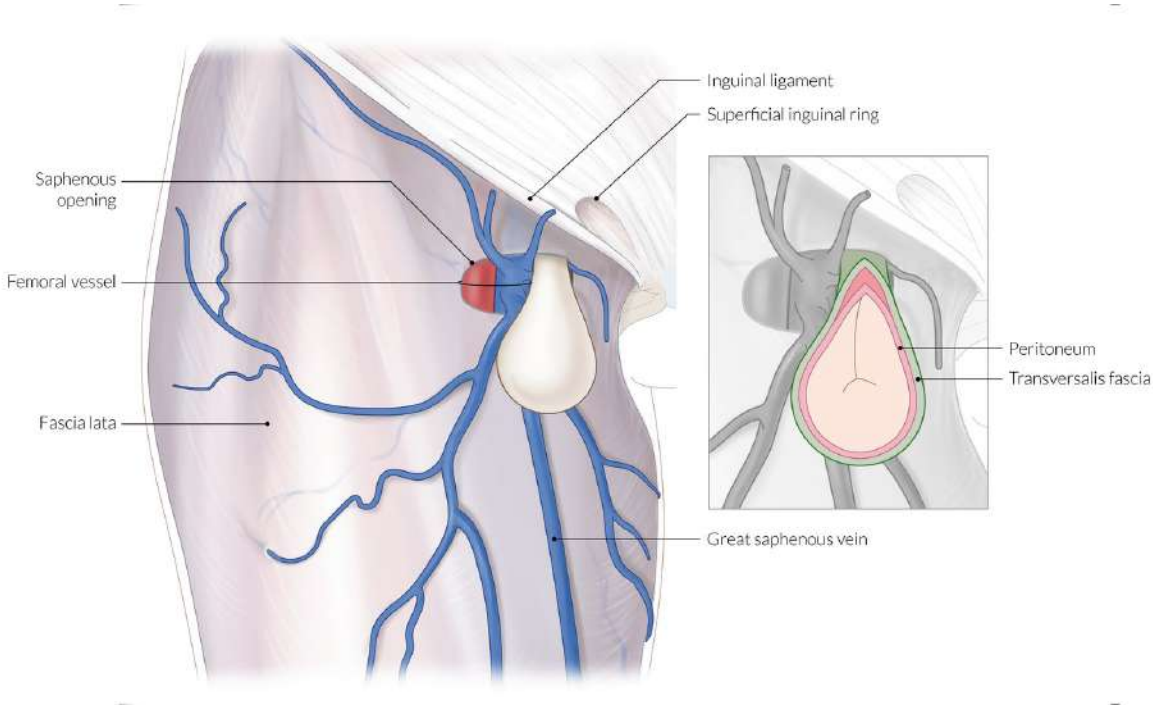
F - Femoral ring

Image



Explanation Why

The femoral ring is the site of protrusion of femoral hernias, which manifest as a groin mass and are prone to strangulation, like the mass seen here. Femoral hernias, however, protrude inferior to the inguinal ligament and medial to the femoral vein rather than medial to the inferior epigastric vessels, and they typically occur in women rather than men.

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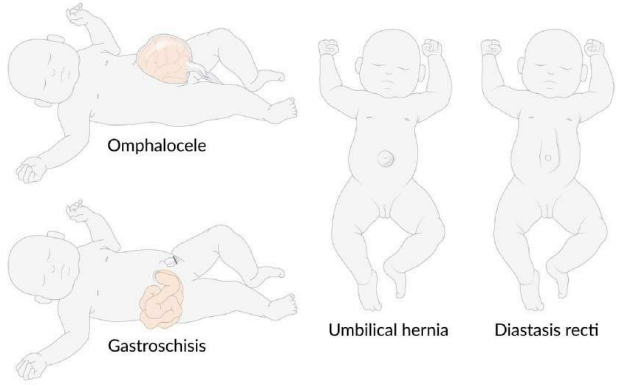
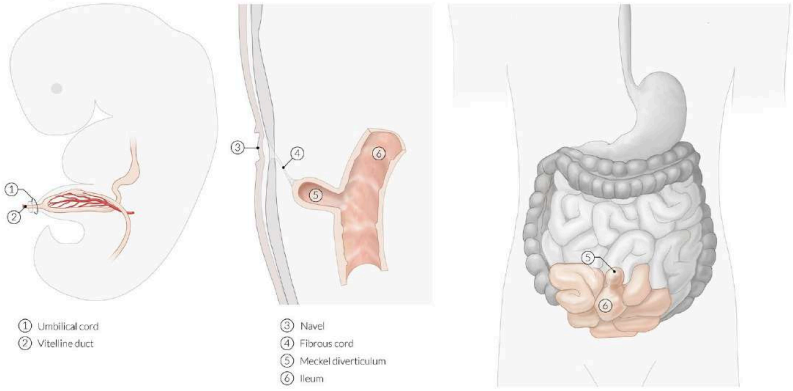
Question # 17

A 22-day-old male newborn is brought to the physician because of poor feeding, lethargy, and an abdominal protrusion. The child was delivered at home and has not yet been evaluated by a physician. The mother has not had routine prenatal care. The patient is at the 25th percentile for height, 50th percentile for weight, and 95th percentile for head circumference. Physical examination shows scleral icterus, pale facies, and an enlarged tongue. The abdomen is distended and there is a protruding mass at the abdominal midline. The skin covering the protrusion appears normal. When the newborn cries during the examination, the mass enlarges but is easily reducible. Which of the following is the most likely cause of the abdominal protrusion?

	Answer	Image
A	Failed convergence of the lateral embryologic folds	
B	Failed obliteration of the vitelline duct	

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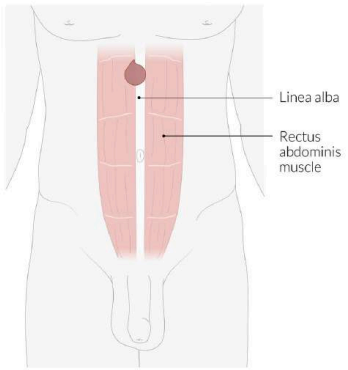
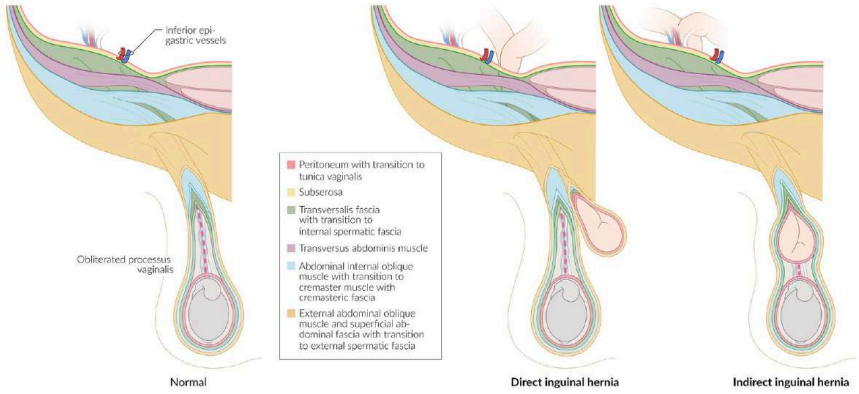
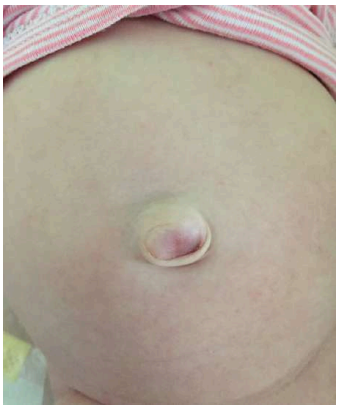
	Answer	Image
C	Congenital weakness of the linea alba	 Epigastric hernia
D	Persistence of a patent processus vaginalis	
E	Failed spontaneous closure of the umbilical ring	

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Hint

This patient has features consistent with congenital hypothyroidism (poor feeding, lethargy, prolonged newborn jaundice, pale facies, increased head circumference, abdominal distention, and macroglossia). His midline abdominal protrusion is a congenital umbilical hernia, a common feature of congenital hypothyroidism.

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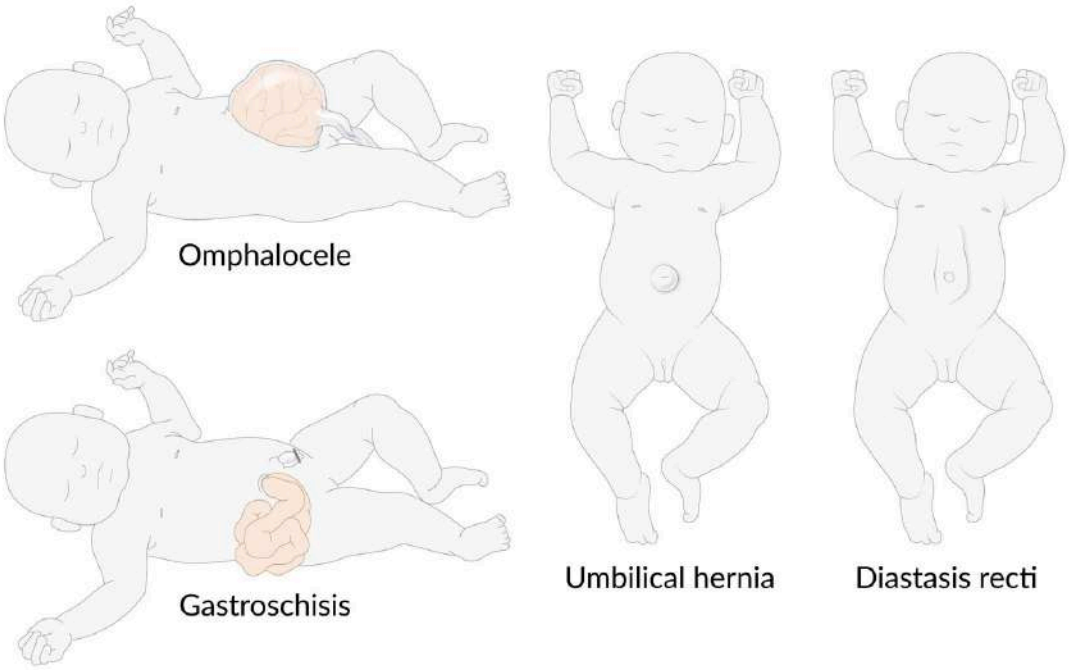
Correct Answer

A - Failed convergence of the lateral embryologic folds

Image



Explanation Why

Failed convergence of the lateral embryologic folds leads to abdominal wall defects such as gastroschisis or omphalocele, which can manifest as a protruding abdominal mass near or in the midline, as seen here. However, in gastroschisis, the intestines herniate uncovered by skin or peritoneum and in omphalocele, the intestines herniate through the umbilical ring covered only by peritoneum. This patient's skin-covered abdominal protrusion has a different cause.

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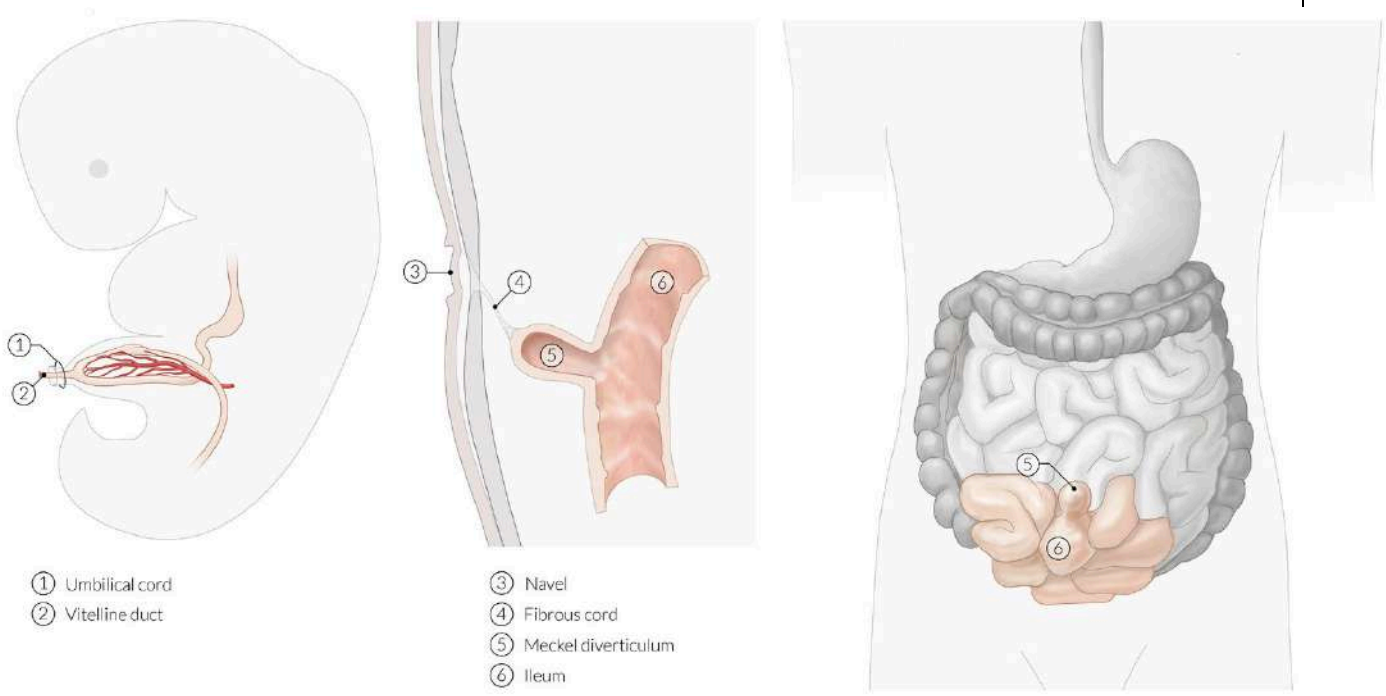
B - Failed obliteration of the vitelline duct

Image



Explanation Why

Complete failure of the vitelline duct to obliterate during the 7th week of development causes a vitelline fistula; partial failure results in Meckel diverticulum. A vitelline fistula causes meconium discharge through the umbilicus. A Meckel diverticulum is asymptomatic in most cases and sometimes manifests with diverticulitis or painless lower gastrointestinal bleeding. Neither of these conditions would manifest with an abdominal protrusion.

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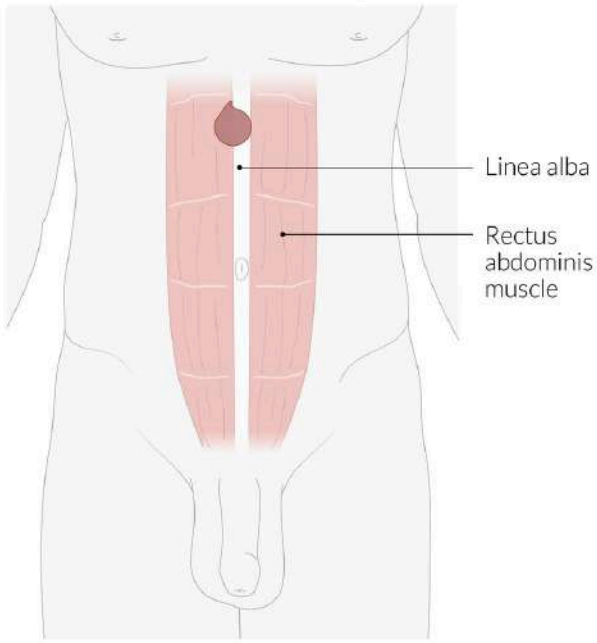
C - Congenital weakness of the linea alba

Image



Epigastric hernia

Explanation Why

Congenital weakness of the linea alba is the cause of an epigastric hernia, which occurs in the abdominal midline (between the xiphoid process and the umbilicus) and can manifest with an abdominal protrusion that enlarges with an increase in abdominal pressure (e.g., during crying), as seen here. However, epigastric hernias typically manifest during adulthood, not during the neonatal period. The abdominal protrusion in this patient has a different cause.

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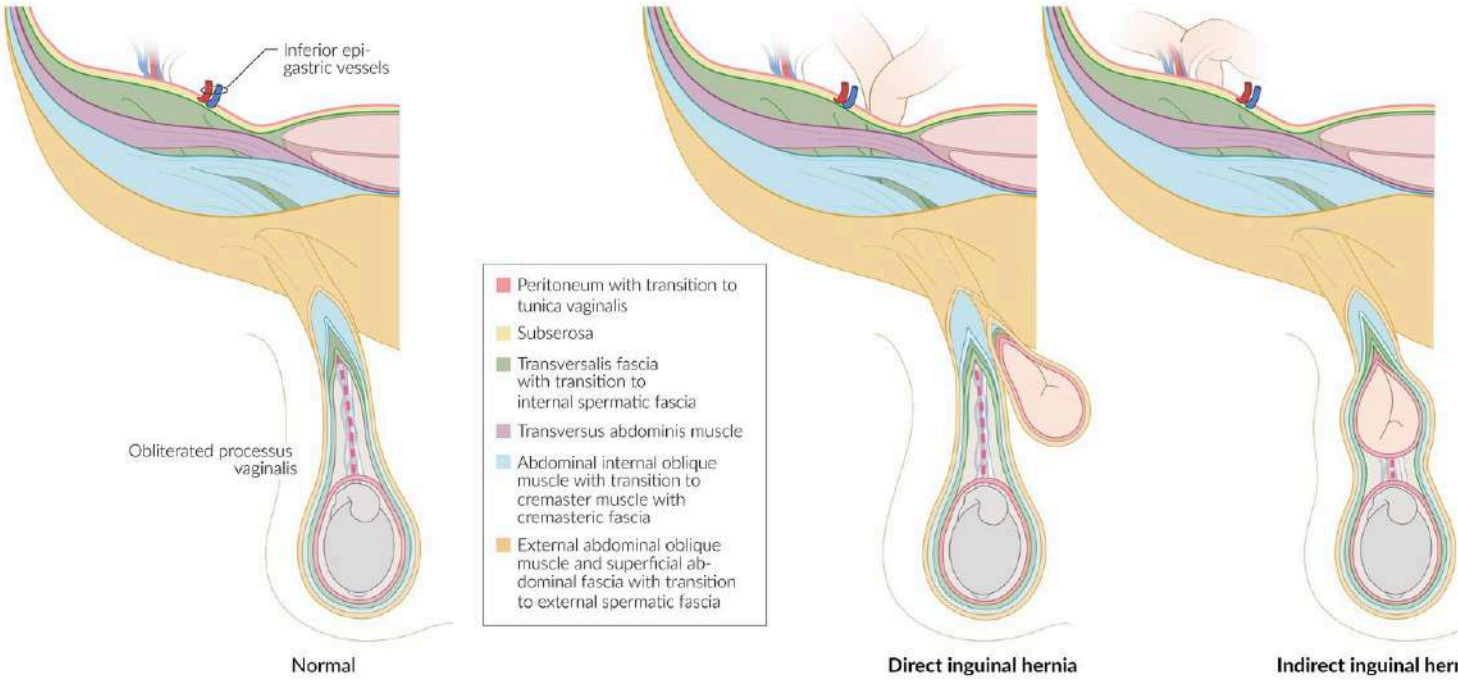
D - Persistence of a patent processus vaginalis

Image



Explanation Why

The persistence of a patent processus vaginalis is the cause of an indirect inguinal hernia, which manifests as a mass that enlarges with increases in abdominal pressure (e.g., during crying), as seen here. However, an indirect inguinal hernia would manifest in the groin, not the abdominal midline.

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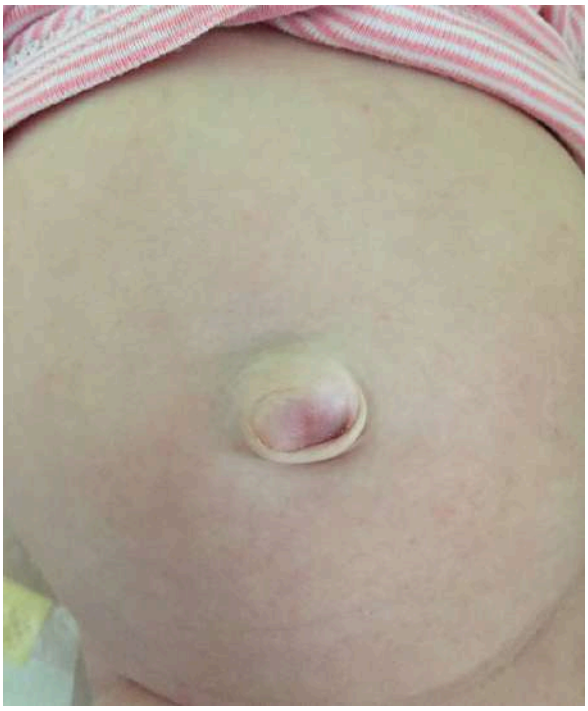
E - Failed spontaneous closure of the umbilical ring

Image



Explanation Why

Failure of the umbilical ring to close during fetal development causes congenital umbilical hernia. The midgut develops outside the abdominal cavity until the second trimester, when it physiologically herniates back into the abdomen. If the umbilical ring fails to close or the fascia in this region is underdeveloped, abdominal content may bulge through the umbilicus. Umbilical hernias are more common in children with chromosomal abnormalities (e.g., Down syndrome, Edwards syndrome) or congenital hypothyroidism, as seen here. Most congenital umbilical hernias resolve spontaneously by 5 years of age.

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Question # 18

A 27-year-old man comes to the emergency department because of nausea and repeated vomiting for the past 30 minutes. Two hours ago, he was at a summer barbecue gathering where he ate spicy, freshly grilled chicken that was fully cooked through with some reheated leftover lime basil rice. He has not had diarrhea. Physical examination shows a mildly tender abdomen with no rigidity or rebound tenderness. The next morning, his symptoms have resolved. Which of the following is the most likely cause of this patient's symptoms?

	Answer	Image
A	Person-to-person transmission of Staphylococcus aureus enterotoxin	
B	Mucosal invasion by Listeria monocytogenes	
C	Intestinal infection with Salmonella enteritidis	
D	Luminal production of heat-stable Escherichia coli toxin	
E	Germination of Clostridium perfringens spores	
F	Ingestion of preformed cereulide toxin	

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Hint

This patient has food poisoning caused by a spore-forming gram-positive rod.

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Correct Answer

A - Person-to-person transmission of Staphylococcus aureus enterotoxin

Explanation Why

Transmission of *Staphylococcus aureus* enterotoxins can lead to a rapid onset of nausea and vomiting, which is seen here. However, the *S. aureus* enterotoxin is transmitted via the ingestion of contaminated food, not from person to person. Furthermore, *S. aureus* food poisoning is typically caused by the inadequate refrigeration of foods such as mayonnaise, potato salad, and custard rather than reheated rice or freshly cooked meat, which this patient has eaten.

B - Mucosal invasion by Listeria monocytogenes

Explanation Why

Listeria monocytogenes causes a foodborne illness that can manifest with nausea and vomiting, which are seen here. Individuals with *L. monocytogenes* gastroenteritis typically become symptomatic 6 hours to 10 days after ingesting contaminated food and usually report diarrhea. This patient, however, only presents with vomiting 90 minutes after eating contaminated food. Moreover, *L. monocytogenes* is typically transmitted via unpasteurized dairy products or ready-to-eat deli meats, not reheated rice or freshly cooked meat.

C - Intestinal infection with Salmonella enteritidis

Explanation Why

Salmonella enteritidis infection is a foodborne illness that can manifest with nausea and vomiting, which are seen here. Symptoms usually develop 3–7 days after the ingestion of undercooked poultry or eggs. This patient, however, developed symptoms 90 minutes after eating reheated rice and properly cooked poultry. Furthermore, patients with this infection typically also present with diarrhea and systemic symptoms (e.g., fever, chills, myalgias), none of which are seen here.

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D - Luminal production of heat-stable Escherichia coli toxin

Explanation Why

A heat-stable enterotoxin is produced in the intestinal lumen by enterotoxigenic *Escherichia coli* (ETEC), which causes a foodborne illness that can manifest with nausea and vomiting, as seen here. However, ETEC also causes watery diarrhea and symptoms typically develop 1–3 days after the ingestion of contaminated food. This patient has not reported diarrhea, and he developed symptoms within 90 minutes of eating contaminated food.

E - Germination of Clostridium perfringens spores

Explanation Why

Clostridium perfringens enterocolitis is a foodborne illness that primarily manifests with diarrhea 6–24 hours after contaminated food is ingested. This patient, however, presents only with vomiting 90 minutes after eating contaminated food. Moreover, *C. perfringens* spores are commonly found in undercooked or poorly refrigerated meat; this patient consumed properly cooked meat and reheated rice.

F - Ingestion of preformed cereulide toxin

Explanation Why

Improperly refrigerated and reheated starch-containing food (e.g., rice), as seen here, is a common source of emetic *Bacillus cereus* food poisoning. *B. cereus* can form spores, which are heat-resistant and survive the cooking process. If the food is cooled too slowly or improperly refrigerated after cooking, these spores can germinate and produce cereulide, a heat-resistant emetic toxin that causes nausea and vomiting, or a heat-labile diarrheal toxin that causes diarrhea. Food poisoning caused by the ingestion of preformed enterotoxins (e.g., from *B. cereus* and *S. aureus*) leads to the rapid onset of symptoms within minutes to hours, as seen here. In comparison, food poisoning caused by bacteria that produce enterotoxins inside the intestines (e.g., enterotoxigenic *E. coli*, *V. cholerae*) has a delayed onset (hours to days after ingestion) and typically manifests with watery diarrhea. Foodborne illnesses that manifest with bloody diarrhea usually indicate invasion of the intestinal

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mucosa by the pathogen (e.g., *Campylobacter*, *Shigella*, nontyphoidal *Salmonella*).

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