

## Jaundice: Review Questions

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### QUESTIONS

Choose the single best answer for each question.

1. An 18-year-old male college freshman is referred to a gastroenterologist for evaluation of painless jaundice. He initially presented to a campus health center for evaluation of a flu-like illness with high fevers, where mild scleral icterus was noted. Initial laboratory studies revealed a normal complete blood count, normal alkaline phosphatase level, and normal alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels as well as a total serum bilirubin of 4 mg/dL and direct serum bilirubin of 0.4 mg/dL. Serologic testing for hepatitis was negative. At this visit, the flu-like illness has spontaneously resolved, and repeat laboratory testing reveals that total serum bilirubin has returned to normal. He has not taken any medications for his illness. What is the most likely cause of this patient's elevated serum bilirubin level?

- (A) Acute viral hepatitis
- (B) Gilbert's syndrome
- (C) Primary biliary cirrhosis (PBC)
- (D) Primary sclerosing cholangitis (PSC)
- (E) Transient biliary obstruction caused by a gallstone

2. A 29-year-old man is referred to a gastroenterologist for evaluation of progressive fatigue, intermittent fevers, and jaundice. He has a history of ulcerative colitis since age 18 years and underwent a proctocolectomy with an ileal pouch-anal anastomosis reconstruction. On physical examination, vital signs are stable and he is afebrile. He has a few spider angiomas on his chest and vague right upper quadrant pain with deep palpation. Laboratory testing reveals the following: AST, 120 U/L; ALT, 138 U/L; alkaline phosphatase, 800 U/L; and total serum



Figure 1. A cholangiogram performed in the patient described in question 2.

bilirubin, 5.6 mg/dL. Complete blood count is normal. The patient undergoes endoscopic retrograde cholangiopancreatography (ERCP) and an occlusion cholangiogram is generated (Figure 1). What is this patient's most likely diagnosis?

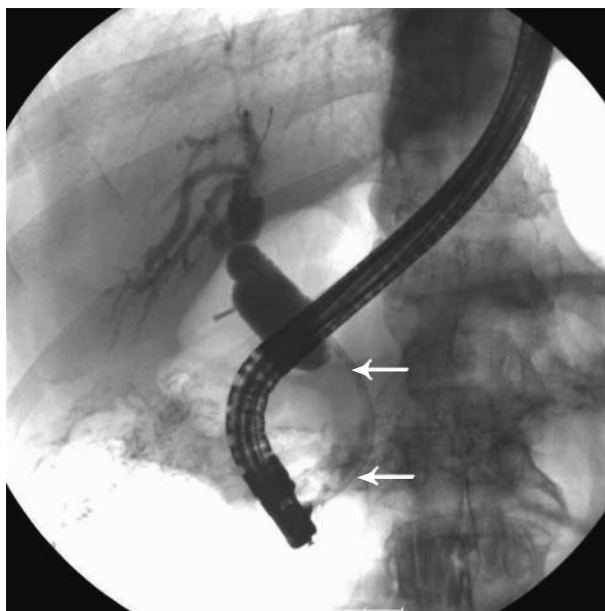
- (A) Acute hepatitis A
- (B) Choledocholithiasis
- (C) PBC
- (D) PSC
- (E) Secondary sclerosing cholangitis (SSC)

Questions 3 and 4 refer to the following case.

A 42-year-old female nurse is referred to a gastroenterologist for evaluation of jaundice. The patient was made aware that she looked jaundiced by her coworkers.

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**Figure 2.** An endoscopic retrograde cholangiopancreatogram performed in the patient described in question 5 demonstrating significant intra- and extrahepatic ductal dilation and a tight biliary stricture (arrows).

She also complains of intense pruritus that has not been relieved by over-the-counter agents such as diphenhydramine. Her appetite and weight are stable, and she has no abdominal symptoms. Physical examination is remarkable for xanthomas on her upper eyelids near the bridge of her nose but is otherwise unremarkable except for jaundice. She takes no medications. Laboratory testing reveals normal ALT and AST levels, a total serum bilirubin level of 7 mg/dL, and an alkaline phosphatase level of 733 U/L. The patient is referred for ERCP due to concern for obstruction, but the cholangiogram is normal.

**3. What is this patient's most likely diagnosis?**

- (A) Acute hepatitis A
- (B) Choledocholithiasis
- (C) PBC
- (D) PSC
- (E) SSC

**4. Which additional blood test would be the most helpful to confirm this patient's diagnosis?**

- (A) Antigliadin antibody
- (B) Antimitochondrial antibody (AMA)
- (C) Antinuclear antibody
- (D) IgG subclass 4
- (E) Serum amylase level

**5. A 62-year-old woman presents for evaluation of sudden-onset, severe, painless jaundice. The patient**

has developed anorexia with a 20-lb weight loss over a 3-month period and recently was diagnosed with diabetes mellitus. Complete blood count is normal, total serum bilirubin is 8.9 mg/dL, direct serum bilirubin is 8.3 mg/dL, alkaline phosphatase is 550 U/L, AST is 120 U/L, and ALT is 134 U/L. The patient undergoes magnetic resonance imaging of the abdomen, but she is unable to tolerate the examination due to claustrophobia. ERCP is performed, which reveals significant intra- and extrahepatic ductal dilation and a tight distal biliary stricture (Figure 2). What is this patient's most likely diagnosis?

- (A) Ampullary cancer
- (B) Cholangiocarcinoma
- (C) Cholecystitis
- (D) Pancreatic adenocarcinoma
- (E) Postoperative biliary stricture

**6. A 28-year-old woman is referred to a gastroenterologist for evaluation of jaundice. The patient has a history of recurrent urinary tract infections, kidney stones, and migraine headaches. She states that the jaundice came on suddenly over the last several days. She has vague right upper quadrant pain but also states she has large kidney stones on the right side, which cause similar pain. Medications include trimethoprim-sulfamethoxazole (TMP-SMX), which she takes 3 times per week to suppress urinary tract infections, as well as acetaminophen and sumatriptan for migraines. Laboratory testing reveals an AST of 59 U/L, ALT of 73 U/L, alkaline phosphatase of 630 U/L, a total serum bilirubin of 6.4 mg/dL, and a direct serum bilirubin of 5.9 mg/dL. A hepatobiliary iminodiacetic acid (HIDA) scan is normal. What is the most likely cause of this patient's jaundice?**

- (A) Acetaminophen
- (B) Cholecystitis
- (C) Choledocholithiasis
- (D) Sumatriptan
- (E) TMP-SMX

**ANSWERS AND EXPLANATIONS**

**1. (B) Gilbert's syndrome.** Gilbert's syndrome is a classic inherited disorder of bilirubin metabolism that presents with an unconjugated hyperbilirubinemia. A mutation in the gene that codes for the uridine diphosphoglucuronate glucuronosyltransferases (UGTs; enzymes that moderate glucuronidation of various compounds including bilirubin) leads to decreased production of bilirubin-UGT, which in turn causes decreased excretion of conjugated bilirubin. In patients with Gilbert's syndrome, elevated serum bilirubin is typically caused by physical stressors, such as dehydration, febrile illnesses, periods of fasting,

extreme physical exertion, and the ingestion of certain drugs. Gilbert's syndrome is a benign condition that is not associated with progressive jaundice or liver disease. Acute viral hepatitis, PBC, PSC, and transient biliary obstruction would not present with an isolated elevation of serum bilirubin without other abnormal liver function tests.

2. **(D) PSC.** PSC is a cholestatic liver disease that results in chronic inflammation, fibrosis, and structuring of the intra- and extrahepatic biliary tree. It can ultimately lead to cirrhosis and hepatic failure in some patients. PSC is frequently seen in patients with inflammatory bowel disease (ulcerative colitis and Crohn's disease). Figure 1 shows diffuse bilateral intrahepatic strictures and loss of high intrahepatic ducts (pruning). These strictures cause episodes of cholangitis with fever. In PBC, the cholangiogram is usually normal. Choledocholithiasis would show stones in the common bile duct (CBD) on ERCP, which are absent in this case. SSC often presents as diffuse intra- and extrahepatic stone disease or develops following a bile duct injury, causing a biliary stricture. A patient with hepatitis A would likely have a normal cholangiogram.

3. **(C) PBC.** PBC is a progressive cholestatic liver disease of unknown etiology. PBC occurs as a result of a T-cell-mediated assault on the small intralobular bile ducts and is almost always seen in middle-aged women. Pruritus is common in patients with PBC and can be severe. Patients with PBC also frequently have periorbital xanthomas caused by hyperlipidemia. In PBC, the cholangiogram is usually normal at presentation, whereas in PSC it is almost always abnormal, demonstrating diffuse intra- and extrahepatic ductal abnormalities. Choledocholithiasis would have been seen during ERCP. SSC can mimic PBC but is typically caused by chronic benign biliary obstruction, which this patient does not have. Acute hepatitis A would manifest with a marked elevation of the patient's transaminase levels.

4. **(B) AMA.** A positive serum AMA assay would essentially confirm the diagnosis of PBC. Sensitivity and specificity for PBC in the setting of a positive AMA are both greater than 95%.<sup>1</sup> Antinuclear antibody is often positive in autoimmune hepatitis; however, the patient does not have biochemical evidence of hepatitis. Serum amylase would be elevated in patients with

acute pancreatitis but normal in PBC. Antigliadin antibody would be elevated in patients with celiac disease but not in PBC. IgG subclass 4 may be elevated in patients with autoimmune pancreatitis.

5. **(D) Pancreatic adenocarcinoma.** The patient presents with classic signs of pancreatic adenocarcinoma—painless jaundice, weight loss, and anorexia in the setting of recently diagnosed diabetes. The cholangiogram demonstrates a long, tight distal CBD stricture (Figure 2). The distal CBD runs through the head of the pancreas (the most common site for pancreatic adenocarcinoma), and in this patient, the CBD is extrinsically compressed by a tumor mass. Cholangiocarcinoma at this site is possible but markedly less common. Although a postoperative biliary stricture is possible, it is very unlikely to develop in the intrapancreatic portion of the CBD due to its limited accessibility. Ampullary cancer could present with similar symptoms and laboratory profile but would likely demonstrate a site of obstruction in the most distal portion of the CBD at the level of the ampulla/duodenal wall and not higher up the duct, as seen in this patient. Cholecystitis is not possible in this patient, as she has undergone cholecystectomy, evidenced by the absence of a gallbladder and the postsurgical clip seen on the cholangiogram.

6. **(E) TMP-SMX.** TMP-SMX is frequently associated with cholestatic liver injury, which can be severe.<sup>2-4</sup> This drug can interfere with normal hepatocyte secretion of bile constituents and typically produces jaundice without significant hepatitis, as seen in this patient. Acetaminophen, which can be highly toxic to the liver if taken in high doses, usually produces a severe drug-induced hepatitis, which this patient does not have. Sumatriptan is not strongly associated with liver disease. A HIDA scan would likely identify cholecystitis or obstructive jaundice from choledocholithiasis but was normal in this patient.

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