

A 16-year-old boy comes to the office for follow-up after having an appendectomy 3 days ago. The patient was hospitalized for abdominal pain, vomiting, and fever; subsequent evaluation revealed early retrocecal appendicitis. He had an emergent appendectomy without any perioperative complications and was discharged home the next day. Today, his family noticed yellowing of his eyes, but he has not had any abdominal pain or nausea since the surgery and is tolerating a normal diet. The patient does not use tobacco or alcohol. Temperature is 37 C (98.6 F), blood pressure is 118/80 mm Hg, and pulse is 68/min. On examination, there is mild scleral icterus. Cardiopulmonary examination is normal. Abdominal surgical incisions are healing well without any surrounding redness. Laboratory results are as follows:

Complete blood count

Hemoglobin	14.4 g/dL
Platelets	260,000/mm <sup>3</sup>
Leukocytes	7,500/mm <sup>3</sup>

Liver function studies

Total bilirubin	3.3 mg/dL
Direct bilirubin	0.4 mg/dL
Alkaline phosphatase	70 U/L
Aspartate aminotransferase	27 U/L
Alanine aminotransferase	24 U/L

Which of the following is the most likely diagnosis?

- ☐ A. Acalculous cholecystitis
- ☐ B. Acute viral hepatitis
- ☐ C. Anesthetic hepatotoxicity
- ☐ D. Gilbert syndrome
- ☐ E. Glucose-6-phosphate dehydrogenase deficiency
- ☐ F. Iatrogenic biliary injury



evaluation revealed early retrocecal appendicitis. He had an emergent appendectomy without any perioperative complications and was discharged home the next day. Today, his family noticed yellowing of his eyes, but he has not had any abdominal pain or nausea since the surgery and is tolerating a normal diet. The patient does not use tobacco or alcohol. Temperature is 37 C (98.6 F), blood pressure is 118/80 mm Hg, and pulse is 68/min. On examination, there is mild scleral icterus. Cardiopulmonary examination is normal. Abdominal surgical incisions are healing well without any surrounding redness. Laboratory results are as follows:

Complete blood count

Hemoglobin	14.4 g/dL
Platelets	260,000/mm <sup>3</sup>
Leukocytes	7,500/mm <sup>3</sup>

Liver function studies

Total bilirubin	3.3 mg/dL
Direct bilirubin	0.4 mg/dL
Alkaline phosphatase	70 U/L
Aspartate aminotransferase	27 U/L
Alanine aminotransferase	24 U/L

Which of the following is the most likely diagnosis?

- ☐ A. Acalculous cholecystitis
- ☐ B. Acute viral hepatitis
- ☐ C. Anesthetic hepatotoxicity
- ☐ D. Gilbert syndrome
- ☐ E. Glucose-6-phosphate dehydrogenase deficiency
- ☐ F. Iatrogenic biliary injury

Submit



A 16-year-old boy comes to the office for follow-up after having an appendectomy 3 days ago. The patient was hospitalized for abdominal pain, vomiting, and fever; subsequent evaluation revealed early retrocecal appendicitis. He had an emergent appendectomy without any perioperative complications and was discharged home the next day. Today, his family noticed yellowing of his eyes, but he has not had any abdominal pain or nausea since the surgery and is tolerating a normal diet. The patient does not use tobacco or alcohol. Temperature is 37 C (98.6 F), blood pressure is 118/80 mm Hg, and pulse is 68/min. On examination, there is mild scleral icterus. Cardiopulmonary examination is normal. Abdominal surgical incisions are healing well without any surrounding redness. Laboratory results are as follows:

Complete blood count

Hemoglobin	14.4 g/dL
Platelets	260,000/mm <sup>3</sup>
Leukocytes	7,500/mm <sup>3</sup>

Liver function studies

Total bilirubin	3.3 mg/dL
Direct bilirubin	0.4 mg/dL
Alkaline phosphatase	70 U/L
Aspartate aminotransferase	27 U/L
Alanine aminotransferase	24 U/L

Which of the following is the most likely diagnosis?

- ☐ A. Acalculous cholecystitis [3%]
- ☐ B. Acute viral hepatitis [1%]
- ☐ C. Anesthetic hepatotoxicity [7%]
- ☒ D. Gilbert syndrome [75%]
- ☐ E. Glucose-6-phosphate dehydrogenase deficiency [5%]
- ☐ F. Iatrogenic biliary injury [8%]



Which of the following is the most likely diagnosis?

- ☐ A. Acalculous cholecystitis [3%]
- ☐ B. Acute viral hepatitis [1%]
- ☐ C. Anesthetic hepatotoxicity [7%]
- ☒ D. **Gilbert syndrome** [75%]
- ☐ E. Glucose-6-phosphate dehydrogenase deficiency [5%]
- ☐ F. Iatrogenic biliary injury [8%]

Proceed to Next Item

Explanation:

User Id: [REDACTED]

Gilbert syndrome	
Epidemiology	<ul style="list-style-type: none"><li>• More common in males</li><li>• Most common inherited disorder of bilirubin glucuronidation</li></ul>
Pathogenesis	<ul style="list-style-type: none"><li>• AR or AD mutation in <i>UGT1A1</i> gene</li><li>• ↓ UDP-glucuronosyltransferase activity → ↑ <b>unconjugated bilirubin</b></li></ul>
Clinical findings	<ul style="list-style-type: none"><li>• Intermittent episodes of mild <b>jaundice</b></li><li>• Provoked by <b>stress</b> (eg, infection, fasting, vigorous exercise, surgery)</li></ul>
Diagnosis	<ul style="list-style-type: none"><li>• Unconjugated hyperbilirubinemia on repeat testing</li><li>• Normal CBC, blood smear, reticulocyte count</li><li>• <b>Normal</b> AST, ALT, alkaline phosphatase</li></ul>
Treatment	<ul style="list-style-type: none"><li>• No specific treatment</li></ul>

AD = autosomal dominant; ALT = alanine aminotransferase; AR = autosomal recessive;  
AST = aspartate aminotransferase; CBC = complete blood count;  
UGT1A1 = UDP glucuronosyltransferase family 1 member A1.

©UWorld

This patient with mild scleral icterus following appendectomy has elevated indirect (unconjugated) bilirubin levels (given his elevated total bilirubin level of 3.3 mg/dL without direct bilirubin predominance) with normal liver function test results and no evidence of



UGT1A1 = UDP glucuronosyltransferase family 1 member A1.

©UWorld

This patient with mild scleral icterus following appendectomy has elevated indirect (unconjugated) bilirubin levels (given his elevated total bilirubin level of 3.3 mg/dL without direct bilirubin predominance) with normal liver function test results and no evidence of hemolysis (given the normal hemoglobin level). This presentation is consistent with **Gilbert syndrome**, the most common inherited disorder of bilirubin glucuronidation.

Gilbert syndrome is characterized by recurrent episodes of mild jaundice due to decreased activity of the **UDP-glucuronosyltransferase enzyme**, responsible for **bilirubin conjugation** in the liver. These episodes may be precipitated by **stressors** (eg, infection, fasting, vigorous exercise, surgery). Gilbert syndrome is diagnosed by elevated levels of **unconjugated bilirubin** on repeat testing with normal liver function test results and complete blood count results. No specific treatment is indicated, but it is important to educate patients about the **benign** nature of the condition and its inheritance pattern to prevent unnecessary diagnostic studies.

**(Choice A)** Acalculous cholecystitis is an inflammatory condition of the gallbladder most commonly seen in critically ill, hospitalized patients. Laboratory results are nonspecific but often show a leukocytosis along with hyperbilirubinemia and sometimes mild elevation in alkaline phosphatase and aminotransferase levels.

**(Choice B)** Patients with acute viral hepatitis present with anorexia, nausea, and vomiting. Aminotransferase levels are extremely elevated (eg, >25x upper limits of normal).

**(Choice C)** Halogenated inhalational anesthetics (eg, halothane) are associated with severe hepatotoxicity. Due to this concern, halothane use is not recommended in adults. There are 2 types of halothane hepatotoxicity: a mild, self-limiting form characterized by mild elevations in aminotransferase levels, and a severe form that causes liver necrosis, fever, and jaundice with grossly elevated aminotransferase levels.

**(Choice E)** Glucose-6-phosphate dehydrogenase (G6PD) deficiency predisposes patients to hemolytic anemias and resultant jaundice due to oxidant damage of red blood cells. Some drugs (eg, antimalarials, sulfonamides) may precipitate acute hemolysis in patients with G6PD deficiency; laboratory studies reveal anemia, elevated lactate dehydrogenase levels, and decreased haptoglobin levels. Heinz bodies and/or **bite cells** can be seen on peripheral smear.

**(Choice F)** Iatrogenic biliary injury occurs most commonly following laparoscopic cholecystectomy but would be unlikely following an appendectomy. Manifestations include jaundice, fever, and epigastric pain.

**Educational objective:**



(eg, infection, fasting, vigorous exercise, surgery). Gilbert syndrome is diagnosed by elevated levels of **unconjugated bilirubin** on repeat testing with normal liver function test results and complete blood count results. No specific treatment is indicated, but it is important to educate patients about the **benign** nature of the condition and its inheritance pattern to prevent unnecessary diagnostic studies.

**(Choice A)** Acalculous cholecystitis is an inflammatory condition of the gallbladder most commonly seen in critically ill, hospitalized patients. Laboratory results are nonspecific but often show a leukocytosis along with hyperbilirubinemia and sometimes mild elevation in alkaline phosphatase and aminotransferase levels.

**(Choice B)** Patients with acute viral hepatitis present with anorexia, nausea, and vomiting. Aminotransferase levels are extremely elevated (eg, >25x upper limits of normal).

**(Choice C)** Halogenated inhalational anesthetics (eg, halothane) are associated with severe hepatotoxicity. Due to this concern, halothane use is not recommended in adults. There are 2 types of halothane hepatotoxicity: a mild, self-limiting form characterized by mild elevations in aminotransferase levels, and a severe form that causes liver necrosis, fever, and jaundice with grossly elevated aminotransferase levels.

**(Choice E)** Glucose-6-phosphate dehydrogenase (G6PD) deficiency predisposes patients to hemolytic anemias and resultant jaundice due to oxidant damage of red blood cells. Some drugs (eg, antimalarials, sulfonamides) may precipitate acute hemolysis in patients with G6PD deficiency; laboratory studies reveal anemia, elevated lactate dehydrogenase levels, and decreased haptoglobin levels. Heinz bodies and/or **bite cells** can be seen on peripheral smear.

**(Choice F)** Iatrogenic biliary injury occurs most commonly following laparoscopic cholecystectomy but would be unlikely following an appendectomy. Manifestations include jaundice, fever, and epigastric pain.

#### Educational objective:

Gilbert syndrome, the most common inherited disorder of bilirubin glucuronidation, is characterized by recurrent episodes of mild jaundice precipitated by stressors (eg, infection, fasting, vigorous exercise, surgery). With the exception of elevated unconjugated bilirubin, liver function test results and complete blood counts are normal.

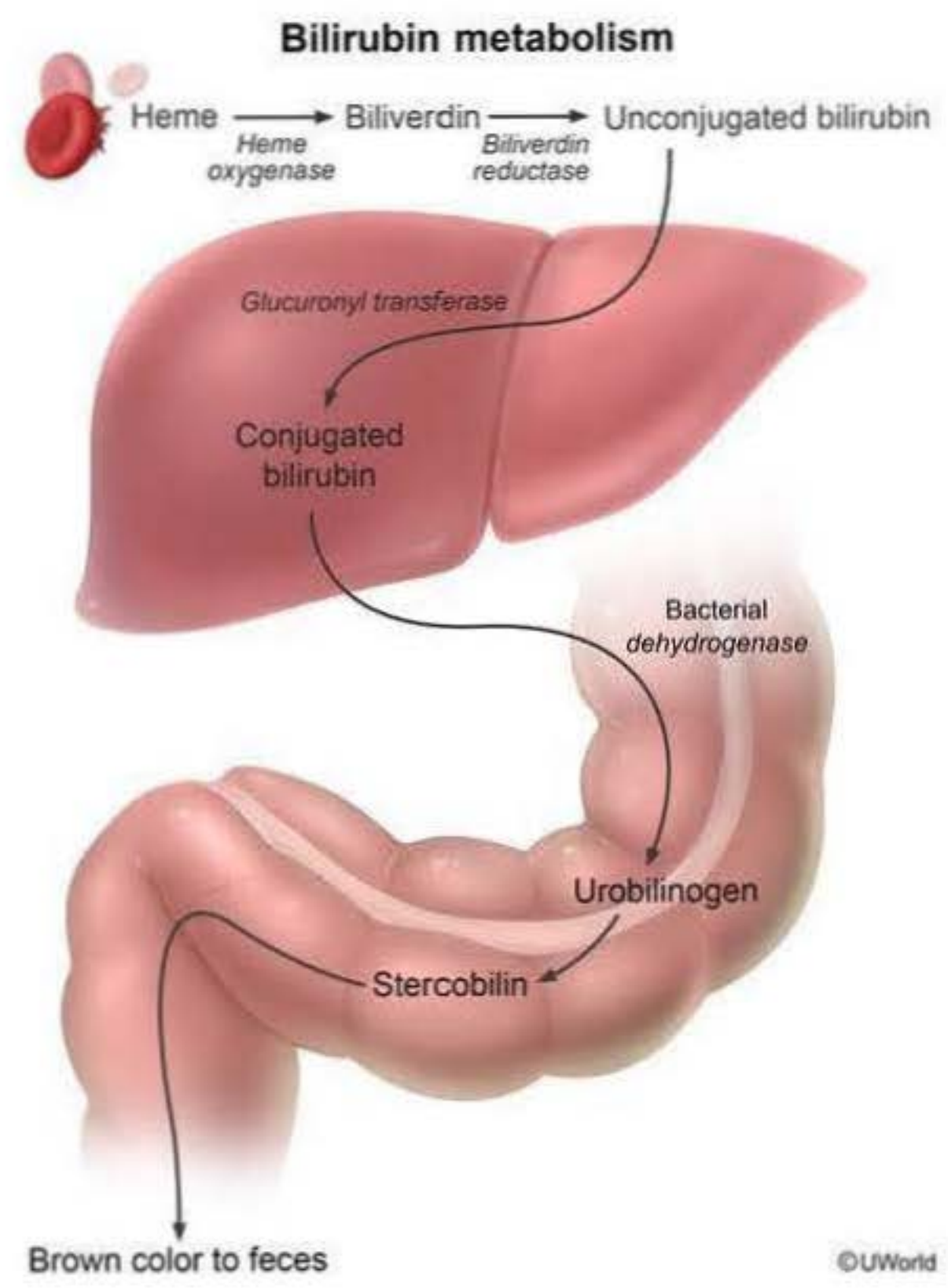
#### References:

1. [Gilbert syndrome.](#)



Media Exhibit

metabolism



Media Exhibit

iciency anemia

