

### Causes of Elevated Bilirubin

#### Elevated unconjugated bilirubin

- ☐ Gilbert's syndrome
- ☐ Crigler-Najjar syndrome
- ☐ Hemolysis (intravascular and extravascular)
- ☐ Ineffective erythropoiesis
- ☐ Resorption of large hematomas
- ☐ Neonatal jaundice
- ☐ Hyperthyroidism
- ☐ Medications
- ☐ Post-blood transfusion

#### Elevated conjugated hyperbilirubinemia

- ☐ Bile duct obstruction
  - ☐ Choledocholithiasis
  - ☐ Malignant obstruction
  - ☐ Bile duct flukes
- ☐ Bile duct stricture
- ☐ AIDS cholangiopathy
- ☐ Viral hepatitis
- ☐ Toxic hepatitis
- ☐ Medications or drug-induced liver injury
- ☐ Acute alcoholic hepatitis
- ☐ Ischemic hepatitis
- ☐ Cirrhosis
- ☐ Primary biliary cirrhosis
- ☐ PSC
- ☐ Infiltrative diseases of the liver
  - ☐ Sarcoid
  - ☐ Granulomatous hepatitis
  - ☐ Tuberculosis
  - ☐ Metastatic cancer
  - ☐ Lymphoma
- ☐ Hepatocellular carcinoma
- ☐ Wilson disease (especially fulminant Wilson's disease)
- ☐ Autoimmune hepatitis
- ☐ Ischemic hepatitis
- ☐ Congestive hepatopathy
- ☐ Sepsis
- ☐ TPN
- ☐ Intrahepatic cholestasis of pregnancy
- ☐ Benign post-operative jaundice
- ☐ ICU or multifactorial jaundice
- ☐ Benign recurrent cholestasis
- ☐ Vanishing bile duct syndrome

### Causes of Elevated Bilirubin (cont)

- ☐ Ductopenia

#### Continued

- ☐ Dubin-Johnson syndrome
- ☐ Rotor syndrome
- ☐ Sickle cell liver crisis
- ☐ Hemophagocytic lymphohistiocytosis

PSC, primary sclerosing cholangitis; TPN, total parenteral nutrition.

### Algorithm Elevated (predominant unconjugated)

#### Elevated total bilirubin (predominant unconjugated)

1. History and physical exam  
Assess liver transaminases and serum alkaline phosphatase
2. Review medications  
Evaluate for hemolysis  
Evaluate for Gilbert's syndrome
3. If persistent elevation is otherwise unexplained, may consider diagnostic testing for Gilbert's syndrome (UGT1A1 genotype) and evaluate for uncommon etiologies in Table 6
4. If persistent elevation is otherwise unexplained, is symptomatic, is worsening over time, and/or associated with abnormal transaminases  
--> consider liver biopsy

### Algorithm Elevated (predominant conjugated)

#### Elevated total bilirubin (predominant conjugated)

1. History & physical exam  
Assess liver transaminases and serum alkaline phosphatase
2. Review medications  
Evaluate for clinically overt etiologies: sepsis, TPN, cirrhosis, & biliary obstruction  
Perform right upper quadrant ultrasound
3. If ductal dilatation --> ERCP or MRCP  
If no ductal dilatation --> check AMA, ANA, and SMA
4. If persistent elevation is otherwise unexplained, is symptomatic, is worsening over time, and/or associated with abnormal transaminases  
--> consider liver biopsy

Source: <http://acgblog.org/wp-content/uploads/2016/12/AJG-Kwo-et-al-ACG-Liver-Chemistries-Guideline-2017.pdf>