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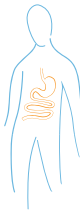

Jaundice

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INTRODUCTION

The term *jaundice* refers to yellow pigmentation of the skin, the conjunctival membranes over the sclera, and other mucous membranes that is caused by elevated serum bilirubin levels (hyperbilirubinemia). The word derives from the French word *jaune*, which means "yellow," and the condition also is known as *icterus* (Greek for "yellow"). Normal serum bilirubin levels range from 0.5 to 1.0 mg/dL, and plasma bilirubin concentrations typically must exceed 2.5 mg/dL before jaundice becomes evident clinically. In most cases, jaundice or hyperbilirubinemia per se is not a pathologic condition but rather a sign of one or more illnesses originating from or affecting the liver and blood. However, there is one notable exception: In newborns, high bilirubin levels can lead to pathologic cerebral changes. In this condition, which is known as *kernicterus* (the word *kern* derives from German and means "nucleus"), sustained high levels of unconjugated bilirubin lead to deposition of unconjugated bilirubin in the cerebral basal ganglia (or nuclei). This process is preventable and treatable and therefore merits special recognition to prevent damage to the developing brain.

BILIRUBIN METABOLISM

Hyperbilirubinemia can be classified based on the three phases of hepatic bilirubin metabolism: uptake, conjugation, and excretion into the bile (the rate-limiting step). In addition, jaundice can be classified into prehepatic, hepatic, and posthepatic causes (Table 40-1). Although the approaches are complementary, we believe that the latter classification is more useful for the practicing clinician.

The main source of bilirubin is the hemoglobin released from senescent red blood cells, and the liver serves as its primary site of metabolism and excretion. Abnormalities at any step—bilirubin production, metabolism, or excretion—can lead to increases in serum bilirubin and clinical jaundice. Under normal conditions, human red blood cells have a life span of about 120 days. As they age, erythrocytes are broken down and removed from the circulation by phagocytes. Most bilirubin (80%) is derived from the breakdown of hemoglobin released from these cells; the remainder is derived from ineffective erythropoiesis and from catabolism of myoglobin and hepatic hemoproteins such as the cytochrome P-450 isoenzymes. The normal rate of bilirubin production is approximately 4 mg/kg body weight per day (E-Fig. 40-1).

TABLE 40-1 CLASSIFICATION OF JAUNDICE AND REPRESENTATIVE CAUSES

PREHEPATIC CAUSES
Predominantly Unconjugated Hyperbilirubinemia
Hemolysis (e.g., sickle cell disease, autoimmune hemolytic anemia, mechanical cardiac valve with accelerated red cell destruction)
Microbe-induced hemolysis (malaria, leptospirosis)
Ineffective erythropoiesis (e.g., megaloblastic anemias)
Hematoma resolution
HEPATIC CAUSES
Unconjugated Hyperbilirubinemia
Decreased hepatic uptake
Therapeutic drugs that interfere with bilirubin uptake (e.g., rifampin, metformin, methimazole, propylthiouracil, clopidogrel, sulfamethoxazole/trimethoprim)
Herbal medicines (e.g., *Teucrium viscidum*, kava-kava, chaparral, greater celandine)
Hyperthyroidism
Diminished uptake and decreased cytosolic binding proteins (e.g., newborn or premature infants)
Shunting of blood away from the liver (portal hypertension or surgical shunt)
Decreased conjugation due to limited glucuronyltransferase activity
Gilbert's syndrome
Crigler-Najjar syndrome types I and II
Neonatal jaundice
Breast-milk jaundice
Drug-induced inhibition (e.g., chloramphenicol)
Predominantly Conjugated Hyperbilirubinemia
Impaired hepatic excretion
Familial cholestasis (Dubin-Johnson syndrome, Rotor's syndrome, benign recurrent cholestasis, cholestasis of pregnancy)
Hepatocellular injury from infiltrative disorders, hemochromatosis, α_1-antitrypsin deficiency, lymphoma, sarcoidosis, extensive metastases)
Liver cirrhosis
Hepatitis
Drug-induced cholestasis (chlorpromazine, erythromycin estolate, isoniazid, halothane, and many others)
Primary biliary cirrhosis
Congestive heart failure
Sepsis
POSTHEPATIC CAUSES
Extrahepatic biliary obstruction
Common bile duct obstruction from gallstones
Benign and malignant tumors of the pancreas
Tumors of bile ducts (cholangiocarcinoma) and ampulla of Vater
Biliary strictures (postsurgical, gallstone-related, primary sclerosing cholangitis)
Congenital disorders (biliary atresia, cystic fibrosis)
Infectious cholangiopathy
Chronic pancreatitis (fibrosis of the head of the pancreas)