

- I. Indirect hyperbilirubinemia
 - A. Hemolytic disorders
 - B. Ineffective erythropoiesis
 - C. Increased bilirubin production
 - 1. Massive blood transfusion
 - 2. Resorption of hematoma
 - D. Drugs
 - 1. Rifampin
 - 2. Probenecid
 - 3. Antibiotics—cephalosporins and penicillins
 - E. Inherited conditions
 - 1. Crigler-Najjar types I and II
 - 2. Gilbert's syndrome
- II. Direct hyperbilirubinemia (inherited conditions)
 - A. Dubin-Johnson syndrome
 - B. Rotor syndrome

Hemolytic disorders that cause excessive heme production may be either inherited or acquired. Inherited disorders include spherocytosis, sickle cell anemia, thalassemia, and deficiency of red cell enzymes such as pyruvate kinase and glucose-6-phosphate dehydrogenase. In these conditions, the serum bilirubin level rarely exceeds 86 $\mu\text{mol/L}$ (5 mg/dL). Higher levels may occur when there is coexistent renal or hepatocellular dysfunction or in acute hemolysis, such as a sickle cell crisis. In evaluating jaundice in patients with chronic hemolysis, it is important to remember the high incidence of pigmented (calcium bilirubinate) gallstones found in these patients, which increases the likelihood of choledocholithiasis as an alternative explanation for hyperbilirubinemia.

Acquired hemolytic disorders include microangiopathic hemolytic anemia (e.g., hemolytic-uremic syndrome), paroxysmal nocturnal hemoglobinuria, spur cell anemia, immune hemolysis, and parasitic infections (e.g., malaria and babesiosis). Ineffective erythropoiesis occurs in cobalamin, folate, and iron deficiencies. Resorption of hematomas and massive blood transfusions both