Assessment of Jaundice in the Hospitalized Patient

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KEYWORDS

• Jaundice • Cholestasis • Hyperbilirubinemia • Benign postoperative jaundice
• Cholestasis of sepsis

KEY POINTS

- Jaundice signifies a disorder in bilirubin metabolism.
- A thorough assessment of the clinical history and physical exam findings together with laboratory analysis and imaging studies are required to determine the cause of jaundice.
- The clinician must be able to recognize which conditions associated with jaundice warrant urgent endoscopy or evaluation for liver transplantation.

OVERVIEW

Jaundice originates from the Latin word "galbinus," which describes a yellow-green color. Icterus comes from the Greek word "ikteros," which meant both yellow bird and jaundice; historically, yellow birds were used as a "cure" for jaundice.[1] However, it has since come to be understood that jaundice is not a disease but rather a feature of disordered bilirubin metabolism that often signifies liver dysfunction. In general, the yellow discoloration occurs as a result of bilirubin deposition in the sclerae, mucosa, and skin when levels rise higher than 3 mg/dL.[2] Management is aimed at identifying and addressing the cause of the dysregulation in bilirubin metabolism.

Jaundice in the hospitalized patient is not an uncommon consultation for the general gastroenterologist. The National Hospital Ambulatory Medical Care Survey analyzed more than 1 billion emergency department visits from 1995 to 2004 and found that 400,000 patients had a diagnosis of jaundice. Nearly 50% of these were older than age 15; certainly the frequency and cause of jaundice depends on the patient population being studied.[3]

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This article provides a systematic approach to evaluating jaundice in adult patients with a focus on conditions that require urgent endoscopic intervention or evaluation for liver transplantation.

PATHOGENESIS

More than 75% of bilirubin is made from senescent red blood cell (RBC) breakdown in the reticuloendothelial system, with the remaining coming from ineffective RBC production or heme proteins, such as myoglobin and cytochrome enzymes.[2,4] Hepatocytes take up and conjugate this bilirubin within the sinusoids before excretion in the biliary tree.

Unconjugated bilirubin is fat-soluble, allowing it to cross the blood-brain barrier. In the newborn, it is this unconjugated hyperbilirubinemia that can lead to kernicterus. Unconjugated bilirubin becomes conjugated via the glucuronosyltransferase enzyme; in this form, the bilirubin becomes soluble in bile. Conjugated bilirubin can then be transported to the gallbladder where it is stored, transported to the duodenum to be excreted in stool, or converted into urobilinogen and excreted via the kidney (**Fig. 1**). The components of bile are integral for fat metabolism, absorption of fat-soluble vitamins, and excretion of bilirubin and its waste products.

It is postulated that bile flow can be altered by specific cytokines (tumor necrosis factor-α, interleukin-1 and -6) by upregulating expression of intercellular adhesion molecules, which in turn alters bile flow.[5] Bile flow can also be affected by endotoxins and exotoxins that are associated with infections or inflammatory states. Thus it is not surprising that common causes of hyperbilirubinemia encompass various viral and bacterial infectious etiologies.

Highlights:

- Bilirubin is produced by senescent RBC breakdown, ineffective RBC production, and heme proteins
- The enzyme glucuronosyltransferase conjugates bilirubin, which is then converted to urobilinogen in the liver before being stored or excreted in the bile ducts
- Bile flow can be altered by cytokines in inflammatory states

DIFFERENTIAL DIAGNOSIS

Rather than providing an exhaustive differential, this article focuses on the most common conditions and those diagnoses that should not be missed.

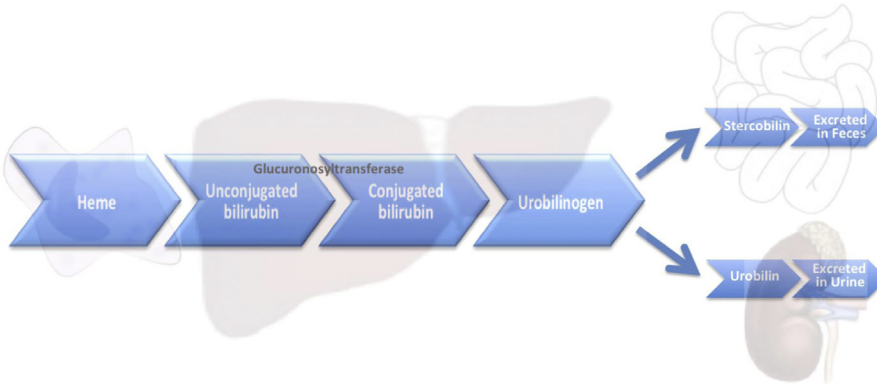

Fig. 1. Overview of bilirubin metabolism.