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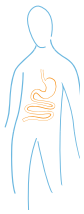
Disorders of the Gallbladder and Biliary Tract



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INTRODUCTION

The gallbladder and biliary tract transport bile from the liver into the intestines, a process central to digestion of fat and absorption of lipids and fat-soluble vitamins. Gallbladder and biliary tract diseases are among the most common and costly of all digestive disorders. This chapter examines the principal gallbladder and biliary tract disorders, focusing on cholelithiasis. The reader is referred to Chapter 40 for a detailed discussion of bilirubin metabolism and the diagnostic approach to jaundice and to Chapter 34 for a review of the various imaging techniques used to study the biliary tract.

NORMAL BILIARY ANATOMY AND PHYSIOLOGY

Figure 44-1 outlines the basic anatomy of the liver and biliary tract. The liver produces 500 to 1500 mL of bile per day. The secretory product of individual hepatocytes contains bile acids, phospholipids, and cholesterol, which are transported across the apical membrane and into the canalicular space between cells. These canaliculi merge to form larger intrahepatic bile ducts and then the common hepatic duct. During fasting, tonic contractions of the sphincter of Oddi, located in the region of the ampulla of Vater, divert about one half of the bile through the cystic duct into the gallbladder, where it is stored and concentrated by water resorption. Cholecystokinin, which is released after food enters the small intestine, causes the sphincter of Oddi to relax, allowing delivery of a timed bolus of bile into the intestine. Bile acids are present in millimolar concentrations. They are detergent molecules that possess both fat-soluble and water-soluble moieties. Cholesterol is secreted by the liver to the intestine, where it undergoes fecal excretion (see E-Fig. 40-1 in Chapter 40). In the intestinal lumen, bile acids solubilize dietary fat and promote its digestion and absorption. Bile acids are, for the most part, efficiently reabsorbed by the small intestinal mucosa, particularly in the terminal ileum. They are then recycled to the liver for re-excretion, a process termed *enterohepatic circulation.*

GALLBLADDER DISORDERS

Gallstones (Cholelithiasis)

Gallstone formation constitutes a significant health problem, affecting 10% to 15% of the adult population. Complications from gallstones are a leading cause for hospital admissions related to gastrointestinal problems. In the United States, gallstone disease leads to more than 750,000 cholecystectomies annually, making this the most common elective abdominal surgery, with estimated costs of $6.5 billion per year. Gallstones are of two types: 75% are made of cholesterol, and 25% are pigmented stones (black or brown). The latter are composed of calcium bilirubinate and other calcium salts. The risk factors for cholelithiasis are shown in Table 44-1.

Pathogenesis of Cholelithiasis

The three main factors that lead to cholesterol gallstone formation are cholesterol supersaturation of bile, nucleation, and gallbladder hypomotility. The liver is the most important organ in regulating total-body cholesterol stores. Once it is secreted, cholesterol, which is insoluble in water, is solubilized in bile through the formation of mixed micelles with bile acids and phospholipids. In most individuals, there is more cholesterol in bile than can be maintained in stable solution. As bile becomes supersaturated, microscopic cholesterol molecules aggregate into coalescent vesicles that crystallize, a process referred to as *nucleation*. The gradual deposition of additional layers of cholesterol leads to the appearance of macroscopic stones. Factors that influence nucleation include bile transit time, gallbladder contraction, bile composition (concentrations of cholesterol, phospholipids, and bile salts), and presence of bacteria, mucin, and glycoproteins, which can act as a nidus to initiate cholesterol crystal formation. The interplay between *pronucleating* and *antinucleating* factors in the gallbladder may determine whether cholesterol gallstones will form from supersaturated bile. Gallbladder sludge is a superconcentrated mixture of bile acids, bilirubin, cholesterol, mucus, and proteins that exhibits various degrees of fluidity and is prone to precipitate into a semisolid or solid form.

The pathophysiologic factors leading to pigment stone formation are less well understood; however, increased production of bilirubin conjugates (hemolytic states), increased biliary calcium (Ca^{2+}) and bicarbonate (HCO_3^-) levels, cirrhosis, and bacterial deconjugation of bilirubin to a less soluble form are all associated with pigment stone formation. Black pigment stones, which are composed primarily of calcium bilirubinate, are formed in sterile bile in the gallbladder and are common in chronic hemolytic states, in cases of cirrhosis, and in patients with ileal resection. Their brown pigment counterparts, composed primarily of calcium salts, are formed in the bile ducts and are seen in the setting of infection of the biliary tract.

Many of the recognized predisposing factors for cholelithiasis and gallbladder sludge can be understood in terms of the pathophysiologic scheme outlined previously: