Pathogenesis. *Acute calculous cholecystitis results from chemical irritation and inflammation of a gallbladder obstructed by stones.* The action of mucosal phospholipases hydrolyzes luminal lecithins to toxic lysolecithins. The normally protective glycoprotein mucus layer is disrupted, exposing the mucosal epithelium to the direct detergent action of bile salts. Prostaglandins released within the wall of the distended gallbladder contribute to mucosal and mural inflammation; distention and increased intraluminal pressure compromise blood flow to the mucosa. *These events occur in the absence of bacterial infection; only later in the course may bacterial contamination develop.* Acute calculous cholecystitis frequently develops in diabetic patients who have symptomatic gallstones.

Acute acalculous cholecystitis, without stone involvement, is thought to result from ischemia. The cystic artery is an end artery with no collateral circulation. Contributing factors may include inflammation and edema of the wall compromising blood flow, gallbladder stasis, and accumulation of microcrystals of cholesterol (biliary sludge), viscous bile, and gallbladder mucus, causing cystic duct obstruction in the absence of stones. It occurs in patients who are hospitalized for unrelated conditions. Risk factors for acute acalculous cholecystitis include: (1) sepsis with hypotension and multisystem organ failure; (2) immunosuppression; (3) major trauma and burns; (4) diabetes mellitus; (5) infections.

MORPHOLOGY

In **acute cholecystitis** the gallbladder is usually enlarged and tense, and it may assume a bright red or blotchy, violaceous to green-black discoloration, imparted by subserosal hemorrhages. The serosal covering is frequently covered by a fibrinous exudate that may be fibrinopurulent in severe cases. There are no specific morphologic differences between acute acalculous and calculous cholecystitis, save the absence of stones in the acalculous form. In **calculous cholecystitis**, an obstructing stone is usually present in the neck of the gallbladder or the cystic duct. The gallbladder lumen may contain one or more stones and is filled with a cloudy or turbid bile that may contain large amounts of fibrin, pus, and hemorrhage. When the exudate is virtually pure pus, the condition is referred to as **gallbladder empyema**. In mild cases the gallbladder wall is thickened, edematous, and hyperemic. In more severe cases it is transformed into a green-black necrotic organ, termed **gangrenous cholecystitis**, with small-to-large perforations. Inflammation is predominantly neutrophilic. The invasion of gas-forming organisms, notably clostridia and coliforms, may cause an **acute "emphysematous" cholecystitis**.

Clinical Features. Individuals with acute calculous cholecystitis usually, but not always, have experienced previous episodes of pain. An attack of acute cholecystitis begins with progressive right upper quadrant or epigastric pain that lasts for more than six hours. It is frequently associated with mild fever, anorexia, tachycardia, sweating, nausea, and vomiting. Most patients are free of jaundice; the presence of hyperbilirubinemia suggests obstruction of the common bile duct. Mild to moderate leukocytosis may be accompanied by mild elevations in serum alkaline phosphatase values. *Acute calculous cholecystitis may appear with remarkable suddenness and constitute an acute surgical emergency or may present with mild symptoms that resolve without medical intervention.* In the absence of medical attention, the attack usually subsides in 7 to 10 days and frequently within 24 hours. However, as many as 25% of patients progressively develop more severe symptoms and require immediate surgical intervention. Recurrence is common in patients who recover without surgery.

Clinical symptoms of acute acalculous cholecystitis tend to be more insidious, since they are obscured by the underlying conditions precipitating the attacks. A higher proportion of patients have no symptoms referable to the gallbladder; diagnosis therefore rests on a high index of suspicion. In the severely ill patient, early recognition of the condition is crucial, since failure to do so almost ensures a fatal outcome. As a result of either delay in diagnosis or the disease itself, the incidence of gangrene and perforation is much higher in acalculous than in calculous cholecystitis. In rare instances, primary bacterial infection can give rise to acute acalculous cholecystitis, by agents such as *Salmonella typhi* and staphylococci. A more indolent form of acute acalculous cholecystitis may occur in the setting of systemic vasculitis, severe atherosclerotic ischemic disease in the elderly, in patients with AIDS, and with biliary tract infection.

Chronic Cholecystitis

Chronic cholecystitis may be a sequel to repeated bouts of mild to severe acute cholecystitis, but in many instances it develops in the apparent absence of antecedent attacks. Since it is associated with *cholelithiasis in more than 90% of cases*, the at-risk patient population is the same as that for gallstones. The evolution of chronic cholecystitis is obscure; it is not clear that gallstones play a direct role in the initiation of inflammation or the development of pain, particularly since chronic acalculous cholecystitis shows symptoms and histology similar to those of the calculous form. Rather, supersaturation of bile predisposes to both chronic inflammation and, in most instances, stone formation. Microorganisms, usually *E. coli* and enterococci, can be cultured from the bile in about one third of cases. Unlike acute calculous cholecystitis, obstruction of gallbladder outflow is not a requisite. Since most gallbladders that are removed at elective surgery for gallstones show features of chronic cholecystitis, one must conclude that biliary symptoms often emerge following long-term coexistence of gallstones and low-grade inflammation.

MORPHOLOGY

The morphologic changes in chronic cholecystitis are extremely variable and sometimes minimal. The serosa is usually smooth and glistening but may be dulled by **subserosal fibrosis**. Dense fibrous adhesions may remain as sequelae of preexistent acute inflammation. On sectioning, the wall is variably thickened, and has an opaque gray-white appearance. In the uncomplicated case the lumen contains green-yellow, mucoid bile and usually stones. The mucosa itself is generally preserved.

On histologic examination the degree of inflammation is variable. In the mildest cases, only scattered lymphocytes, plasma