Pathophsiology

Disorder of gastrointestinal(GI) and hepatobiliary system

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Stomach

- The stomach is divided into four major anatomic regions: the cardia, fundus, body, and antrum.
- The cardia is lined mainly by mucin-secreting foveolar cells that form shallow glands.
- The antral glands are similar but also contain endocrine cells, such as G cells, that release gastrin to stimulate luminal acid secretion by parietal cells within the gastric fundus and body.
- The well-developed glands of the body and fundus also contain chief cells that produce and secrete digestive enzymes such as pepsin.

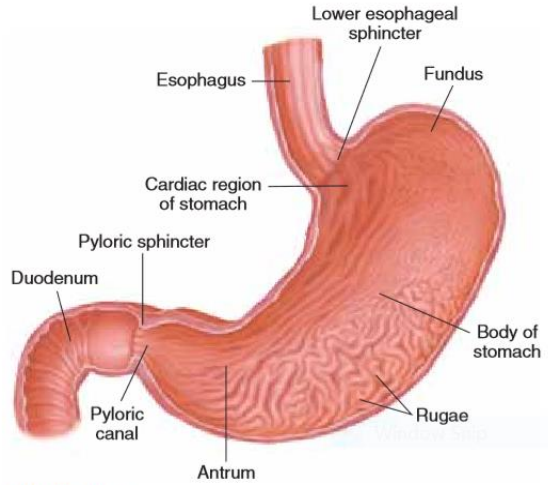
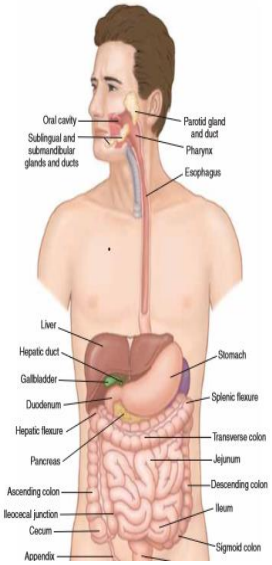


FIGURE 28-2. Structures of the stomach.



Inflammatory Disease Of The Stomach

Acute Gastritis

Acute gastritis is a transient mucosal inflammatory process that may be asymptomatic or cause variable degrees of epigastric pain, nausea, and vomiting. In more severe cases there may be mucosal erosion, ulceration, hemorrhage, hematemesis, melena, or, rarely, massive blood loss.

Acute gastritis is most commonly associated with :-

- local irritants such aspirin or other NSAIDs, alcohol, or bacterial toxins.
- Oral administration of corticosteroid drugs, which inhibit prostaglandin synthesis, may also cause acute hemorrhagic gastritis.

- Any serious illness or trauma that is accompanied by profound physiologic stress renders the gastric mucosa more vulnerable to acute hemorrhagic gastritis.
- Uremia, treatment with cancer chemotherapy drugs, and gastric radiation are other causes of acute gastritis.

Acute gastritis usually is a self-limiting disorder, with complete regeneration and healing occurring within several days of removal of the inciting agent.

Acute gastritis can progress to acute gastric ulceration.

Acute Peptic Ulceration

Focal, acute peptic injury is a well-known complication of therapy with NSAIDs as well as severe physiologic stress. Such lesions include

- **Stress ulcers**, most commonly affecting critically ill patients with shock, sepsis, or severe trauma .
- **Curling ulcers**, occurring in the proximal duodenum and associated with severe burns or trauma .
- **Cushing ulcers**, arising in the stomach, duodenum, or esophagus of persons with intracranial disease, have a high incidence of perforation.

Mechanisms of gastric injury and protection

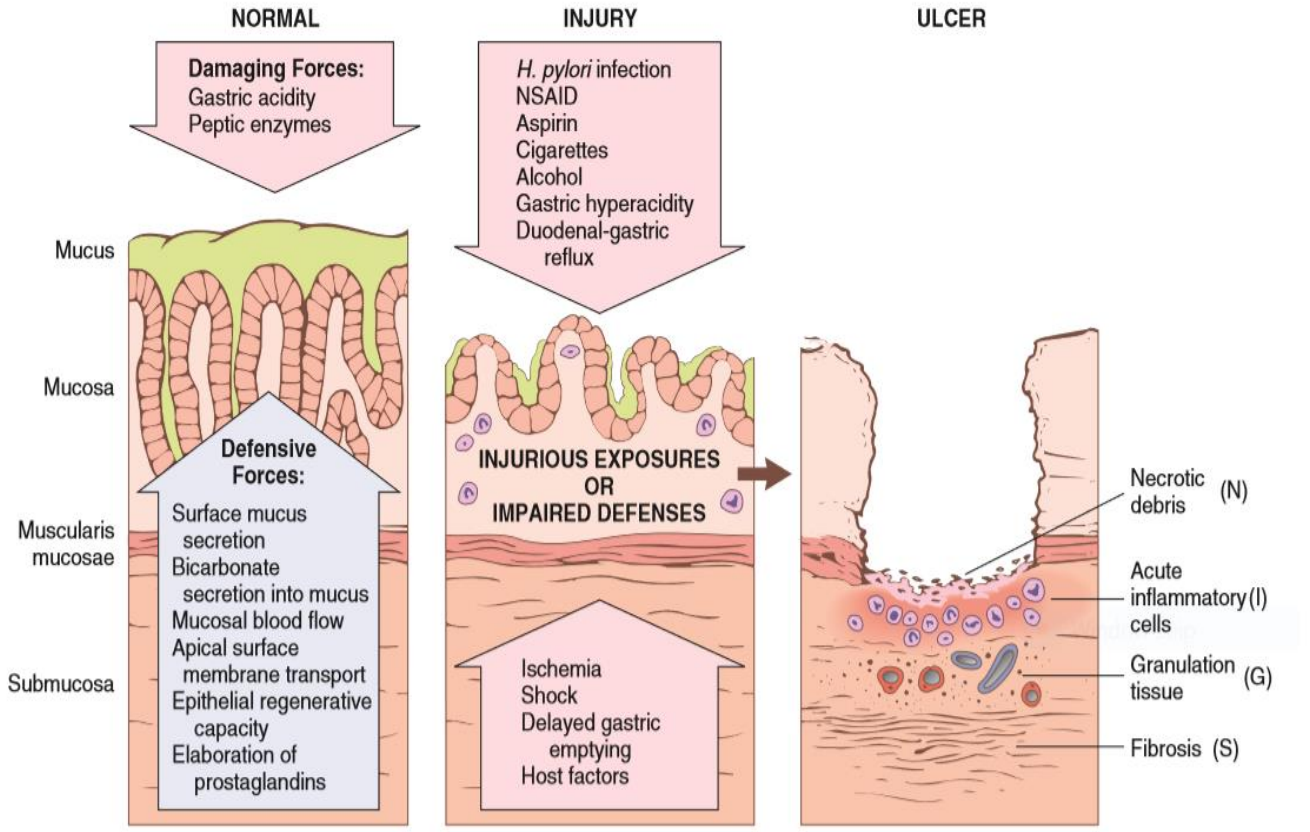


Figure 14–13 Mechanisms of gastric injury and protection. This diagram illustrates the progression from more mild forms of injury to ulceration that may occur with acute or chronic gastritis. Ulcers include layers of necrotic debris *(N)*, inflammation *(I)*, and granulation tissue *(G)*; a fibrotic scar *(S)*, which develops over time, is present only in chronic lesions.

Chronic Gastritis

The symptoms and signs associated with chronic gastritis typically are less severe but more persistent than those of acute gastritis. Nausea and upper abdominal discomfort may occur, sometimes with vomiting, but hematemesis is uncommon. The most common cause of chronic gastritis is infection with the bacillus Helicobacter pylori. Autoimmune gastritis, the most common cause of atrophic gastritis, represents less than 10% of cases of chronic gastritis and is the most common form of chronic gastritis in patients without H. pylori infection. Less common causes include radiation injury and chronic bile reflux.

Peptic Ulcer Disease

Peptic ulcer disease is a term used to describe a group of ulcerative disorders that occur in any portion of the gastrointestinal tract exposed to acidic gastric juices(pepsin) but is most common in the gastric antrum and first portion of the duodenum. Peptic ulcer disease (PUD) most often is associated with H. pylori infection or NSAID use.

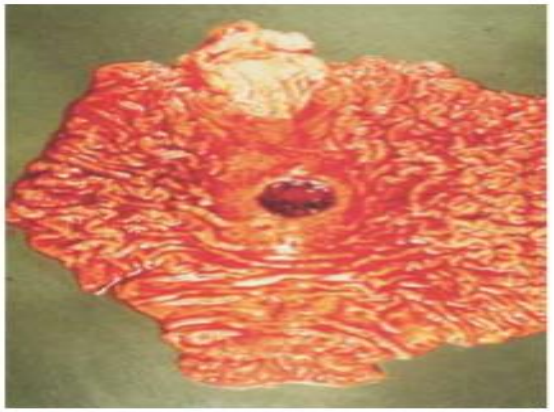


FIGURE 29-5. Gastric ulcer. The stomach has been opened to reveal a sharply demarcated, deep peptic ulcer on the lesser curvature. (From Rubin E., Farber J.L. [Eds.]. [1999]. *Pathology* [3rd ed., p. 693]. Philadelphia: Lippincott Williams & Wilkins.)

FIGURE 29-4. Infective gastritis. *Helicobacter pylori* appear on silver staining as small, curved rods on the surface of the gastric mucosa. (From Mitos F.A., Rubin E. [2008]. The gastrointestinal tract. In Rubin R., Strayer D.S. [Eds.], *Rubin's pathophysiology: Clinicopathologic foundations of medicine* [5th ed., p. 563]. Philadelphia: Lippincott Williams & Wilkins.)

Pathogenesis

H. pylori infection and NSAID use are the primary underlying causes of PUD. The imbalances of mucosal defenses and damaging forces that cause chronic gastritis are also responsible for PUD. Thus, PUD generally develops on a background of chronic gastritis. Although more than 70% of PUD cases are associated with H. pylori infection, only 5% to 10% of H. pylori–infected persons develop ulcers. It is probable that host factors as well as variation among H. pylori strains determine the clinical outcomes. Gastric hyperacidity is fundamental to the pathogenesis of PUD. The acidity that drives PUD may be caused by H. pylori infection, parietal cell hyperplasia, excessive secretory responses, or impaired inhibition of stimulatory mechanisms such as gastrin release. For example, **Zollinger-Ellison syndrome**, characterized by multiple peptic ulcerations in the stomach, duodenum, and even jejunum, is caused by uncontrolled release of gastrin by a tumor and the resulting massive acid production.

Cofactors in peptic ulcerogenesis include chronic NSAID use, as noted; cigarette smoking, which impairs mucosal blood flow and healing; and high-dose corticosteroids, which suppress prostaglandin synthesis and impair healing.

Peptic ulcers are more frequent in persons with alcoholic cirrhosis, chronic obstructive pulmonary disease, chronic renal failure, and hyperparathyroidism. In the latter two conditions, hypercalcemia stimulates gastrin production and therefore increases acid secretion. Finally, psychologic stress may increase gastric acid production and exacerbate PUD.

Abdominal Hernia

Any weakness or defect in the wall of the peritoneal cavity may permit protrusion of a serosa-lined pouch of peritoneum called a hernia sac. Acquired hernias most commonly occur anteriorly, through the inguinal and femoral canals or umbilicus, or at sites of surgical scars. These are of concern because of visceral protrusion (external herniation). This is particularly true of inguinal hernias, which tend to have narrow orifices and large sacs. Small bowel loops are herniated most often, but portions of omentum or large bowel also protrude, and any of these may become entrapped. Pressure at the neck of the pouch may impair venous drainage, leading to stasis and edema. These changes increase the bulk of the herniated loop, leading to permanent entrapment, or incarceration, and over time, arterial and venous compromise, or strangulation, can result in infarction.

Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is characterized by chronic and relapsing bdominal pain, bloating, and changes in bowel habits including diarrhea and constipation. The pathogenesis is poorly defined but involves psychologic stressors, diet, and abnormal gastrointestinal motility. Despite very real symptoms, no gross or microscopic abnormalities are found in most IBS patients. Thus, the diagnosis depends on clinical symptoms. IBS typically manifests between 20 and 40 years of age, and there is a significant female predominance.Variability in diagnostic criteria makes it difficult to establish the incidence, but reported prevalence rates in developed countries typically are between 5% and 10%. In patients with diarrhea, microscopic colitis, celiac disease, giardiasis, lactose intolerance, small bowel bacterial overgrowth, bile salt malabsorption, colon cancer, and inflammatory bowel disease must be excluded (although IBS is common in patients with inflammatory bowel disease).

Diarrheal Disease

Diarrhea is a common symptom of many intestinal diseases, including those due to infection, inflammation, ischemia, malabsorption, and nutritional deficiency

Diarrhea is defined as an increase in stool mass, frequency, or fluidity, typically to volumes greater than 200 mL per day. In severe cases stool volume can exceed 14 L per day and, without fluid resuscitation, result in death. Painful, bloody, small-volume diarrhea is known as dysentery

Diarrhea can be classified into four major categories:

- **Secretory diarrhea** is characterized by isotonic stool and persists during fasting.
- **Osmotic diarrhea**, such as that occurring with lactase deficiency, is due to osmotic forces exerted by unabsorbed luminal solutes. The condition abates with fasting.
- **Malabsorptive diarrhea** caused by inadequate nutrient absorption is associated with steatorrhea and is relieved by fasting.
- **Exudative diarrhea** is due to inflammatory disease and characterized by purulent, bloody stools that continue during fasting.

Celiac Disease

Celiac disease, also known as celiac sprue or gluten-sensitive enteropathy, is an immune-mediated enteropathy triggered by the ingestion of gluten-containing cereals, such as wheat or barley, in genetically predisposed persons. The primary treatment for celiac disease is a gluten free diet. Despite the challenges of adhering to such a diet, it does result in symptomatic improvement for most patients.

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a chronic condition resulting from inappropriate mucosal immune activation. IBD encompasses two major entities, **Crohn disease** and **ulcerative colitis**. The distinction between ulcerative colitis and Crohn disease is based, in large part, on the distribution of affected sites and the morphologic expression of disease at those sites . Ulcerative colitis is limited to the colon and rectum and extends only into the mucosa and submucosa. By contrast, Crohn disease, which also has been referred to as regional enteritis (because of frequent ileal involvement), may involve any area of the gastrointestinal tract and frequently is transmural.

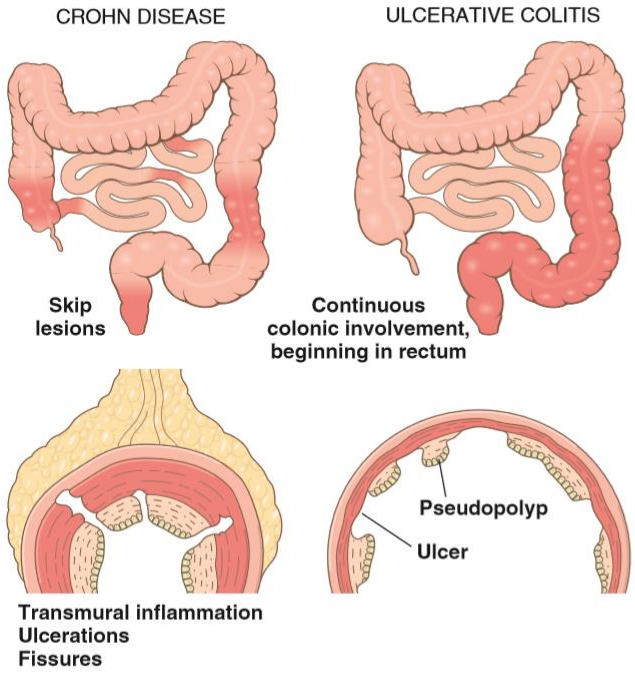


Figure 14–26 Distribution of lesions in inflammatory bowel disease. The distinction between Crohn disease and ulcerative colitis is based primarily on morphology.

Table 14–5 Features That Differ Between Crohn Disease and Ulcerative Colitis

Feature	Crohn Disease	Ulcerative Colitis
Macroscopic		
Bowel region affected	Ileum ± colon	Colon only
Rectal involvement	Sometimes	Always
Distribution	Skip lesions	Diffuse
Stricture	Yes	Rare
Bowel wall appearance	Thick	Thin
Inflammation	Transmural	Limited to mucosa and submucosa
Pseudopolyps	Moderate	Marked
Ulcers	Deep, knifelike	Superficial, broad-based
Lymphoid reaction	Marked	Moderate
Fibrosis	Marked	Mild to none
Serositis	Marked	No
Granulomas	Yes (–35%)	No
Fistulas/sinuses	Yes	No
Clinical		
Perianal fistula	Yes (in colonic disease)	No
Fat/vitamin malabsorption	Yes	No
Malignant potential	With colonic involvement	Yes
Recurrence after surgery	Common	No
Toxic megacolon	No	Yes

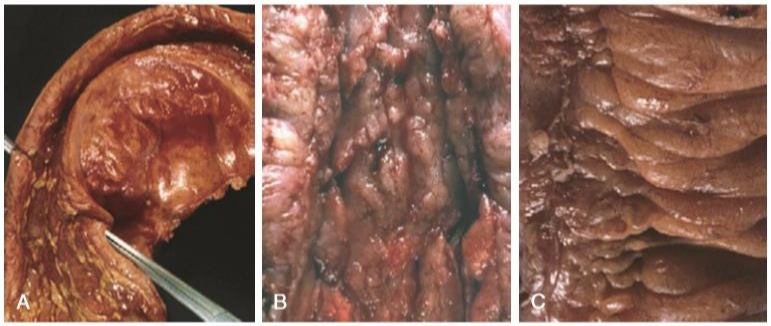


Figure 14–28 Gross pathology of Crohn disease. **A,** Small intestinal stricture. **B,** Linear mucosal ulcers and thickened intestinal wall. **C,** Creeping fat.

Hepatitis

Hepatitis refers to the acute or chronic inflammation of the liver. Although hepatitis viruses account for many cases of chronic hepatitis, there are many other causes including chronic alcoholism, drug toxicities, and auto immune disorders.

Viral Hepatitis Viral hepatitis refers to hepatic infections due to a group of viruses known as hepatotropic viruses (hepatitis A [HAV], hepatitis B [HBV], hepatitis C [HCV], hepatitis D [HDV], and hepatitis E [HEV]) that are have a particular affinity for the liver. Although all of the hepatotropic viruses cause hepatitis, they differ in terms of their mode of transmission and incubation period; mechanism, degree, and chronicity of liver damage; and ability to evolve to a carrier state. Acute hepatitis may also occur in the course of other viral infections such as infectious mononucleosis, caused by the Epstein-Barr virus; and cytomegalovirus infection, particularly in newborn or immunosuppressed persons. These other forms of hepatitis must be distinguished from hepatitis caused by hepatotropic viruses.

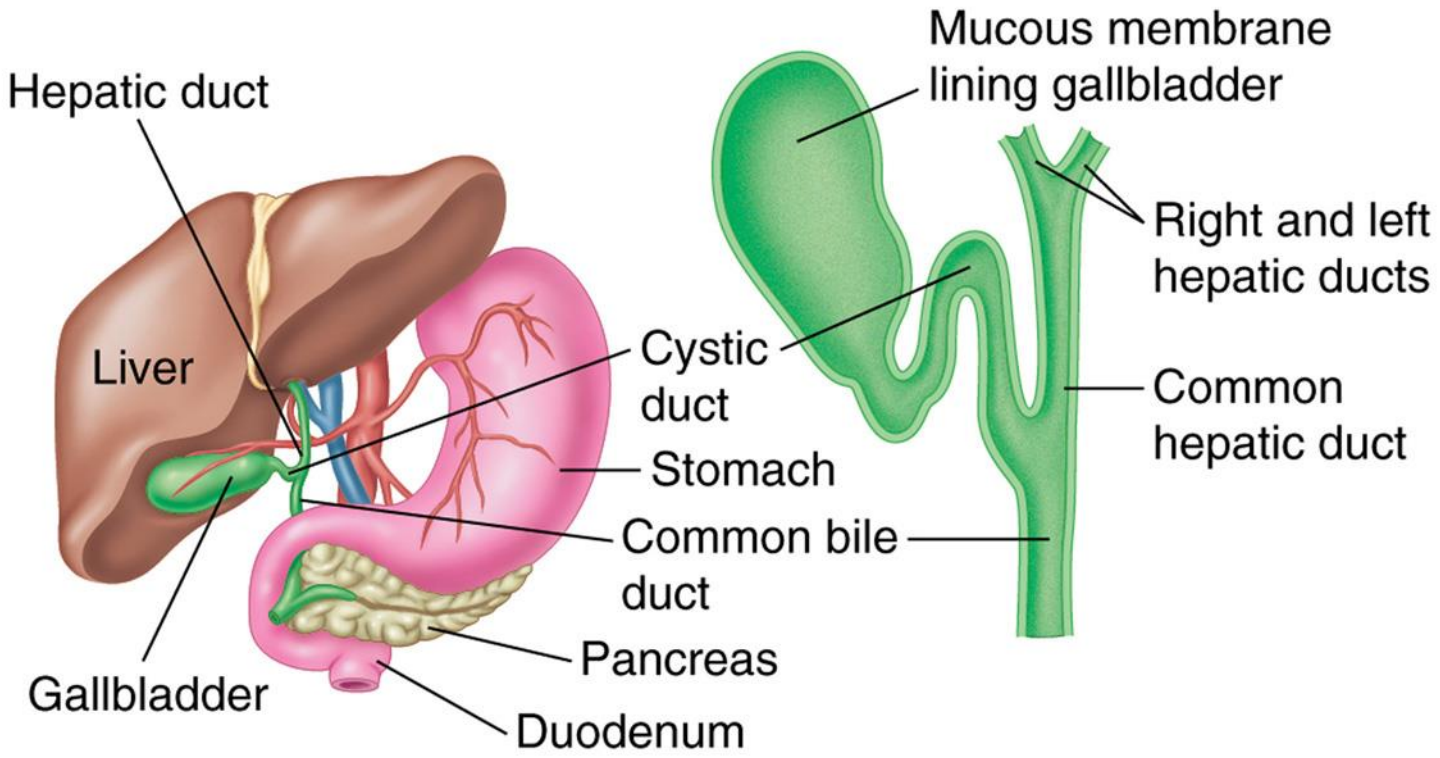


Figure 10-9: Bile duct system of the liver and gallbladder.

The hepatic viruses

Table 15–6 The Hepatitis Viruses

Virus	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
Type of virus	ssRNA	Partially dsDNA	ssRNA	Circular defective ssRNA	ssRNA
Viral family	Hepatovirus; related to picornavirus	Hepadnavirus	Flaviridae	Subviral particle in Deltaviridae family	Hepevirus
Route of transmission	Fecal-oral (contaminated food or water)	Parenteral, sexual contact, perinatal •	Parenteral; intranasal cocaine use is a risk factor	Parenteral	Fecal-oral
Incubation period	2–6 weeks	4–26 weeks	2–26 weeks	Same as for HBV	2–8 weeks
Frequency of chronic liver disease	Never	10%	~80%	5% (coinfection); ≤70% for superinfection	Never
Laboratory diagnosis	Detection of serum IgM antibodies	Detection of HBsAg or antibody to HBcAg	PCR assay for HCV RNA; 3rd-generation ELISA for antibody detection	Detection of IgM and IgG antibodies; HDV RNA serum; HDAg in liver	PCR assay for HEV RNA; detection of serum IgM and IgG antibodies

dsDNA, double-stranded DNA; ELISA, enzyme-linked immunosorbent assay; HBcAg, hepatitis B core antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HDAg, hepatitis D antigen; HDV, hepatitis D virus; HEV, hepatitis E virus; IgG, IgM, immunoglobulins G and M; PCR, polymerase chain reaction; ssRNA, single-stranded RNA.
From Washington K: Inflammatory and infectious diseases of the liver. In Iacobuzio-Donahue CA, Montgomery EA (eds): Gastrointestinal and Liver Pathology. Philadelphia, Churchill Livingstone, 2006.

Clinical Features and Outcomes for Viral Hepatitis

A number of clinical syndromes may develop after exposure to hepatitis viruses:

- Asymptomatic acute infection: serologic evidence only
- Acute hepatitis: anicteric or icteric
- Fulminant hepatitis: submassive to massive hepatic necrosis with acute liver failure
- Chronic hepatitis: with or without progression to cirrhosis
- Chronic carrier state: asymptomatic without apparent disease

Primary Biliary Cirrhosis

Primary biliary cirrhosis (PBC) is a chronic, progressive, and sometimes fatal cholestatic liver disease characterized by destruction of intrahepatic bile ducts, portal inflammation and scarring, and the development of cirrhosis and liver failure over years to decades. The cardinal feature of PBC is a nonsuppurative destruction of small and medium-sized intrahepatic bile ducts. PBC is primarily a disease of middle-aged women, with peak incidence between the ages of 40 and 50 years. The name is a bit of a misnomer, because end-stage PBC is not always cirrhotic. Some patients may die or undergo transplantation because of severe portal hypertension in the absence of fully establishe cirrhosis, although others, usually displaying severe intractable cholestasis, are fully cirrhotic.

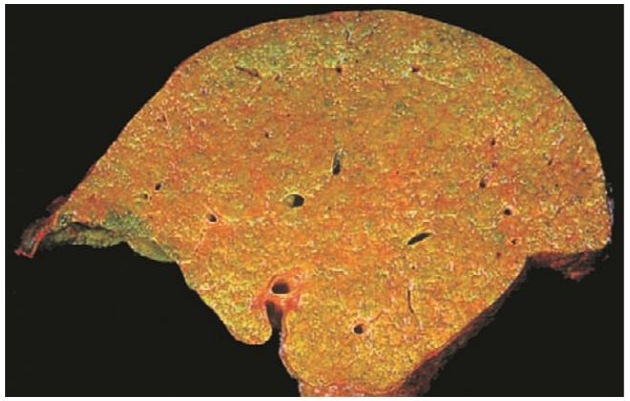


Figure 15–23 Primary biliary cirrhosis, end stage. This sagittal section demonstrates liver enlargement, nodularity indicative of cirrhosis, and green discoloration due to cholestasis.

Secondary Biliary Cirrhosis

Prolonged obstruction of the extrahepatic biliary tree results in profound damage to the liver itself. The most common cause of obstruction is extrahepatic cholelithiasis. Other obstructive conditions include biliary atresia , malignancies of the biliary tree and head of the pancreas, and strictures resulting from previous surgical procedures. The initial morphologic features of cholestasis were described earlier and are entirely reversible with correction of the obstruction. However, secondary inflammation resulting from biliary obstruction initiates periportal fibrogenesis, which eventually leads to scarring and nodule formation, generating secondary biliary cirrhosis

Hepatic Failure

The most severe clinical consequence of liver disease is hepatic failure. It generally develops as the end point of progressive damage to the liver, either through insidious piecemeal destruction of hepatocytes or by repetitive waves of symptomatic parenchymal damage. Less commonly, hepatic failure is the result of sudden, massive destruction. Whatever the sequence, 80% to 90% of hepatic function must be lost before hepatic failure ensues. In many cases, the balance is tipped toward decompensation by intercurrent conditions or events that place demands on the liver. These include systemic infections, electrolyte disturbances, major surgery, heart failure, and gastrointestinal bleeding.

The patterns of injury that cause liver failure fall into three categories:

- **Acute liver failure with massive hepatic necrosis**. Most often caused by drugs or viral hepatitis, acute liver failure denotes clinical hepatic insufficiency that progresses from onset of symptoms to hepatic encephalopathy within 2 to 3 weeks.

A course extending as long as 3 months is called subacute failure. The histologic correlate of acute liver failure is massive hepatic necrosis, whatever the underlying cause. It is an uncommon but lifethreatening condition that often necessitates liver transplantation.

- **Chronic liver disease**. This is the most common route to hepatic failure and is the end point of relentless chronic liver damage. While all structural components of the liver are involved in end-stage chronic liver disease, the processes that initiate and drive chronic damage to the liver can usually be classified as either primarily hepatocytic (or parenchymal), biliary, or vascular. Regardless of the initiating factors, chronic damage to the liver often ends in cirrhosis, as described later.
- **Hepatic dysfunction without overt necrosis**. Less commonly than the forms described above, hepatocytes may be viable but unable to perform their normal metabolic function. Settings where this is seen most often are mitochondrial injury in Reye syndrome, acute fatty liver of pregnancy, and some drug- or toxin-mediated injuries.

Cholelithiasis (Gallstones)

Gallstones afflict 10% to 20% of adults residing in Western countries in the Northern Hemisphere, 20% to 40% in Latin American countries, and only 3% to 4% in Asian countries. In the United States, about 1 million new cases of gallstones are diagnosed annually, and two thirds of persons so affected undergo surgery, with retrieval of as much as 25 to 50 million tons of stones! There are two main types of gallstones: cholesterol stones, containing crystalline cholesterol monohydrate (80% of stones in the West), and pigment stones, made of bilirubin calcium salts.

Pathogenesis

Bile formation is the only significant pathway for elimination of excess cholesterol from the body, either as free cholesterol or as bile salts. Cholesterol is rendered water-soluble by aggregation with bile salts and lecithins. When cholesterol concentrations exceed the solubilizing capacity of bile (supersaturation), cholesterol can no longer remain dispersed and crystallizes out of solution. Cholesterol gallstone formation is enhanced by hypomobility of the gallbladder (stasis), which promotes nucleation, and by mucus hypersecretion, with consequent trapping of the crystals, thereby enhancing their aggregation into stones. Formation of pigment stones is more likely in the presence of unconjugated bilirubin in the biliary tree, as occurs in hemolytic anemias and infections of the biliary tract. The precipitates are primarily insoluble calcium bilirubinate salts.

Cholelithiasis (Gallstones)

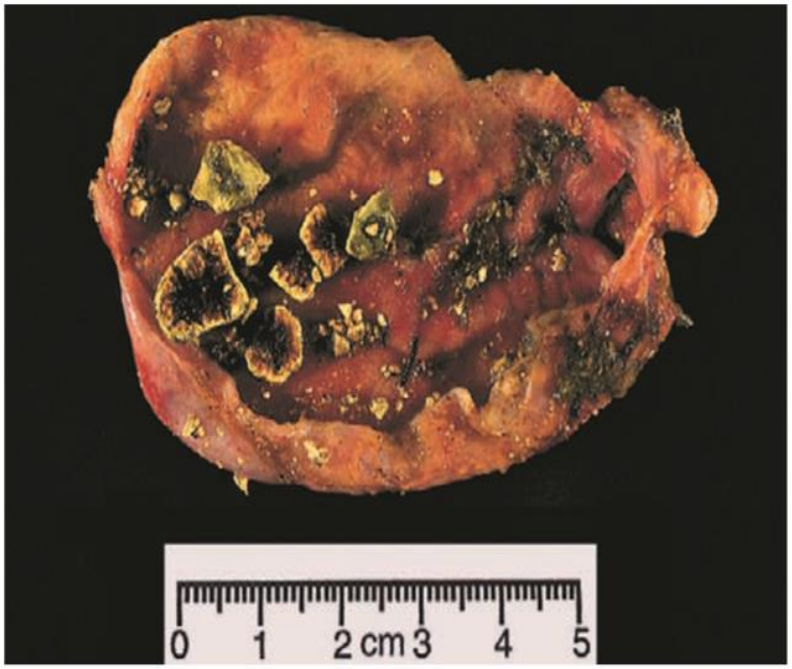


Figure 15–35 Cholesterol gallstones. Mechanical manipulation during laparoscopic cholecystectomy has caused fragmentation of several cholesterol gallstones, revealing interiors that are pigmented because of entrapped bile pigments. The gallbladder mucosa is reddened and irregular as a result of coexistent acute and chronic cholecystitis.

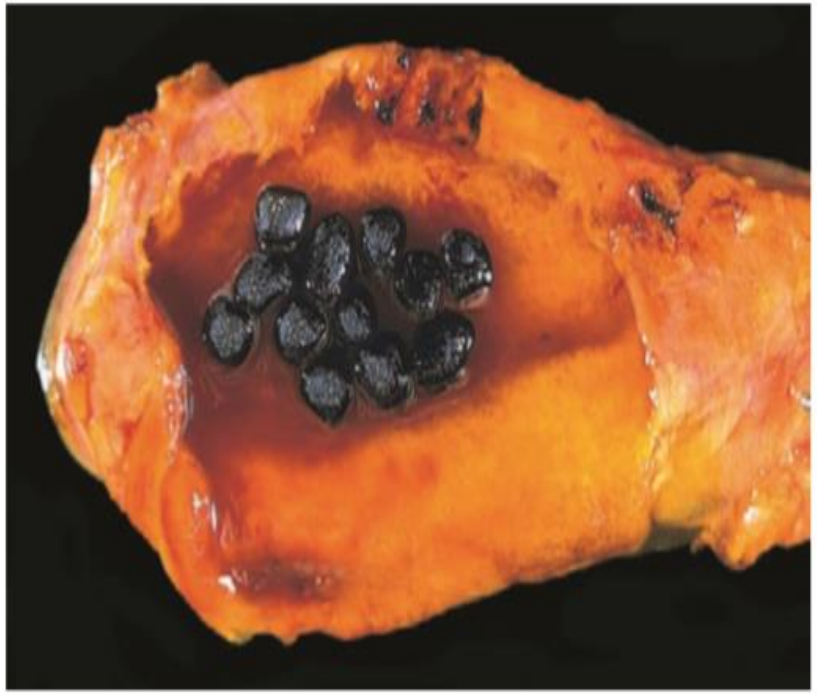


Figure 15–36 Pigmented gallstones. Several faceted black gallstones are present in this otherwise unremarkable gallbladder removed from a patient who had a mechanical mitral valve prosthesis, leading to chronic intravascular hemolysis.

References

-Robbins Basic Pathology 9th edition

- Carol Mattson Porth - Essentials of Pathophysiology 3rd edition.