:
Title: *Professional Guide to Diseases, 9th Edition*

5

Hepatobiliary disorders

Introduction

The liver is the largest internal organ in the body, weighing slightly more than 3 lb (1,200 to 1,600 g) in the average adult. It's also one of the busiest, performing well over 100 separate functions. The most important of these are the formation and secretion of bile; detoxification of harmful substances; storage of vitamins; metabolism of carbohydrates, fats, and proteins; and production of plasma proteins. This remarkably resilient organ serves as the body's warehouse and is essential to life.

Lobular structure

Located above the right kidney, stomach, pancreas, and intestines and immediately below the diaphragm, the liver divides into a left and a right lobe separated by the falciform ligament. The right lobe is six times larger than the left. Glisson's capsule, a network of connective tissue, covers the entire organ and extends into the parenchyma along blood vessels and bile ducts. Within the parenchyma, cylindrical lobules comprise the basic functional units of the liver, consisting of cellular plates that radiate from a central vein, somewhat like spokes in a wheel. Small bile canaliculi fit between the cells in the plates and empty into terminal bile ducts, which join two larger

ones that merge into a single hepatic duct upon leaving the liver. The hepatic duct then joins the cystic duct to form the common bile duct.

The liver receives blood from two major sources: the hepatic artery and the portal vein. The two vessels carry approximately 1,500 ml of blood to the liver per minute, nearly 75% of which is supplied by the portal vein. Sinusoids — offshoots of the hepatic artery and portal vein — run between each row of hepatic cells. Phagocytic Kupffer's cells, part of the reticuloendothelial system, line the sinusoids, destroying old or defective red blood cells and detoxifying harmful substances. The liver has a large lymphatic supply; consequently, cancer frequently metastasizes there.

Liver function

One of the liver's most important functions is the conversion of bilirubin, a breakdown product of hemoglobin, into bile. Liberated by the spleen into plasma and bound loosely to albumin, bilirubin reaches the liver in an unconjugated (water-insoluble) state. The liver then conjugates or dissociates it, converting it to a water-soluble derivative before excreting it as bile. All hepatic cells continually form bile.

The liver also detoxifies many substances through inactivation or through conjugation. Inactivation involves reduction, oxidation, and hydroxylation. An important liver function is the inactivation of many drugs that are metabolized primarily in the liver. Such drugs must be used with caution in hepatic disease because their effects may be markedly prolonged.

ELDER TIP

In elderly people, the blood supply to the liver decreases, and certain liver enzymes become less active. As a result, the liver loses some of its ability to metabolize drugs, and higher levels of drugs remain in the circulation, causing more intense drug effects. This increases the risk of drug toxicity.

As still another example of its amazing versatility, the liver forms vitamin A from certain vegetables and stores vitamins K, D, and B_{12}. It also stores iron in the form of ferritin.

Metabolic functions

The liver figures indispensably in the metabolism of the three major food groups: carbohydrates, fats, and proteins. In carbohydrate metabolism, the liver plays one of its most vital roles by extracting excess glucose from the blood and reserving it for times when blood glucose levels fall below normal, when it releases glucose into the circulation, and then replenishes the supply by a process called glyconeogenesis. To prevent dangerously low blood glucose levels, the liver can also convert galactose or amino acids into glucose (gluconeogenesis). The liver also forms many critical chemical compounds from the intermediate products of carbohydrate metabolism.

The liver performs more than half the body's preliminary breakdown of fats because liver cells metabolize fats more quickly and efficiently than do other body cells. Liver cells break fats down into glycerol and fatty acids and convert the fatty acids into small molecules that can be oxidized. The liver also produces substantial quantities of cholesterol and phospholipids, manufactures lipoproteins, and synthesizes fat from carbohydrates and proteins to be transported in lipoproteins for eventual storage in adipose tissue.

Like so many of its functions, the liver's role in protein metabolism is essential to life. The liver deaminates amino acids so they can be used for energy or converted into fats or carbohydrates. It forms urea to remove ammonia from body fluids and forms all plasma proteins (as much as 50 to 100 g/day) except gamma globulin. The liver is such an effective synthesizer of protein that it can replenish as much as half its plasma proteins in 4 to 7 days. The liver also synthesizes nonessential amino acids and forms other important chemical compounds from amino acids.

Production of plasma proteins

The liver synthesizes most of the body's large molecules of plasma proteins, including all of the albumin, which binds many substances in plasma and maintains colloid osmotic pressure.

Normally, plasma proteins and amino acid levels maintain equilibrium in the blood. When amino acid levels decrease,

the plasma proteins split into amino acids to restore this equilibrium. Reacting to decreased levels of amino acids, the liver steps up production of the plasma proteins. The liver may synthesize approximately 400 g of protein daily; for this reason, significant liver damage leads to hyperproteinemia, which in turn disrupts the colloid osmotic pressure and amino acid levels.

The liver also produces most of the plasma proteins necessary for blood coagulation, including prothrombin and fibrinogen, which are the most abundant. The liver forms prothrombin in a process dependent on vitamin K and the production of bile. Fibrinogen, a large-molecule protein formed entirely by the liver, is an essential factor in the coagulation cascade.

Together, the plasma proteins maintain colloid osmotic pressure throughout the capillaries. Because the plasma protein molecules are too large to cross the capillary membrane, they concentrate at the capillary line and produce an osmotic pressure of pull. This constant colloid osmotic pressure at the arteriolar and venular sections of the capillary provides the major osmotic force regulating the return of fluid to the intravascular compartment.

Because of their large molecular size, the plasma proteins don't easily cross into the interstitial spaces. Their only route for return to the bloodstream is through lymphatic drainage. The lymphatic vessels drain into the lymphatic and thoracic ducts, which drain directly into the superior vena cava.

Assessing for liver disease

In many cases, a careful physical examination and patient history can detect hepatic disease. Watch especially for its cardinal signs: jaundice (a result of increased serum bilirubin levels), ascites (commonly with hemoconcentration, edema, and oliguria), and hepatomegaly. Other signs and symptoms may include right upper quadrant abdominal pain, lassitude, anorexia, nausea, and vomiting. To detect hepatomegaly, palpate the liver's left lobe, in the epigastrium between the xiphoid process and the umbilicus. Another primary sign is portal hypertension (portal vein pressure greater than 6 to 12 cm H_2O) revealed by

auscultation of a venous hum over the patient's abdomen. Surgical insertion of a catheter into the portal vein allows measurement of portal vein pressure.

ALERT

Carefully assess the patient's neurologic status because neurologic symptoms, such as those associated with hepatic encephalopathy (confusion, muscle tremors, and asterixis), may signal the onset of life-threatening hepatic failure.

Other common signs of hepatic disease include pallor (commonly linked to cirrhosis or carcinoma), parotid gland enlargement (in alcohol-induced liver damage), Dupuytren's contracture, gynecomastia, testicular atrophy, decreased axillary or pubic hair, bleeding disorders (ecchymosis and purpura), spider angiomas, and palmar erythema.

Careful abdominal palpation and auscultation can also detect hepatocellular carcinoma or metastasis, which turns the liver rock-hard and causes abdominal bruits. In hepatitis, the liver is usually enlarged; palpation may elicit tenderness at the liver's edge. In cirrhosis, the atrophic liver is difficult to palpate. In neoplastic disease or hepatic abscess, auscultation may detect a pleural friction rub.

Comprehensive history essential

Ask if the patient has ever had jaundice, anemia, or a splenectomy. Ask about occupational or other exposure to toxins (carbon tetrachloride, beryllium, or vinyl chloride), which may predispose him to hepatic disease. Consider recent travel or contact with persons who have traveled to areas where hepatic disease is endemic.

Make sure to ask about alcohol consumption, a significant factor in suspected hepatic disease. Remember, an alcoholic may deliberately underestimate his alcohol intake, so interview the patient's family as well. Ask about recent contact with a jaundiced person and about any recent blood or plasma transfusions, blood tests, body piercings, tattoos, or dental work. Find out if the patient takes any drugs that may cause liver damage, such as sedatives, tranquilizers, analgesics, and

diuretics that cause potassium loss. Ask if the onset of symptoms was abrupt or insidious or if it

followed abdominal injury that could have damaged the liver. Ask if the patient bruises or bleeds easily. Check the color of stools and urine, and ask about any change in bowel habits. Also ask if the patient's weight has fluctuated recently.

Liver function studies

Numerous tests are available to detect hepatic disease. Perhaps the most useful tests are liver function studies, which measure serum enzymes and other substances. Typical findings in hepatic disease include:

- increased bilirubin levels
- increased alkaline phosphatase and 5′-nucleotidase levels
- elevated levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT): possible hepatocellular damage, viral hepatitis, or acute hepatic necrosis
- elevated gamma-glutamyltransferase levels: especially helpful because this enzyme level rises even when hepatic damage is still minimal
- hypoalbuminemia: subacute or massive hepatic necrosis or cirrhosis
- hyperglobulinemia: chronic inflammatory disorders
- prolonged prothrombin time or partial thromboplastin time: hepatitis or cirrhosis
- elevated serum ammonia levels: hepatic encephalopathy
- decreased serum total cholesterol levels: liver disease
- positive lupus erythematosus cell test (in chronic active hepatitis and the presence of hepatitis B antigen).

Liver function studies are less reliable after liver trauma. For instance, tests done long after the injury might miss an initial rise in serum AST and ALT levels. Several less specific blood tests for detecting hepatic

disease are urine urobilinogen, lactate dehydrogenase, and ornithine carbamoyltransferase.

Other useful diagnostic tests include the following:

- Plain abdominal X-rays may indicate gross hepatomegaly and hepatic masses by elevation or distortion of the diaphragm and may show calcification in the gallbladder, biliary tree, pancreas, and liver.
- Barium studies may indicate an elevated left hepatic lobe by displacing the barium-filled stomach laterally and posteriorly.
- Oral cholecystography is useful because parenchymal dysfunction and impaired bile excretion decrease the excretion of the contrast material and prevent visualization of the gallbladder.
- Percutaneous transhepatic cholangiography distinguishes mechanical biliary obstruction from intrahepatic cholestasis.
- Angiography demonstrates hepatic arterial circulation (altered in cirrhosis) and helps diagnose primary or secondary hepatic tumor masses.
- Radioisotope liver scans (scintiscans) may show an area of decreased uptake (a “hole”) using a colloidal or bengal scan or an area of increased uptake (a “hot spot”) using a gallium scan in hepatoma or hepatic abscess.
- Computed tomography scan produces in-depth, three-dimensional images of the biliary tract (the liver as well as the pancreas) that help distinguish between obstructive and nonobstructive jaundice and also helps identify space-occupying hepatic lesions.
- Portal and hepatic vein manometry localizes obstructions in the extrahepatic portion of the portal vein and portal inflow system or increased pressure in the presinusoidal vessels.
- Percutaneous or transvenous liver biopsy can determine the cause of unexplained hepatomegaly, hepatosplenomegaly, cholestasis, or persistently abnormal liver function tests; it's also useful when systemic infiltrative disease (such as sarcoidosis) or primary or metastatic hepatic tumors are suspected.
- Laparoscopy visualizes the serosal lining, liver, gallbladder, spleen, and other organs and is useful in unexplained hepatomegaly, ascites,

or an abdominal mass.

Gallbladder anatomy

The gallbladder is a pear-shaped organ that lies in the fossa on the underside of the liver and is capable of holding 50 ml of bile. Attached to the large organ above by connective tissue, the peritoneum, and blood vessels, the gallbladder is divided into four parts: the fundus, or broad inferior end;

the body, which is funnel-shaped and bound to the duodenum; the neck, which empties into the cystic duct; and the infundibulum, which lies between the body and the neck and sags to form Hartmann's pouch. The hepatic artery supplies the cystic and hepatic ducts with blood, which drains out of the gallbladder through the cystic vein. Rich lymph vessels in the submucosal layer also drain the gallbladder as well as the head of the pancreas.

The biliary duct system provides a passage for bile from the liver to the intestine and regulates bile flow. The gallbladder itself collects, concentrates, and stores bile. The normally functioning gallbladder also removes water and electrolytes from hepatic bile, increases the concentration of the larger solutes, and reduces its pH to less than 7. In gallbladder disease, bile becomes more alkaline, altering bile salts and cholesterol and predisposing the organ to stone formation.

Mechanisms of contraction

The gallbladder responds to sympathetic and parasympathetic innervation. Sympathetic stimulation inhibits muscle contraction, mild vagal stimulation causes the gallbladder to contract and the sphincter of Oddi to relax, and stronger stimulation causes the sphincter to contract. The gallbladder also responds to substances released by the intestine. For instance, after chyme (semiliquid, partially digested food) enters the duodenum from the stomach, the duodenum releases cholecystokinin (CCK) and pancreozymin (PCZ) into the bloodstream and stimulates the gallbladder to contract. The gallbladder also produces secretin, which stimulates the liver to secrete bile and CCK-PCZ. The gallbladder may also respond to some type of hormonal control, a theory

based in part on the fact that the gallbladder empties more slowly during pregnancy.

Assessing for gallbladder disease

During your physical examination of a patient with suspected gallbladder disease, look for its telltale signs and symptoms: pain, jaundice (a result of blockage of the common bile duct), fever, chills, indigestion, nausea, and intolerance of fatty foods. Pain may range from vague discomfort (as when pressure within the common bile duct gradually increases) to deep visceral pain (as when the gallbladder suddenly distends). Abrupt onset of pain with epigastric distress indicates gallbladder inflammation or obstruction of bile outflow by a stone or spasm.

The onset of jaundice also varies. If the gallbladder is healthy, jaundice may be delayed several days after bile duct blockage; if the gallbladder is absent or diseased, jaundice may appear within 24 hours after the blockage. Other effects of obstruction—pruritus, steatorrhea, and bleeding tendencies — may accompany jaundice. Gallbladder disorders rarely cause internal bleeding, but when they do—as in cholecystitis or obstructive clots in the biliary tree from GI bleeding — they can be fatal.

Diagnostic tests

After taking a thorough patient history and carefully assessing the clinical features, the next step in accurate diagnosis of gallbladder disease is cholecystography, in which X-rays are taken of the gallbladder after the patient has ingested radiopaque dye. However, visualization depends on absorption of the dye from the small intestine, the liver's capacity to remove the dye from the blood and excrete it in bile, the patency of the ductal system, and the ability of the gallbladder to concentrate and store the dye. Normally, the gallbladder fills about 13 hours after ingestion of the dye. Presence of stones or failure to visualize the gallbladder is significant.

Other diagnostic tests for gallbladder disease include the following:

- Percutaneous transhepatic cholangiography differentiates extrahepatic from intrahepatic obstructive jaundice and helps detect biliary masses and calculi. Needle insertion in a bile duct permits withdrawal of bile and injection of dye. Fluoroscopic tests evaluate

the filling of the hepatic and biliary trees. The test also permits palliative internal or external placement of biliary catheters for free flow of bile.

- Duodenal drainage diagnoses cholelithiasis, choledocholithiasis, biliary obstruction, hepatic cirrhosis, and pancreatic disease and differentiates types of jaundice. A

  tube is passed through the GI tract into the duodenum, and CCK-PCZ is given to stimulate the gallbladder, permitting measurement of bile flow and also specimen collection, which is examined for mucus, blood, cholesterol crystals, pancreatic enzymes, cancer cells, bacteria, or calcium bilirubinate. Duodenal drainage is especially useful when gallbladder function is poor or absent, when cholecystography fails to visualize the gallbladder or yields negative results despite continuing symptoms, or when cholecystography is contraindicated because of the patient's condition.
- In endoscopic retrograde cholangiopancreatography, duodenal endoscopy with dye injection and fluoroscopy are used to cannulate and visualize biliary and pancreatic ducts. This test is useful in locating obstruction, calculi, carcinoma, or stricture and for obtaining bile or pancreatic juice for analysis. Internal stents can be inserted to allow free flow of bile or pancreatic juice.
- In gallbladder ultrasound, sound waves are used to visualize the gallbladder and locate obstruction, stones, and tumors. This test is 95% accurate in detecting stones.

Other appropriate tests for biliary disease are the same as those for hepatic disease.

LIVER DISORDERS

Viral hepatitis

Viral hepatitis is a fairly common systemic disease, marked by hepatic cell destruction, necrosis, and autolysis, leading to anorexia, jaundice, and hepatomegaly. In most patients, hepatic cells eventually regenerate with little or no residual damage. However, old age and serious

underlying disorders make complications more likely. The prognosis is poor if edema and hepatic encephalopathy develop.

Hepatitis occurs in these forms:

- Type A (infectious or short-incubation hepatitis) is an acute-onset infection and most often affects children and young adults.
- Type B (serum or long-incubation hepatitis) is an insidious-onset infection and affects all age groups. Routine screening of donor blood for the hepatitis B surface antigen (HBsAg) has decreased the incidence of posttransfusion cases, but transmission by needles shared by drug abusers remains a major problem.
- Type C accounts for about 20% of all viral hepatitis cases and for most posttransfusion cases.
- Type D (delta hepatitis) is responsible for about 50% of all cases of fulminant hepatitis, which has a high mortality. Developing in 1% of patients, fulminant hepatitis causes unremitting liver failure with encephalopathy. It progresses to coma and commonly leads to death within 2 weeks. In the United States, type D is confined to people who are frequently exposed to blood and blood products, such as I.V. drug users and patients with hemophilia.
- Type E (formerly grouped with type C under the name non-A, non-B hepatitis) occurs primarily among patients who have recently returned from an endemic area (such as India, Africa, Asia, or Central America); it's more common in young adults and more severe in pregnant women.
- Hepatitis G is a newly discovered form of hepatitis. Transmission is by the blood-borne route and it's more common in those who receive blood transfusions.

Causes and incidence

The major forms of viral hepatitis result from infection with the causative viruses: A, B, C, D, E, or G.

Type A hepatitis is highly contagious and is usually transmitted by the fecal-oral route. However, it may also be transmitted parenterally, sexually (especially with oral or anal contact) and perinatally. Hepatitis

A usually results from ingestion of contaminated food, milk, or water. Many outbreaks of this type are traced to ingestion of seafood from polluted water. In 2004, there were more than 5,000 acute cases of hepatitis A infection reported in the United States.

Type B hepatitis, once thought to be transmitted only by the direct exchange of contaminated blood, is now known to be

transmitted also by contact with human secretions and feces. As a result, nurses, physicians, laboratory technicians, and dentists are frequently exposed to type B hepatitis, in many cases as a result of wearing defective gloves. Transmission also occurs during intimate sexual contact as well as through perinatal transmission. An estimated 50,000 new cases of hepatitis B virus (HBV) and 5,000 deaths from HBV occurred in the United States in 2004.

Although specific type C hepatitis viruses have been isolated, only a small percentage of patients have tested positive for them—perhaps reflecting the test's poor specificity. Usually, this type of hepatitis is transmitted through transfused blood from asymptomatic donors. Hepatitis C accounted for 26,000 new infections and 8,000 to 10,000 deaths in the United States in 2004. Most exposures (60%) occur through the use of illicit I.V. drugs. However, sexual transmission is responsible for 20% of cases. More than 170 million people have the hepatitis C virus worldwide.

Type D hepatitis is found only in patients with an acute or chronic episode of hepatitis B and requires the presence of HBsAg. The type D virus depends on the double-shelled type B virus to replicate. For this reason, type D infection can't outlast a type B infection. About 15 million people are infected with hepatitis D worldwide. It's more common in adults than in children. People with a history of illicit I.V. drug use and people who live in the Mediterranean basin have a higher incidence.

Type E hepatitis is transmitted enterically, much like type A. Because this virus is inconsistently shed in feces, detection is difficult. In the United States, the prevalence of hepatitis E is less than 2%. It's typically found in developing countries that lie near the equator. Incidence is highest among people ages 15 to 40.

Type G may be transmitted in a manner similar to that of hepatitis C. It may also be transmitted by sexual contact, and its incidence may be higher than previously suspected. It's associated with acute and chronic liver disease, but studies haven't clearly implicated the hepatitis G virus as an etiologic agent.

Other proposed causative factors, such as non-ABCDE viral hepatitis and type F, are under investigation.

Complications

- Chronic active hepatitis (with late hepatitis B)
- Primarily liver cancer (hepatitis B or C)
- Pancreatitis
- Cirrhosis
- Myocarditis
- Aplastic anemia
- Peripheral neuropathy

Signs and symptoms

Assessment findings are similar for the different types of hepatitis. Typically, signs and symptoms progress in several stages.

In the prodromal (preicteric) stage, the patient typically complains of easy fatigue and anorexia (possibly with mild weight loss), generalized malaise, depression, headache, weakness, arthralgia, myalgia, photophobia, and nausea with vomiting. He also may describe changes in his senses of taste and smell.

Assessment of the patient's vital signs may reveal a fever of 100° to 102° F (37.8° to 38.9° C). As the prodromal stage ends, usually 1 to 5 days before the onset of the clinical jaundice stage, inspection of urine and stool specimens may reveal darkcolored urine and clay-colored stools.

If the patient has progressed to the clinical jaundice stage, he may report pruritus, abdominal pain or tenderness, and indigestion. Early in this stage, he may complain of anorexia; later, his appetite may return.

Inspection of the sclerae, mucous membranes, and skin may reveal jaundice, which can last for 1 to 2 weeks. Jaundice indicates that the damaged liver is unable to remove bilirubin from the blood; however, its presence doesn't indicate the severity of the disease. Occasionally, hepatitis occurs without jaundice.

During the clinical jaundice stage, inspection of the skin may detect rashes, erythematous patches, or urticaria, especially if the patient has hepatitis B or C. Palpation may disclose abdominal tenderness in the right upper quadrant, an enlarged and tender liver and, in some cases, splenomegaly and cervical adenopathy.

During the recovery (posticteric) stage, most of the patient's symptoms decrease or subside. On palpation, a decrease in liver enlargement may be noted. The recovery phase commonly lasts from 2 to 12 weeks, although sometimes this phase lasts longer in the patient with hepatitis B, C, or E. Little is known about hepatitis G.

Diagnosis

A hepatitis profile, which identifies antibodies specific to the causative virus and establishes the type of hepatitis, is routine in suspected viral hepatitis.

- Type A: Detection of an antibody to hepatitis A confirms the diagnosis.
- Type B: The presence of HBsAg and hepatitis B antibodies confirms the diagnosis.
- Type C: Diagnosis depends on serologic testing for the specific antibody 1 or more months after the onset of acute hepatitis. Until then, the diagnosis is established primarily by obtaining negative test results for hepatitis A, B, and D.
- Type D: Detection of intrahepatic delta antigens or immunoglobulin (Ig) antidelta antigens in acute disease (or IgM and IgG in chronic disease) establishes the diagnosis.
- Type E: Detection of hepatitis E antigens supports the diagnosis; however, the diagnosis may also be determined by ruling out hepatitis C.

- Type G: Detection of hepatitis G antigen supports the diagnosis but doesn't clearly implicate infection; the patient may be otherwise asymptomatic.

Additional findings from liver function studies support the diagnosis:

- Serum aspartate aminotransferase and serum alanine aminotransferase levels are increased in the prodromal stage of acute viral hepatitis.
- Serum alkaline phosphatase levels are slightly increased.
- Serum bilirubin levels are elevated. Levels may continue to be high late in the disease, especially in severe cases.
- Prothrombin time is prolonged (more than 3 seconds longer than normal indicates severe liver damage).
- White blood cell counts commonly reveal transient neutropenia and lymphopenia followed by lymphocytosis.
- Liver biopsy is performed if chronic hepatitis is suspected; however, it's performed for acute hepatitis only if the diagnosis is questionable.

Treatment

No specific drug therapy has been developed for hepatitis, with the exception of hepatitis B and hepatitis C. Chronic hepatitis B has been successfully treated with a synthetic thymidine nucleoside analogue called telbividine(Tyzeka). Hepatitis C has been treated somewhat successfully with interferon alfa-2b (Intron A) and peginterferon alfa-2a (Pegasys). Instead, patients are advised to rest in the early stages of the illness and to combat anorexia by eating small, high-calorie, high-protein meals. (Protein intake should be reduced if signs or symptoms of pre-coma—lethargy, confusion, and mental changes—develop.) Large meals are usually better tolerated in the morning because many patients experience nausea late in the day.

In acute viral hepatitis, hospitalization usually is required only for the patient with severe symptoms or complications. Parenteral nutrition may be required if the patient experiences persistent vomiting and is unable to maintain oral intake.

Antiemetics may be given 30 minutes before meals to relieve nausea and prevent vomiting; phenothiazines have a cholestatic effect and should be avoided. For severe pruritus, the resin cholestyramine may be given.

Special considerations

Use enteric precautions when caring for patients with type A or E hepatitis. Practice standard precautions for all patients.

- Inform visitors about isolation precautions.
- Provide rest periods throughout the day. Schedule treatments and tests so that the patient can rest between bouts of activity.
- Because inactivity may make the patient anxious, include diversionary activities as part of his care. Gradually add activities to his schedule as he begins to recover.

- Encourage the patient to eat. Don't overload his meal tray or overmedicate him because this will diminish his appetite.
- Encourage fluids (at least 4 qt [4 L] per day). Encourage the anorectic patient to drink fruit juice. Also offer chipped ice and effervescent soft drinks to maintain hydration without inducing vomiting.
- Administer supplemental vitamins and commercial feedings, as ordered. If symptoms are severe and the patient can't tolerate oral intake, provide I.V. therapy and parenteral nutrition, as ordered by the physician.
- Record the patient's weight daily, and keep intake and output records. Observe stools for color, consistency, and amount and record the frequency of bowel movements.
- Watch for signs of fluid shift, such as weight gain and orthostasis.
- Watch for signs of hepatic coma, dehydration, pneumonia, vascular problems, and pressure ulcers.
- In fulminant hepatitis, maintain electrolyte balance and a patent airway, prevent infections, and control bleeding. Correct hypoglycemia and other complications while awaiting liver regeneration and repair.

- Before discharge, emphasize the importance of having regular medical checkups for at least 1 year. The patient will have an increased risk of developing hepatoma. Warn the patient against using alcohol or over-the-counter drugs during this period. Teach him to recognize the signs of a recurrence.
- Inform the patient about the availability of support groups for people with all types of hepatitis and provide contact information if he's interested.

PREVENTION

Review the following with your patient to prevent the spread of hepatitis:

- *Stress the importance of thorough and frequent hand washing.*
- *Tell the patient not to share food, eating utensils, or toothbrushes.*
- *If the patient has hepatitis A or E, warn him not to contaminate food or water with fecal matter, because the disease is transmitted by the fecal-oral route.*
- *If the patient has hepatitis B, C, D, or G, explain that transmission occurs thorugh exchange of blood or body fluids that contain blood. While infected, he shouldn't donate blood or have sexual contact.*
- *Advise the patient to take extra care to avoid cutting himself.*

Nonviral hepatitis

Nonviral inflammation of the liver is a form of hepatitis that is classified as toxic, drug-induced (idiosyncratic), or autoimmune. Most patients recover from this illness, although a few develop fulminating hepatitis or cirrhosis.

Causes and incidence

Various hepatotoxins—carbon tetrachloride, acetaminophen, trichloroethylene, poisonous mushrooms, and vinyl chloride —can cause the toxic form of this disease. Following exposure to these agents, liver damage usually occurs within 24 to 48 hours, depending on the size of the dose or degree of exposure. Alcohol, anoxia, and preexisting liver disease exacerbate the toxic effects of some of these agents.

Drug-induced (idiosyncratic) hepatitis may stem from a hypersensitivity reaction unique to the affected individual, unlike toxic hepatitis, which appears to affect all people indiscriminately. Among the drugs that may cause this type of hepatitis are niacin, halothane, sulfonamides, isoniazid, methyldopa, and phenothiazines (cholestasis-induced hepatitis). In hypersensitive people, symptoms of hepatic dysfunction may appear at any time during or after exposure to these drugs but usually emerge after 2 to 5 weeks of therapy. Not all adverse drug reactions are toxic. Hormonal contraceptives, for example, may impair liver function and produce jaundice without causing necrosis, fatty infiltration of liver cells, or hypersensitivity.

Autoimmune hepatitis, also known as lupoid hepatitis, is a disease in which the body's immune system attacks liver cells, causing them to become inflamed. Researchers think a genetic factor may predispose some people to autoimmune diseases. About 70% of those with autoimmune hepatitis

are women, most age 15 to 40. It's usually chronic and can lead to cirrhosis.

Complications

- Cirrhosis
- Hepatitis
- Liver failure

Signs and symptoms

Clinical features of toxic and drug-induced hepatitis vary with the severity of the liver damage and the causative agent. In most patients, signs and symptoms resemble those of viral hepatitis: anorexia, nausea,

vomiting, jaundice, dark urine, hepatomegaly, possible abdominal pain (with acute onset and massive necrosis), and clay-colored stools or pruritus with the cholestatic form of hepatitis. Carbon tetrachloride poisoning also produces headache, dizziness, drowsiness, and vasomotor collapse; halothane-related hepatitis produces fever, moderate leukocytosis, and eosinophilia; chlorpromazine toxicity produces abrupt fever, rash, arthralgia, lymphadenopathy, and epigastric or right upper quadrant pain.

Diagnosis

Diagnostic findings include elevations in serum aspartate aminotransferase and alanine aminotransferase, total and direct bilirubin (with cholestasis), alkaline phosphatase, white blood cell (WBC) count, and eosinophil count (possible in drug-induced type). To diagnose autoimmune hepatitis, antibodies, including antinuclear antibodies (ANA), smooth muscle cells antibodies (SMA), or liver and kidney microsomes (anti-LKM), will be elevated. Liver biopsy may help identify the underlying pathology, especially infiltration with WBCs and eosinophils. Liver function tests have limited value in distinguishing between nonviral and viral hepatitis.

Treatment

Effective treatment must remove the causative agent by lavage, catharsis, or hyperventilation, depending on the route of exposure. Acetylcysteine (Acetadote) may serve as an antidote for toxic hepatitis caused by acetaminophen poisoning but doesn't prevent drug-induced hepatitis caused by other substances. Corticosteroids may be ordered for patients with the drug-induce and autoimmune type. Azathioprine (Imuran), an immune suppressant, may also be used in conjunction with corticosteroids to treat autoimmune hepatitis.

Special considerations

- Monitor laboratory studies and note trends.
- Monitor the patient's vital signs and provide support to maintain vital functioning, depending on the severity of his symptoms.

- Preventive measures should include instructing the patient about the proper use of drugs and the proper handling of cleaning agents and solvents.

Cirrhosis and fibrosis

Cirrhosis is a chronic hepatic disease characterized by diffuse destruction and fibrotic regeneration of hepatic cells. As necrotic tissue yields to fibrosis, this disease alters liver structure and normal vasculature, impairs blood and lymph flow, and ultimately causes hepatic insufficiency. The prognosis is better in noncirrhotic forms of hepatic fibrosis, which cause minimal hepatic dysfunction and don't destroy liver cells.

Causes and incidence

These clinical types of cirrhosis reflect its diverse etiology:

- Portal, nutritional, or alcoholic (Laennec's) cirrhosis, the most common type, occurs in 30% to 50% of cirrhotic patients, up to 90% of whom have a history of alcoholism. Liver damage results from malnutrition, especially of dietary protein, and chronic alcohol ingestion. Fibrous tissue forms in portal areas and around central veins.
- Biliary cirrhosis (15% to 20% of patients) results from injury or prolonged obstruction.
- Postnecrotic (posthepatic) cirrhosis (10% to 30% of patients) stems from various types of hepatitis.
- Pigment cirrhosis (5% to 10% of patients) may result from disorders such as hemochromatosis.

- Cardiac cirrhosis (rare) refers to liver damage caused by right-sided heart failure.
- Idiopathic cirrhosis (about 10% of patients) has no known cause.

Noncirrhotic fibrosis may result from schistosomiasis or congenital hepatic fibrosis or may be idiopathic.

Complications

- Portal hypertension
- Bleeding esophageal varices
- Hepatic encephalopathy
- Hepatorenal syndrome

Signs and symptoms

Clinical manifestations of cirrhosis and fibrosis are similar for all types, regardless of the cause. Early indications are vague, but usually include GI signs and symptoms (anorexia, indigestion, nausea, vomiting, constipation, or diarrhea) and a dull abdominal ache. Major and late signs and symptoms develop as a result of hepatic insufficiency and portal hypertension:

- Respiratory—pleural effusion and limited thoracic expansion due to abdominal ascites, interfering with efficient gas exchange and leading to hypoxia
- Central nervous system—progressive signs or symptoms of hepatic encephalopathy —lethargy, mental changes, slurred speech, asterixis (flapping tremor), peripheral neuritis, paranoia, hallucinations, extreme obtundation, and coma
- Hematologic—bleeding tendencies (nosebleeds, easy bruising, and bleeding gums) and anemia
- Endocrine—testicular atrophy, menstrual irregularities, gynecomastia, and loss of chest and axillary hair
- Skin—severe pruritus, extreme dryness, poor tissue turgor, abnormal pigmentation, spider angiomas, palmar erythema, and possibly jaundice
- Hepatic—jaundice, hepatomegaly, ascites, edema of the legs, hepatic encephalopathy, and hepatorenal syndrome comprise the other major effects of full-fledged cirrhosis
- Miscellaneous—musty breath, enlarged superficial abdominal veins, muscle atrophy, pain in the right upper abdominal quadrant that

worsens when the patient sits up or leans forward, palpable liver or spleen, and temperature of 101° to 103° F (38.3° to 39.4° C). Bleeding from esophageal varices results from portal hypertension.

Diagnosis

CONFIRMING DIAGNOSIS

Liver biopsy, the definitive test for cirrhosis, detects destruction and fibrosis of hepatic tissue.

Liver scan shows abnormal thickening and a liver mass. Cholecystography and cholangiography visualize the gallbladder and the biliary duct system, respectively; splenoportal venography visualizes the portal venous system. Percutaneous transhepatic cholangiography differentiates extrahepatic from intrahepatic obstructive jaundice and discloses hepatic pathology and the presence of gallstones.

Laboratory findings that are characteristic of cirrhosis include:

- decreased white blood cell count, hemoglobin level and hematocrit, albumin, serum electrolyte levels (sodium, potassium, chloride, and magnesium), and cholinesterase
- elevated levels of globulin, serum ammonia, total bilirubin, alkaline phosphatase, serum aspartate aminotransferase, serum alanine aminotransferase, and lactate dehydrogenase and increased thymol turbidity
- anemia, neutropenia, and thrombocytopenia, characterized by prolonged prothrombin and partial thromboplastin times
- deficiencies of folic acid, iron, and vitamins A, B_{12}, C, and K.

Treatment

Treatment is designed to remove or alleviate the underlying cause of cirrhosis or fibrosis, prevent further liver damage, and prevent or treat complications. The patient may benefit from a high-calorie and moderate-to high-protein diet, but developing hepatic encephalopathy mandates restricted protein intake. In addition, sodium is usually

restricted to 200 to 500 mg/day and fluids to 1 to 1½ qt (about 1 to 1.5 L)/day.

If the patient's condition deteriorates, he may need tube feedings or total parenteral nutrition. He also may need supplemental vitamins—A, B complex, D, and K—to

compensate for the liver's inability to store them and vitamin B_{12}, folic acid, and thiamine for deficiency anemia. Rest, moderate exercise, and avoidance of infections and toxic agents are essential.

UNDERSTANDING PORTAL HYPERTENSION AND ESOPHAGEAL VARICES

Portal hypertension—elevated pressure in the portal vein—occurs when blood flow meets increased resistance. The disorder is a common result of cirrhosis, but may also stem from mechanical obstruction and occlusion of the hepatic veins (Budd-Chiari syndrome). As portal pressure rises, blood backs up into the spleen and flows through collateral channels to the venous system, bypassing the liver. Consequently, portal hypertension produces splenomegaly with thrombocytopenia, dilated collateral veins (esophageal varices, hemorrhoids, or prominent abdominal veins), and ascites. Nevertheless, in many patients, the first sign of portal hypertension is bleeding from esophageal varices—dilated tortuous veins in the submucosa of the lower esophagus. Bleeding esophageal varices commonly cause massive hematemesis, requiring emergency treatment to control hemorrhage and prevent hypovolemic shock.

Diagnosis and treatment

These procedures help diagnose and correct esophageal varices.

- Endoscopy identifies the ruptured varix as the bleeding site and excludes other potential sources in the upper

GI tract.

- Angiography may aid diagnosis, but is less precise than endoscopy.
- Vasopressin infused into the superior mesenteric artery may temporarily stop bleeding. When angiography is unavailable, vasopressin may be infused by I.V. drip or diluted with 5% dextrose in water (except in patients with coronary vascular disease), but this route is usually less effective.
- A Sengstaken-Blakemore or Minnesota tube may also help control hemorrhage by applying pressure on the bleeding site. Iced saline lavage through the tube may help control bleeding.

The use of vasopressin or a Minnesota or Sengstaken-Blakemore tube is a temporary measure, especially in the patient with a severely deteriorated liver. Fresh blood and fresh frozen plasma, if available, are preferred for blood transfusions to replace clotting factors. Treatment with lactulose promotes elimination of old blood from the GI tract, which combats excessive ammonia production and accumulation.

Appropriate surgical bypass procedures include portosystemic anastomosis, splenorenal shunt, and mesocaval shunt. A portacaval or a mesocaval shunt decreases pressure within the liver and reduces ascites, plasma loss, and the risk of hemorrhage by directing blood from the liver into collateral vessels. Emergency shunts carry a mortality of 25% to 50%. Clinical evidence suggests that portosystemic bypass doesn't prolong the patient's survival time; however, he will eventually die of hepatic coma rather than of hemorrhage.

Patient care

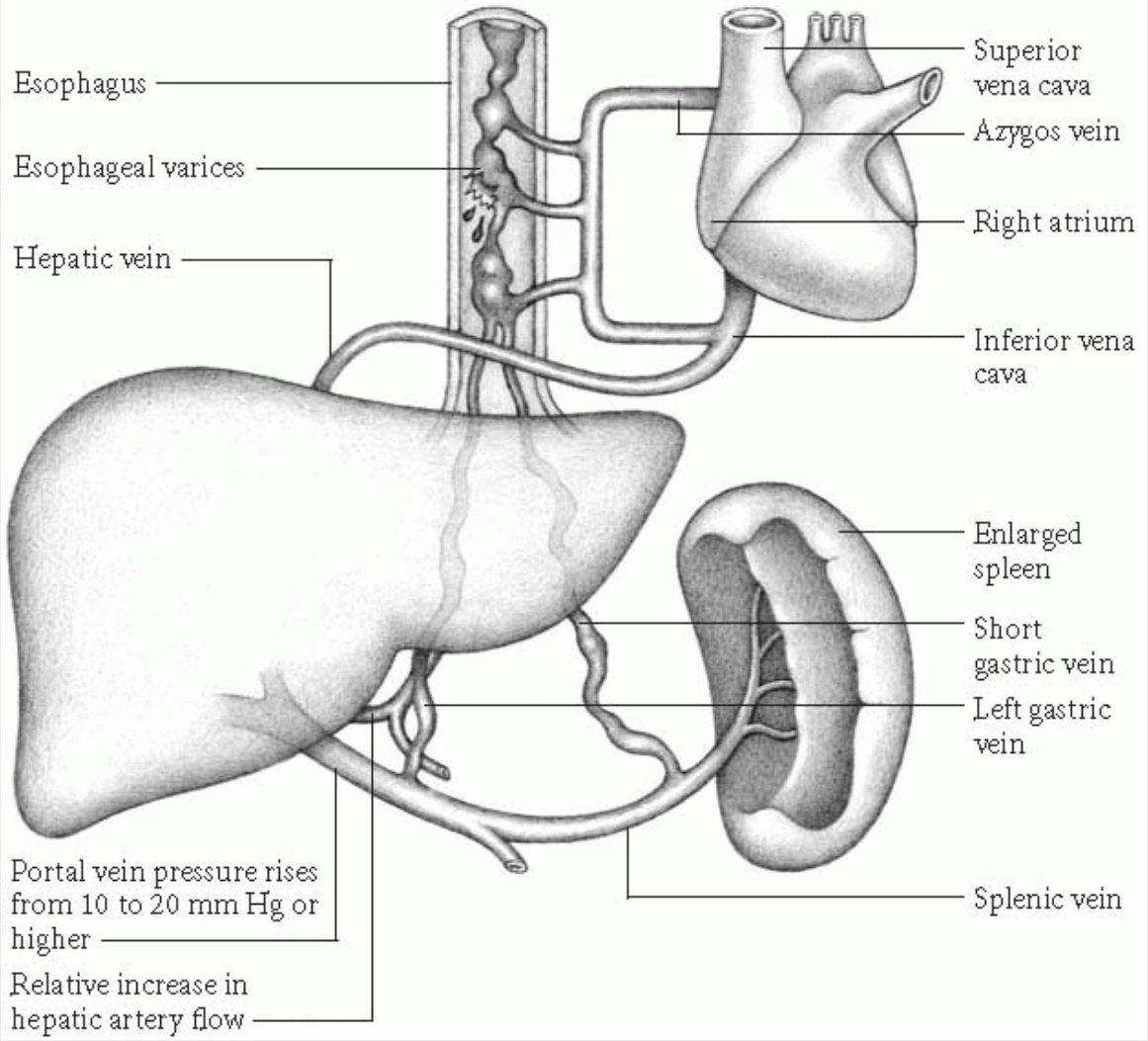
Care for the patient who has portal hypertension with esophageal varices focuses on careful monitoring for signs and symptoms of hemorrhage and subsequent hypotension, compromised oxygen supply, and altered level of consciousness (LOC).

- Monitor the patient's vital signs, urine output, and central venous pressure to determine fluid volume status.
- Assess the patient's LOC often.
- Provide emotional support and reassurance after massive GI bleeding, which is always frightening.
- Keep the patient as quiet and comfortable as possible, but remember that tolerance of sedatives and tranquilizers may be decreased because of liver damage.
- Clean the patient's mouth, which may be dry and flecked with dried blood.
- Carefully monitor the patient with a Minnesota or Sengstaken-Blakemore tube in place for persistent bleeding in gastric drainage, signs of asphyxiation from tube displacement, proper inflation of balloons, and correct traction to maintain tube placement.

PATHOPHYSIOLOGY

CIRCULATION IN PORTAL HYPERTENSION

As portal vein pressure rises, blood backs up into the spleen and flows through collateral channels to the venous system, bypassing the liver and resulting in esophageal varices.



Drug therapy requires special caution because the cirrhotic liver can't detoxify harmful substances efficiently. If required, vasopressin may be prescribed for esophageal varices, and diuretics may be given for edema. However, diuretics require careful monitoring because fluid and electrolyte imbalance may precipitate hepatic encephalopathy. Encephalopathy is treated with lactulose. Antibiotics are used to decrease intestinal bacteria and reduce ammonia production, which causes encephalopathy. Coagulopathy may be treated with blood products or vitamin K.

Paracentesis and infusions of salt-poor albumin, in addition to fluid and salt restriction, may alleviate ascites. Surgical procedures include treatment of varices by upper endoscopy with banding or sclerosis, splenectomy, esophagogastric resection, and splenorenal or portacaval

anastomosis to relieve portal hypertension. (See *Understanding portal hypertension and esophageal varices* and *Circulation in portal hypertension.*)

Low-protein diets are controversial. They aid in managing acute hepatic encephalopathy but are rarely necessary in chronic conditions because of the underlying protein-calorie malnutrition.

ALERT

If cirrhosis progresses and becomes life-threatening, a liver transplant should be considered.

Special considerations

The patient with cirrhosis needs close observation, first-rate supportive care, and sound nutritional counseling.

- Check the patient's skin, gums, stools, and vomitus regularly for bleeding. Apply pressure to injection sites to prevent bleeding. Warn him against taking nonsteroidal anti-inflammatory drugs, straining at stool, and blowing his nose or sneezing too vigorously. Suggest using an electric razor and soft toothbrush.

ALERT

Observe the patient closely for changes in behavior or personality. Report increasing stupor, lethargy, hallucinations, or neuromuscular dysfunction. Awaken him periodically to determine his level of consciousness. Watch for asterixis, a sign of developing hepatic encephalopathy.

- To assess fluid retention, weigh the patient and measure abdominal girth at least daily, inspect his ankles and sacrum for dependent edema, and accurately record intake and output. Carefully evaluate the patient before, during, and after paracentesis; this drastic loss of fluid may induce shock.
- To prevent skin breakdown associated with edema and pruritus, avoid using soap when you bathe the patient; instead, use lubricating lotion

or moisturizing agents. Handle him gently, and turn and reposition him often to keep his skin intact.

- Tell the patient that rest and good nutrition will conserve his energy and decrease metabolic demands on the liver. Urge him to eat frequent, small meals. Stress the need to avoid infections and abstain from alcohol. Refer him to Alcoholics Anonymous, if necessary.

Liver abscess

A liver abscess occurs when bacteria or protozoa destroy hepatic tissue, producing a cavity, which fills with infectious organisms, liquefied liver cells, and leukocytes. Necrotic tissue then walls off the cavity from the rest of the liver.

Although liver abscess is relatively uncommon, it carries a mortality of 10% to 20%. Complications include rupture into the peritoneum, pleura, or pericardium, significantly increasing mortality.

Causes and incidence

In pyogenic liver abscesses, the common infecting organisms are *Escherichia coli, Klebsiella, Staphylococcus, Streptococcus, Bacteroides,* and enterococcus. The infecting organisms may invade the liver directly after a liver wound or they may spread from the lungs, skin, or other organs by the hepatic artery, portal vein, or biliary tract. Pyogenic abscesses are generally multiple and commonly follow cholecystitis, peritonitis, pneumonia, and bacterial endocarditis.

An amebic abscess results from infection with the protozoa *Entamoeba histolytica,* the organism that causes amebic dysentery. Amebic liver abscesses usually occur singly, in the right lobe.

There are 8 to 16 cases of liver abscess for every 100,000 people hospitalized, and the mortality rate is 5% to 30%. Most cases occur in people in their 60s and 70s.

Complication

- Abscess rupture into pleura, peritoneum, or pericardium

Signs and symptoms

The clinical manifestations of a liver abscess depend on the degree of involvement. Some patients are acutely ill; in others, the abscess is recognized only at autopsy, after death from another illness. The onset of symptoms of a pyogenic abscess is usually sudden; in an amebic abscess, the onset is more insidious. Common signs and symptoms include right abdominal and shoulder pain, weight loss, fever, chills, diaphoresis, nausea, vomiting, and anemia. Signs of right pleural effusion, such as dyspnea and

pleural pain, develop if the abscess extends through the diaphragm. Liver damage may cause jaundice.

Diagnosis

CONFIRMING DIAGNOSIS

Ultrasound and computed tomography (CT) scan with contrast medium can accurately define intrahepatic lesions and assess intra-abdominal pathology. Percutaneous needle aspiration of the abscess can be performed to identify the causative organism.

Magnetic resonance imaging with contrast medium may also be accurate for diagnosing liver abscess, Relevant laboratory values include elevated serum aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and bilirubin levels; increased white blood cell count; and decreased serum albumin levels. In pyogenic abscess, a blood culture can identify the bacterial agent; in amebic abscess, a stool culture and serologic and hemagglutination tests can assist in diagnosis.

Treatment

If the organism causing the liver abscess is unknown, long-term antibiotic therapy begins immediately. When culture results are obtained, antibiotics are prescribed specific to treat the organism. I.V. antibiotic therapy usually continues for 14 days and then is replaced with an oral preparation to complete a 6-week course. Surgery is usually

avoided, but it may be done for a single pyogenic abscess or for an amebic abscess that fails to respond to antibiotics. Placement of drains (using CT scanning or ultrasound) particularly in large abscesses, reduces the need for abdominal surgery. In acutely toxic patients, percutaneous needle aspiration and decompression may be needed to remove the abscess.

Special considerations

- Provide supportive care, monitor the patient's vital signs (especially temperature), and maintain fluid and nutritional intake.
- Administer anti-infectives and antibiotics as ordered, and watch for possible adverse effects. Stress the importance of compliance with therapy.
- Explain diagnostic and surgical procedures.
- Watch carefully for complications of abdominal surgery, such as hemorrhage or sepsis.

Fatty liver

Fatty liver, also known as *steatosis,* or nonalcoholic steatohepatitis, is a common clinical finding consisting of accumulated triglycerides and other fats in liver cells. In severe fatty liver, fat comprises as much as 40% of the liver's weight (as opposed to 5% in a normal liver), and the weight of the liver may increase from 3.31 lb (1.5 kg) to as much as 11 lb (4.9 kg). Minimal fatty changes are temporary and asymptomatic; severe or persistent changes may cause liver dysfunction. Fatty liver is usually reversible by simply eliminating the cause; however, this disorder may result in recurrent infection or sudden death from fat emboli in the lungs.

Causes and incidence

Chronic alcoholism is the most common cause of fatty liver in the United States and in Europe, with the severity of hepatic disease directly related to the amount of alcohol consumed. (Fatty liver can occur in people who consume as little as 10 oz of alcohol per week.)

Other causes of nonalcoholic steatohepatitis include malnutrition (especially protein deficiency), obesity, diabetes mellitus, jejunoileal bypass surgery, Cushing's syndrome, Reye's syndrome, pregnancy, large doses of hepatotoxins such as I.V. tetracycline, carbon tetrachloride intoxication, prolonged parenteral nutrition, and DDT poisoning. Whatever the cause, fatty infiltration of the liver probably results from mobilization of fatty acids from adipose tissues or altered fat metabolism.

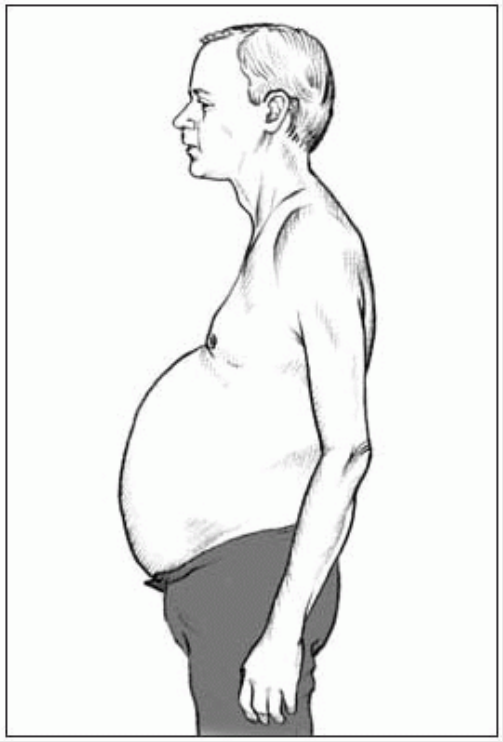
Complications

- Permanent liver damage
- Portal hypertension
- Metabolic disturbances
- Disseminated intravascular coagulation

- Renal failure
- Coma

MASSIVE ASCITES IN FATTY LIVER

Massive ascites may result from fatty liver. Emaciated extremities and upper thorax are also typical of ascites.



Signs and symptoms

Clinical features of fatty liver vary with the degree of lipid infiltration, and many patients are asymptomatic. The most typical sign is a large, tender liver (hepatomegaly). Common signs and symptoms include right upper quadrant pain (with massive or rapid infiltration), ascites, edema, jaundice, and fever (all with hepatic necrosis or biliary stasis). (See *Massive ascites in fatty liver.*) Nausea, vomiting, and anorexia are less common. Splenomegaly usually accompanies cirrhosis. Rarer changes are spider angiomas, varices, transient gynecomastia, and menstrual disorders.

Diagnosis

Typical clinical features—especially in patients with chronic alcoholism, malnutrition, poorly controlled diabetes mellitus, or obesity—suggest fatty liver.

CONFIRMING DIAGNOSIS

A liver biopsy confirms excessive fat in the liver. These liver function tests support this diagnosis:

- *Albumin—somewhat low*
- *Globulin—usually elevated*
- *Cholesterol—usually elevated*
- *Total bilirubin—elevated*
- *Alkaline phosphatase—elevated*
- *Transaminase—elevated*
- *Prothrombin time—possibly prolonged.*

Other findings may include anemia, leukocytosis, elevated white blood cell count, albuminuria, hyperglycemia or hypoglycemia, and iron, folic acid, and vitamin B_{12} deficiencies.

Treatment

Treatment of fatty liver is essentially supportive and consists of correcting the underlying condition or eliminating its cause. For instance, when fatty liver results from parenteral nutrition, decreasing the rate of carbohydrate infusion may correct the disease. In alcoholic fatty liver, abstinence from alcohol and a proper diet can begin to correct liver changes within 4 to 8 weeks. Such correction requires comprehensive patient teaching.

Special considerations

Providing support to the patient and his family is an important element in the care of the patient with steatosis.

- Suggest counseling for the alcoholic patient and provide emotional support for his family.
- Teach the patient with diabetes—and his family—about proper care, such as the purpose of insulin injections, diet, and exercise. Refer him to home health nurses or to group classes, as necessary, to promote compliance with treatment. Emphasize the need for long-term

medical supervision and urge him to report any changes in his health immediately.

- Instruct an obese patient and his family about proper diet. Warn against fad diets, which are usually nutritionally inadequate. Recommend medical supervision for a patient who's more than 20% overweight. Encourage attendance at group diet and exercise programs and, if necessary, suggest behavior modification programs to correct

eating habits. Be sure to follow up on his progress and provide positive reinforcement for any weight loss.

- Assess for malnutrition, especially protein deficiency, in the patient with chronic illness. Suggest dietary changes and refer the patient to a dietitian.
- Advise patients receiving hepatotoxins and those who risk occupational exposure to DDT to watch for and immediately report signs of toxicity.
- Inform the patient that fatty liver is reversible *only* if he strictly follows the therapeutic program; otherwise, he risks permanent liver damage.

Hepatic encephalopathy

Hepatic encephalopathy, also known as *portosystemic encephalopathy* or *hepatic coma,* is a neurologic syndrome that develops as a complication of chronic liver disease. Most common in patients with cirrhosis, this syndrome is due primarily to ammonia intoxication of the brain. It may be acute and self-limiting or chronic and progressive. Treatment requires correction of the precipitating cause and reduction of blood ammonia levels. In advanced stages, the prognosis is extremely poor despite vigorous treatment.

Causes and incidence

Hepatic encephalopathy follows rising blood ammonia levels. Normally, the ammonia produced by protein breakdown in the bowel is metabolized to urea in the liver. When portal blood shunts past the liver,

ammonia directly enters the systemic circulation and is carried to the brain. Such shunting may result from the collateral venous circulation that develops in portal hypertension or from surgically created portosystemic shunts. Cirrhosis further compounds this problem because impaired hepatocellular function prevents conversion of ammonia that reaches the liver.

Other factors that predispose rising ammonia levels include excessive protein intake, sepsis, excessive accumulation of nitrogenous body wastes (from constipation or GI hemorrhage), and bacterial action on protein and urea to form ammonia. Certain other factors heighten the brain's sensitivity to ammonia intoxication: hypoxia, azotemia, impaired glucose metabolism, infection, and administration of sedatives, narcotics, and general anesthetics. Depletion of the intravascular volume, from bleeding or diuresis, reduces hepatic and renal perfusion and leads to contraction alkalosis. In turn, hypokalemia and alkalosis increase ammonia production and impair its excretion.

Complication

- Irreversible coma

Signs and symptoms

Clinical manifestations of hepatic encephalopathy vary (depending on the severity of neurologic involvement) and develop in four stages:

- In the *prodromal* stage, early signs and symptoms are commonly overlooked because they're so subtle: slight personality changes (disorientation, forgetfulness, and slurred speech) and a slight tremor.
- During the *impending* stage, tremor progresses into asterixis (liver flap and flapping tremor), the hallmark of hepatic encephalopathy. Asterixis is characterized by quick, irregular extensions and flexions of the wrists and fingers, when the wrists are held out straight and the hands flexed upward. Lethargy, aberrant behavior, and apraxia also occur.
- At the *stuporous* stage, hyperventilation occurs; the patient is typically stuporous, but becomes noisy and abusive when aroused.

- In the *comatose* stage, the patient has hyperactive reflexes, a positive Babinski's sign, fetor hepaticus (musty, sweet odor to the breath), and coma.

Diagnosis

CONFIRMING DIAGNOSIS

Clinical features, a history of liver disease, and elevated serum ammonia levels in venous and arterial samples confirm hepatic encephalopathy.

Other supportive laboratory values include an EEG that slows as the disease progresses, an increase in spinal fluid glutamine, elevated bilirubin, and prolonged

prothrombin time. Recently, evoked potential testing has been advocated as a more specific indicator of encephalopathy, but its benefit over an EEG isn't yet clear.

Treatment

Effective treatment stops progression of encephalopathy by reducing blood ammonia levels. Treatment includes eliminating ammonia-producing substances from the GI tract by administering neomycin to suppress bacterial flora (preventing them from converting amino acids into ammonia), performing sorbitol-induced catharsis to produce osmotic diarrhea and continuous aspiration of blood from the stomach, and reducing dietary protein intake.

Lactulose, which traps ammonia in the bowel and promotes its excretion, is administered to reduce blood ammonia levels. Bacterial enzymes change lactulose to lactic acid, thereby rendering the colon too acidic for bacterial growth. At the same time, the resulting increase in free hydrogen ions prevents diffusion of ammonia through the mucosa; lactulose promotes conversion of systemically absorbable ammonia to ammonium, which is poorly absorbed and can be excreted. It's usually given orally. However, if the patient is in a coma, it may be administered by retention enema.

Treatment may also include potassium supplements to correct alkalosis due to increased ammonia levels, especially if the patient is taking diuretics. Hemodialysis may sometimes be used to clear toxic blood temporarily. Salt-poor albumin may be used to maintain fluid and electrolyte balance, replace depleted albumin levels, and restore plasma. Sedatives, tranquilizers, and other medications metabolized or excreted by the liver should be avoided if possible. Medications containing ammonium (including certain antacids) should also be avoided.

Special considerations

Patient care includes monitoring symptoms and support.

- Assess and record the patient's level of consciousness frequently. Continually orient him to place and time. Keep a daily record of his handwriting to monitor the progression of neurologic involvement.
- Monitor the patient's intake, output, and fluid and electrolyte balance. Check daily weight and measure abdominal girth. Watch for, and immediately report, signs of anemia (decreased hemoglobin level), infection, alkalosis (increased serum bicarbonate), and GI bleeding (melena and hematemesis).
- If the encephalopathy is acute, ask the dietary department to provide the specified low-protein diet, with carbohydrates supplying most of the calories.
- Promote rest, comfort, and a quiet atmosphere. Discourage stressful exercise.
- Use restraints, if necessary, but avoid sedatives. Protect the comatose patient's eyes from corneal injury by using artificial tears or eye patches.
- Provide emotional support for the patient's family in the terminal stage of encephalopathy.

GALLBLADDER AND DUCT DISORDERS

Cholelithiasis and related disorders

Diseases of the gallbladder and biliary tract are common and, in many cases, painful conditions that usually require surgery and may be life-threatening. They are generally associated with deposition of calculi and inflammation. (See *Common sites of calculi formation.*)

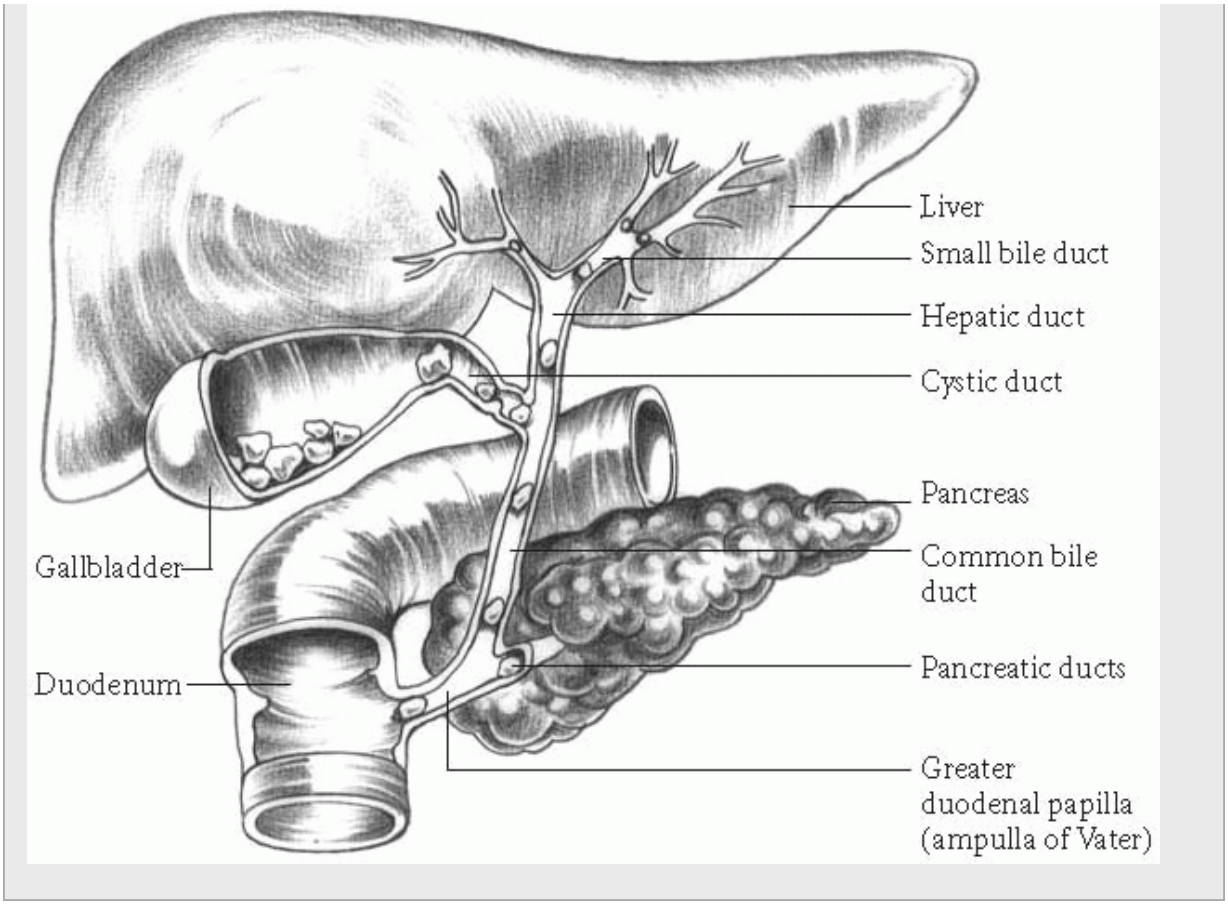
Causes and incidence

Cholelithiasis, stones or calculi (gallstones) in the gallbladder, results from changes in bile components. Gallstones are made of cholesterol, calcium bilirubinate, or a mixture of cholesterol and bilirubin pigment. They arise during periods of sluggishness in the gallbladder due to pregnancy, hormonal contraceptives, diabetes mellitus, celiac disease, cirrhosis of the liver, and pancreatitis. Cholelithiasis is a common health problem, affecting about 1 out of

every 1,000 people. The prognosis is usually good with treatment unless infection occurs, in which case the prognosis depends on its severity and response to antibiotics.

COMMON SITES OF CALCULI FORMATION

The illustration below shows sites where calculi typically collect. Calculi vary in size; small calculi may travel.



One out of every 10 patients with gallstones develops *choledocholithiasis,* or gallstones in the common bile duct (sometimes called “common duct stones”). This occurs when stones passed out of the gallbladder lodge in the hepatic and common bile ducts and obstruct the flow of bile into the duodenum. Prognosis is good unless infection occurs.

Cholangitis, infection of the bile duct, is commonly associated with choledocholithiasis and may follow percutaneous transhepatic cholangiography or occlusion of endoscopic stents. Predisposing factors may include bacterial or metabolic alteration of bile acids. Widespread inflammation may cause fibrosis and stenosis of the common bile duct. The prognosis for this rare condition is poor without stenting or surgery.

Cholecystitis, acute or chronic inflammation of the gallbladder, is usually associated with a gallstone impacted in the cystic duct, causing painful distention of the gallbladder. Cholecystitis accounts for 10% to 25% of all patients requiring gallbladder surgery. The acute form is most

common during middle age; the chronic form usually occurs among elderly patients. The prognosis is good with treatment.

Cholesterolosis, polyps or crystal deposits of cholesterol in the gallbladder's submucosa, may result from bile secretions containing high concentrations of cholesterol and insufficient bile salts. The polyps may be localized or speckle the entire gallbladder. Cholesterolosis, the most common pseudotumor, isn't related to widespread inflammation of the mucosa or lining of the gallbladder. The prognosis is good with surgery.

Biliary cirrhosis, ascending infection of the biliary system, sometimes follows viral destruction of liver and duct cells, but the primary cause is unknown. This condition usually leads to obstructive jaundice and involves the portal and periportal spaces of the liver. It's nine times more common among women ages 40 to 60 than among men. The prognosis is poor without liver transplantation.

Gallstone ileus results from a gallstone lodging at the terminal ileum; it's more common in the elderly. The prognosis is good with surgery.

Postcholecystectomy syndrome commonly results from residual gallstones or stricture of the common bile duct. It occurs in 1% to 5% of all patients whose gallbladders have been surgically removed and may produce right upper quadrant abdominal pain, biliary colic, fatty food intolerance, dyspepsia, and indigestion. The prognosis is good with selected radiologic procedures, endoscopic procedures, or surgery.

Acalculous cholecystitis is more common in critically ill patients, accounting for about 5% of cholecystitis cases. It may result from primary infection with such organisms as *Salmonella typhi, Escherichia coli,* or *Clostridium* or from obstruction of the cystic duct due to lymphadenopathy or a tumor. It appears that ischemia, usually related to a low cardiac output, also has a role in the pathophysiology of this disease. Signs and symptoms of acalculous cholecystitis include unexplained sepsis, right upper quadrant pain, fever, leukocytosis, and a palpable gallbladder.

Each of these disorders produces its own set of complications. Cholelithiasis may lead to any of the disorders associated with gallstone formation: cholangitis, cholecystitis, choledocholithiasis, and gallstone ileus. Cholecystitis can progress to gallbladder complications, such as

empyema, hydrops or mucocele, or gangrene. Gangrene may lead to perforation, resulting in peritonitis, fistula formation, pancreatitis, limy bile, and porcelain gallbladder. Other complications include chronic cholecystitis and cholangitis.

Choledocholithiasis may lead to cholangitis, obstructive jaundice, pancreatitis, and secondary biliary cirrhosis. Cholangitis, especially in the suppurative form, may progress to septic shock and death. Gallstone ileus may cause bowel obstruction, which can lead to intestinal perforation, peritonitis, septicemia, secondary infection, and septic shock.

In most cases, gallbladder and bile duct diseases occur in people who are older than age 40 and are more prevalent in women and Native Americans.

Complications

Each of these disorders produces a set of complications.

- Cholelithiasis may lead to any of the disorders associated with gallstone formation: cholangitis, cholecystitis, choledocholithiasis, and gallstone ileus.
- Cholecystitis can progress to gallbladder complications, such as empyema, hydrops or mucocele, and gangrene. Gangrene may lead to perforation, resulting in peritonitis, fistula formation, pancreatitis, limy bile, and porcelain gallbladder. Other complications include chronic cholecystitis and cholangitis
- Cholecholithiasis may lead to cholangitis, obstructive jaundice, pancreatitis, and secondary biliary cirrhosis.
- Cholangitis may progress to septic shock and death, especially in the suppurative form.
- Gallstone ileus may cause bowel obstruction, which can lead to intestinal perforation, peritonitis, septicemia, secondary infection and septic shock.

Signs and symptoms

Although gallbladder disease may produce no symptoms, acute cholelithiasis, acute cholecystitis, choledocholithiasis, and cholesterolosis produce the symptoms of a classic gallbladder attack. Attacks usually follow meals rich in fats or may occur at night, suddenly awakening the patient. They begin with acute abdominal pain in the right upper quadrant that may radiate to the back, between the shoulders, or to the front of the chest; the pain may be so severe that the patient seeks emergency department care. Other features may include recurring fat intolerance, biliary colic, belching, flatulence, indigestion, diaphoresis, nausea, vomiting, chills, low-grade fever, jaundice (if a stone obstructs the common bile duct), and clay-colored stools (with choledocholithiasis).

Clinical features of cholangitis include a rise in eosinophils, jaundice, abdominal pain, high fever, and chills; biliary cirrhosis may produce jaundice, related itching, weakness, fatigue, slight weight loss, and abdominal pain. Gallstone ileus produces signs and symptoms of small-bowel obstruction —nausea, vomiting, abdominal distention, and absent bowel sounds if the bowel is completely obstructed. Its most telling symptom is intermittent recurrence of colicky pain over several days.

Diagnosis

Echography and X-rays detect gallstones. Other tests may include the following:

- Abdominal computed tomography scan or ultrasound reflects stones in the gallbladder.
- Percutaneous transhepatic cholangiography, done under fluoroscopic control, distinguishes between gallbladder or bile duct disease and cancer of the pancreatic head in patients with jaundice.
- Endoscopic retrograde cholangiopancreatography visualizes the biliary tree after insertion of an endoscope down the esophagus into the duodenum, cannulation of the common bile and pancreatic ducts, and injection of contrast medium.
- HIDA scan of the gallbladder detects obstruction of the cystic duct.

- Oral cholecystography shows stones in the gallbladder and biliary duct obstruction.

An elevated icteric index and total bilirubin, urine bilirubin, and alkaline phosphatase levels support the diagnosis. The white blood cell count is slightly elevated during a cholecystitis attack. Differential diagnosis is essential because gallbladder disease can mimic other diseases (myocardial infarction, angina, pancreatitis, pancreatic head cancer, pneumonia, peptic ulcer, hiatal hernia, esophagitis, and gastritis). Serum amylase levels distinguish gallbladder disease from pancreatitis. With suspected heart disease, serial cardiac enzyme tests and electrocardiography should precede gallbladder and upper GI diagnostic tests.

Treatment

Surgery, usually elective, is the treatment of choice for gallbladder and bile duct diseases and may include open or laparoscopic cholecystectomy, cholecystectomy with operative cholangiography, and possibly exploration of the common bile duct. Electrohydraulic shock wave lithotripsy can be used to fragment gallstones if they're few in number; it may be used with ursodeoxycholic acid to improve dissolution. Other treatments include a low-fat diet to prevent attacks and vitamin K for itching, jaundice, and bleeding tendencies due to vitamin K deficiency. Treatment during an acute attack may include insertion of a nasogastric tube and an I.V. line and, possibly, antibiotic administration.

A nonsurgical treatment for choledocholithiasis involves placement of a catheter through the percutaneous transhepatic cholangiographic route. Guided by fluoroscopy, the catheter is directed toward the stone. A basket is threaded through the catheter, opened, twirled to entrap the stone, closed, and withdrawn. This procedure can be performed endoscopically.

Chenodeoxycholic acid, which dissolves radiolucent stones, provides an alternative for patients who are poor surgical risks or who refuse surgery.

Special considerations

Patient care for gallbladder and bile duct diseases focuses on supportive care and close postoperative observation.

- Before surgery, teach the patient to deep-breathe, cough, expectorate, and perform leg exercises that are necessary after surgery. Also teach splinting, repositioning, and ambulation techniques. Explain the procedures that will be performed before, during, and after surgery to help ease the patient's anxiety and to help ensure his cooperation.
- After surgery, monitor the patient's vital signs for signs of bleeding, infection, or atelectasis.
- Evaluate the incision site for bleeding. Serosanguineous drainage is common during the first 24 to 48 hours if the patient has a wound drain. If, after a choledochostomy, a T-tube drain is placed in the duct and attached to a drainage bag, make sure that the drainage tube has no kinks. Also check that the connecting tubing from the T-tube is well secured to the patient to prevent dislodgment.
- Measure and record T-tube drainage daily (200 to 300 ml is normal).
- Teach patients who will be discharged with a T-tube how to perform dressing changes and routine skin care.
- Monitor the patient's intake and output. Allow him nothing by mouth for 24 to 48 hours or until bowel sounds return and nausea and vomiting cease (postoperative nausea may indicate a full bladder).
- If the patient doesn't void within 8 hours (or if the amount voided is inadequate based on I.V. fluid intake), percuss over the symphysis pubis for bladder distention (especially in the patient receiving anticholinergics). The patient who has had a laparoscopic cholecystectomy may be discharged the same day or within 24 hours after surgery. He should have minimal pain, be able to tolerate a regular diet within 24 hours after surgery, and be able to return to normal activity within a few days to a week.
- Encourage deep-breathing and leg exercises every hour. The patient should ambulate after surgery. Provide elastic stockings to support the leg muscles and promote venous blood flow, thus preventing stasis and clot formation.

- Evaluate the location, duration, and character of any pain. Administer adequate medication to relieve pain, especially before such activities as deep breathing and ambulation, which increase pain.
- At discharge, advise the patient against heavy lifting or straining for 6 weeks. Urge him to walk daily. Tell him that food restrictions are unnecessary unless he has an intolerance to a specific food or some underlying condition (such as diabetes, atherosclerosis, or obesity) that requires such restriction.
- Instruct the patient to notify the surgeon if he has pain for more than 24 hours or notices any jaundice, anorexia, nausea or vomiting, fever, or tenderness in the abdominal area because these may indicate a biliary tract injury from cholestectomy, requiring immediate attention.

Selected references

Burt, A.D., and Portmann, B.C. *MacSween's Pathology of the Liver*, 5th ed. London: STM Books, 2006.

Claven, P., and Baillie, J. *Diseases of the Gallbladder and Bile Ducts: Diagnosis and Treatment*, 2nd ed. Boston: Blackwell Publishing, 2006.

Der, G., et al. "Primary Sclerosing Cholangitis: A Case Presentation," *Gastroenterology Nursing* 28(1):13-16, January-February 2005.

Ginsberg, G., and Ahmad, N. *The Clinician's Guide to Pancreaticobiliary Disorders*. Thoro fare, N.J.: Slack Incorporated, 2006.

Knight, J. "Liver Function Tests: Their Role in the Diagnosis of Hepatobiliary Diseases," *Journal of Infusion Nursing* 28(2):108-17, March-April 2005.

Leone, N. "The ABCs of Hepatitis," *Gastroenterology Nursing* 28(2):171, March-April 2005.