

Chapter 80: Hepatic Disorders

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FIGURE 80–1.

INTRODUCTION AND EPIDEMIOLOGY

This chapter discusses the ED presentation, evaluation, and treatment of acute and chronic liver disease as well as fulminant liver failure. Specific entities addressed in this chapter include viral and toxic hepatitis, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), and complications of cirrhosis including coagulopathy, ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, and hepatic encephalopathy. Cholecystitis and biliary colic are addressed in [chapter 79](#), "Pancreatitis and Cholecystitis." Variceal bleeding is addressed in [chapter 75](#), "Upper Gastrointestinal Bleeding."

Liver disease is associated with many ED complaints: abdominal pain, vomiting, shortness of breath, altered mental status, GI bleeding, and even nonspecific malaise can all be attributed to malfunction of the liver. Globally, hepatitis A, B, C, D, and E are major public health problems. About two billion people are infected with hepatitis B and 150 million with hepatitis C, and cancer and cirrhosis resulting from these infections account for about 3% of deaths worldwide.¹ Cirrhosis is the 12th leading cause of death in the United States, and hepatitis C is the leading cause of cirrhosis in the United States, followed by alcoholic liver disease.² Acute, or fulminant, liver failure is uncommon and is caused primarily by acetaminophen poisoning (46%), with hepatitis B being the most common infectious cause.³

PATHOPHYSIOLOGY

Acute hepatitis is caused by an infectious, toxic, or metabolic injury to hepatocytes. The initial injury leads to inflammation, cellular death, and eventual scarring in the liver. In chronic disease, liver parenchyma is replaced by fibrous tissue, which separates the functioning hepatocytes into isolated nodules. This disruption of the normal tissue structure can become severe and lead to the central characteristics of liver failure: loss of metabolic and synthetic function at the cellular level, progressive development of portal hypertension, ascites formation, and portal-systemic shunting at the gross level.

The liver's synthetic functions include the production of **coagulation and anticoagulation factors**. The liver is responsible for production of the vitamin K–dependent clotting factors II, VII, IX, and X; proteins C and S; and other elements of the clotting and thrombolytic processes.⁴ Inadequate production of these clotting factors makes uncontrolled bleeding one of the life-threatening features of liver disease and a potentially dramatic complication of hepatic failure.

Portal hypertension is increased hydrostatic pressure in the portal vein and its feeder vessels, caused by resistance to blood flow through the cirrhotic liver. It eventually causes esophageal and gastric varices and portal-systemic shunting. The increased hydrostatic pressure in the intraperitoneal veins, hypoalbuminemia, and poor renal management of sodium and water lead to ascites in the cirrhotic patient. Ascites can cause respiratory compromise and lead to spontaneous bacterial peritonitis (SBP), which occurs when normal flora translocate across an edematous bowel wall into the peritoneum. Bacteremia and infection of preexisting ascitic fluid ensue.⁵

Encephalopathy is a pivotal characteristic of chronic liver disease and is a hallmark of liver failure. Ammonia is often presumed to be the cause of confusion and lethargy in encephalopathic patients, but in fact, the pathophysiology is not completely understood. In cirrhosis, portal hypertension allows ammonia formed by colonic bacteria to enter the general circulation through portal-systemic shunting. Large intestinal protein loads, such as a high protein meal or GI bleeding, fuel this process. Although levels of ammonia do not reliably correlate with mental status, it is reasonable to think of ammonia as a contributing factor to alterations in mental status. In fulminant liver failure, cerebral edema and increased intracranial pressure can develop. In this end-stage state, loss of autoregulation of cerebral blood flow, ammonia-related edema, and a systemic inflammatory response are all thought to contribute to this deadly complication.⁶

Jaundice can be present in any stage of liver disease. Jaundice is caused by elevated levels of bilirubin in the circulation, leading to bile pigment deposits in the skin, sclerae, and mucous membranes. Hyperbilirubinemia can occur for one of three reasons: overproduction, inadequate cellular processing, or decreased excretion of bilirubin. Another way to think about this is prehepatic, hepatic, and posthepatic jaundice. Prehepatic jaundice is caused by any form of hemolysis, including inborn errors of bilirubin metabolism, which overwhelm the liver's ability to conjugate bilirubin. Viral infection and ingested toxins are typical causes of hepatic jaundice. When hepatocytes necrose, the liver's ability to conjugate bilirubin is impaired, and the level of unconjugated bilirubin rises in the blood. Unlike prehepatic and hepatic jaundice, which present with elevated unconjugated or indirect bilirubin, posthepatic jaundice produces a rise in conjugated bilirubin. Typical causes of post-hepatic jaundice are a pancreatic tumor or a gallstone in the common bile duct. Parasitic infestation and biliary atresia are rare causes in the United States but are more common in other parts of the world.

CLINICAL FEATURES

Clinical features of hepatitis are listed in [Table 80–1](#).

Table 80-1

Clinical Features of Hepatitis

	Acute Hepatitis	Chronic Disease/Cirrhosis	Acute Liver Failure
Symptoms			
Nausea/vomiting/diarrhea	+	±	+
Fever	+	–	–
Pain	+	±	±
Altered mental status	–	±	+
Bruising/bleeding	–	±	+
Physical examination			
Jaundice	+	+	+
Hepatomegaly	+	–	±
Ascites	–	+	+
Edema	–	+	–
Skin findings (bruising, vascular malformations)	–	+	+
Lab abnormalities			
Elevated ALT/AST	+	+	±
AST/ALT >2	+	±	±
Elevated PT/INR	–	±	+
Elevated ammonia	–	±	+
Low albumin	–	+	+
Direct bilirubinemia	–	+	±

	Acute Hepatitis	Chronic Disease/Cirrhosis	Acute Liver Failure
Indirect bilirubinemia	+	+	±
Urobilinogen	+	+	+
Elevated blood urea nitrogen/creatinine	–	–	±
Radiologic findings			
Ascites	–	+	+
Fatty liver	+	–	–
Cirrhosis	–	+	+

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; PT = prothrombin time; + = typically present; – = typically absent; ± = variable.

At ED presentation, a **chief complaint** of jaundice, nausea, vomiting, diarrhea, right upper quadrant or epigastric pain, pruritus, inappropriate bruising or bleeding, or altered mental status should raise the question of liver disease. In the **history of present illness**, pay attention to onset of symptoms after eating out or after ingestion of acetaminophen (in one-time overdose or chronically high doses), mushrooms, or raw oysters. Note the duration of symptoms to characterize acuity. **Past medical history** can identify comorbidities or risk factors for liver disease. Risk factors include chronic hepatitis, transfusion of blood products, positive human immunodeficiency virus status, frequent use of pain medications, or depression. Obesity, type 2 diabetes, and hyperlipidemia are risk factors specific to NASH. High-risk medications include acetaminophen and acetaminophen-containing pain medications, vitamin A, isoniazid, propylthiouracil, phenytoin, and valproate, as well as a variety of herbal remedies.⁷ Statins raise concern for hepatic toxicity but are rarely implicated in significant liver injury. Three percent of patients taking statins have mild transaminase elevations; clinically significant hepatotoxicity is rare.⁸ A **social history** positive for injection drug use, chronic alcohol abuse, sexual promiscuity, or travel to countries with endemic parasitic liver diseases represents increased risk for liver disease.

The **review of systems** in the patient with suspected liver disease can identify important signs and symptoms. Cholestasis causes white (acholic) stools and brown or tea-colored urine. Stools can be black or bloody from variceal or other GI bleeding. Patients may notice yellow skin or sclerae, indicating elevated bilirubin. Ascites can increase abdominal girth or cause shortness of breath, and portal hypertension leads to generalized weakness, encephalopathic changes in mental status, and lower extremity edema. Lightheadedness or near-syncope can result from intravascular depletion and abnormalities in renal sodium and water excretion.

A number of findings on **physical examination** are hallmarks of liver disease. Liver enlargement and tenderness with or without jaundice are characteristic of acute hepatitis. Chronic liver disease is accompanied by a number of

physical findings, including sallow or jaundiced complexion, extremity muscle atrophy, Dupuytren's contracture, palmar erythema, cutaneous spider nevi, distended abdomen with a fluid wave, enlarged veins on the surface of the abdomen (caput medusae), and asterixis. Extraordinary bruising or other signs of bleeding diathesis can be seen in liver failure.

ACUTE, CHRONIC, OR FULMINANT HEPATIC DISEASE

Liver disease can be categorized as acute, chronic, or fulminant. Accurately differentiating the acuity and severity of the disease process guides appropriate evaluation, treatment, and disposition.

Acute hepatitis typically presents with nausea, vomiting, and right upper quadrant abdominal pain. The patient with acute hepatitis can also have fever, jaundice, bilirubinuria, and an enlarged, tender liver. The most common causes are viral infection and toxic ingestion. Alcohol and acetaminophen are the most common toxic causes.

Patients with **chronic hepatitis** display evidence of long-standing hepatocellular damage. Cirrhotic patients with portal hypertension complain of abdominal pain and/or distention, abnormal bleeding (bruising, bleeding gums, epistaxis, blood in the stool), and lower body edema. They may also exhibit signs of infection, encephalopathy, ascites, and electrolyte derangement. Skin examination may reveal spider nevi, caput medusae, and other manifestations of abnormal shunting of blood to surface vessels.

Liver failure is the potential final common pathway for both acute and chronic liver disease. If there is a delay in seeking medical attention or a rapid acute course, **fulminant liver failure** can be the presenting disorder. For cirrhotic patients, the transition to liver failure is marked by the advent of coagulopathy, encephalopathy, abnormal fluid shifts, and hepatorenal syndrome.

ACUTE HEPATITIS—VIRAL

Hepatitis A virus, hepatitis B virus, and hepatitis C virus are the most prevalent forms of viral hepatitis encountered in the ED. **Hepatitis A virus** is transmitted by fecal-oral contamination. Although it is popularly associated with improper food handling or oyster consumption, the most common transmission occurs from asymptomatic children to adults. Implementation of the hepatitis A vaccine in children has dramatically decreased overall rates of infection. Hepatitis A virus infection has an incubation period of 15 to 50 days, followed by a prodrome of nausea, vomiting, and malaise. About a week into the illness, patients may note dark urine (bilirubinuria). A few days later, they develop clay-colored stools and jaundice. Hepatitis A virus does not have a chronic component, and death from hepatic failure is rare.⁹

Hepatitis B virus is transmitted sexually, by blood transfusion, by contaminated needles, and by perinatal transmission. Incubation period is 1 to 3 months, and patients can be infectious for 5 to 15 weeks after onset of symptoms if they clear the infection. Individuals who develop chronic disease will remain infectious indefinitely. Chronic infection occurs in only 6% to 10% of patients who contract hepatitis B virus as adults, whereas 90% of infants and 30% of children under the age of 5 progress to chronic status, which underlines the importance of vaccination of infants and women of childbearing age.¹⁰ In the acute phase of hepatitis B virus, presentation to the ED is similar to that for hepatitis A virus, including complaints of malaise, nausea, vomiting, fever, abdominal pain, and jaundice.

Hepatitis C virus transmission occurs primarily through exposure to contaminated blood or blood products. In contrast to hepatitis A virus and hepatitis B virus, hepatitis C virus is most often asymptomatic in the acute phase of infection, and >75% of patients advance to the chronic stage. The rate of progression to liver failure varies and depends on the natural course of the virus and cofactors such as alcoholism and human immunodeficiency virus. Along with hepatitis B virus, hepatitis C virus is one of the most common causes of hepatocellular carcinoma. Of the patients who develop chronic hepatitis C virus, 1% to 5% will die of either cirrhosis or liver cancer.¹¹

Hepatitis D virus is uncommon and is typically seen in people with preexisting chronic hepatitis B virus infection. Hepatitis D superinfection can result in a rapidly progressive or fulminant form of liver disease that carries a high short-term mortality rate. This variety of infection is most commonly associated with injection drug use.¹¹

Acute illness with liver function test abnormalities also occurs with infection by other hepatotropic viruses such as cytomegalovirus, herpes simplex virus, Coxsackie virus, and Epstein-Barr virus. These agents are unlikely to cause clinically significant hepatitis in an otherwise healthy host.

ACUTE HEPATITIS—TOXIC

A toxic insult to the liver can cause acute hepatitis and/or fulminant liver failure. The most common of these is acetaminophen overdose. **Acetaminophen** accounts for >40% of liver failure cases in the United States and one third of deaths secondary to toxic ingestion. Patients develop nausea, vomiting, and abdominal pain. They may also give a history of an acute overdose of acetaminophen or chronic use of one or more acetaminophen-containing pain medicines. Up to 28% of patients with acetaminophen overdose will develop liver failure. The likelihood of liver failure depends on time from ingestion to presentation, the dose ingested, and the baseline health status of the patient.¹² Tylenol overdose is reviewed more completely in [chapter 190](#), "Acetaminophen."

In addition to acetaminophen, there are a variety of **prescription medications** (antibiotics and statins prominent among them), **herbal remedies**, and **dietary supplements** that have been associated with acute hepatitis and liver failure. The list of prescription medications that have been implicated in liver disease is so long that it is prudent to refer to a pharmaceutical database to identify a potential culprit when toxic insult is suspected. Some of the most common herbal remedies that have been implicated in hepatic injury are listed in [Table 80-2](#).

Table 80–2

Common Herbal Remedies Known to Cause Hepatic Toxicity

Herbal Remedy	Application	Nature of Injury
Black cohosh (<i>Actea racemosa/cimiifuga racemosa</i>)	Menopausal symptoms	Hepatic necrosis and bridging fibrosis
Chaparral (<i>Larrea tridentata</i>)	Antioxidant, health tonic	Cholestasis, chronic hepatitis, cholangitis, cirrhosis
Comfrey (<i>Symphytum</i>)	Broken bones, wound healing, reduce joint inflammation	Hepatic veno-occlusive disease
Echinacea (<i>E. angustifolia</i> , <i>E. pallida</i> , <i>E. purpurea</i>)	Respiratory infections, fever, immune booster	Acute cholestatic autoimmune hepatitis
Kava (<i>Piper methysticum</i>)	Anxiolytic, sleeping aid	Acute and chronic hepatitis, cholestasis, fulminant hepatic failure
Kombucha "mushroom" tea	Weight loss, increasing T-cell count, well-being, antiaging	Acute liver failure, hepatitis, acute renal failure with hyperthermia and lactic acidosis
Ma huang (<i>Ephedra sinica</i>)	Weight loss	Acute hepatitis
Mistletoe (<i>Viscum album</i>)	Hypertension, insomnia, epilepsy, asthma, infertility, urinary disorders	Acute hepatitis
Noni juice (<i>Morinda citrifolia</i>)	Health tonic	Subacute hepatic failure, acute hepatitis
Prostata (<i>Serenoa repens</i>); saw palmetto	Benign prostatic hyperplasia	Cholestatic hepatitis
Senna (<i>Cassia angustifolia</i>)	Laxative	Acute hepatitis, acute cholestatic hepatitis, acute liver failure
Skullcap (<i>Scutellaria baicalensis</i>)	Sedative, anti-inflammatory	Hepatic veno-occlusive disease, cholestasis, hepatitis
St John's wort (<i>Hypericum perforatum</i>)	Anti-depressant	Cytochrome P-450 induction, serotonin syndrome

Herbal Remedy	Application	Nature of Injury
Valerian (<i>Valeriana officinalis</i>)	Sedative, anxiolytic	Hepatitis

Source: Adapted with permission from Abdualmjid RJ, Sergi C: Hepatotoxic botanicals: an evidence-based systematic review. *J Pharm Pharm Sci* 16: 376, 2013.

Alcoholic liver disease can range from asymptomatic, reversible fatty liver to acute alcoholic hepatitis, cirrhosis, or a combination of acute and cirrhotic features. The diagnosis of alcoholic liver disease carries a 35% 5-year survival rate. If a patient has asymptomatic liver disease (i.e., fatty liver seen on imaging), but the patient's drinking continues and acute alcoholic hepatitis develops, the mortality can be much higher.¹³ A history of consistent heavy alcohol use (mean intake at presentation of 100 grams or more) is thought to be required for development of significant alcoholic liver disease.¹⁴ However, information is often difficult to elicit from the patient or family, and the patient may have stopped drinking before ED presentation. Other nonhepatic features of alcohol abuse, such as malnutrition, stocking-glove neuropathy, and cardiomyopathy, can be clues to alcohol-induced liver disease.

Mushroom poisoning is an uncommon but important cause of acute hepatitis with a high risk of liver failure. *Amanita phalloides* ("death cap") is the most lethal of the more than 50 types of mushrooms that are toxic to humans. For detailed discussion, see [chapter 219](#), "Mushroom Poisoning."

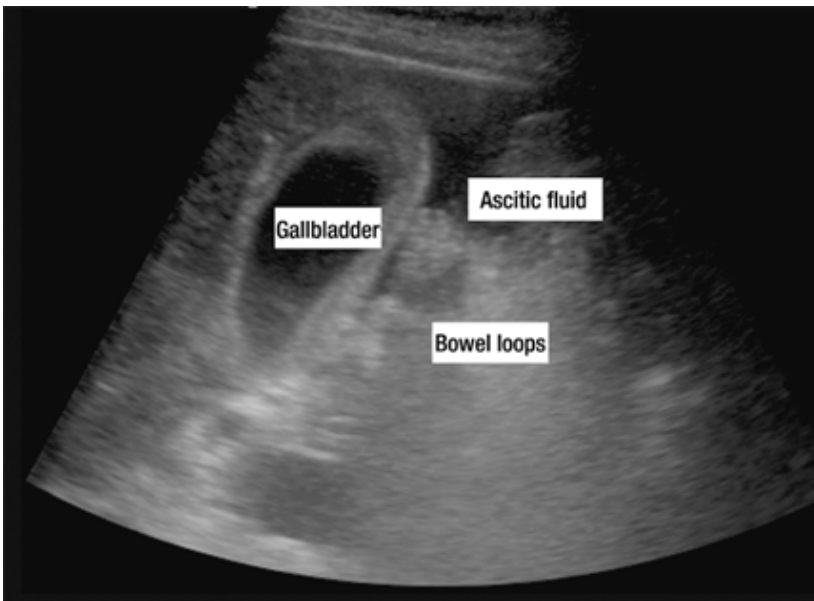
CHRONIC HEPATITIS AND CIRRHOSIS

Most patients live for years with hepatitis B virus, hepatitis C virus, NASH, or alcoholic hepatitis without symptoms. During the asymptomatic period, normal liver parenchyma is being gradually replaced by scar tissue, and hepatic disease can manifest as mild transaminase elevation or, in cases of NASH and alcoholic hepatitis, as an incidental finding of fatty liver on abdominal imaging studies. When a critical amount of liver parenchyma is replaced by fibrotic tissue, symptoms of cirrhosis develop, such as abdominal pain, ascites, SBP, general weakness resulting from electrolyte derangement, or altered mental status due to hepatic encephalopathy.

Ascites

One of the hallmarks of cirrhosis, ascites causes a protuberant abdomen, and a fluid wave is produced on physical exam. Intra-abdominal fluid can displace the diaphragm upward and produce sympathetic pleural effusion with the possibility of respiratory compromise. Smaller amounts of ascites can be difficult to identify on examination; bedside ultrasound can be particularly helpful in patients in whom the presence of ascites is uncertain ([Figure 80–1](#)).

FIGURE 80–1. Sonographic image of ascitic fluid showing bowel loops and an edematous gallbladder wall, a common finding in patients with ascites. [Courtesy of and used with permission of Michael S. Antonis, DO, sonographer.]



Source: J.E. Tintinalli, J.S. Stapczynski, O.J. Ma, D.M. Yealy, G.D. Meckler, D.M. Cline: Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 8th Edition
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Spontaneous Bacterial Peritonitis

SBP is a subtle yet crucial complication of ascites. The survival rate for patients with a first episode of SBP is 68.1% at 1 month and 30.8% at 6 months. This is probably a result of acute infection occurring in the fragile setting of advanced liver disease.¹⁵ Although common in cirrhotic patients—roughly 30% of ascitic patients will develop SBP in a given year—SBP is difficult to diagnose because signs of abdominal pain and fever are not always present, and physical examination does not always demonstrate abdominal tenderness. Consequently, patients who are diagnosed with ascites for the first time, or who have ascites and develop fever, abdominal pain, GI bleeding, or encephalopathy, should undergo paracentesis to check for SBP.

Hepatorenal Syndrome

Hepatorenal syndrome is a complication of cirrhosis that often accompanies SBP. It is defined as acute renal failure in a patient with histologically normal kidneys in the presence of preexisting chronic or acute hepatic failure. The cause is not well understood. There are two types of hepatorenal syndrome. Type 1 is more serious and is identified by progressive oliguria and doubling of serum creatinine over a 2-week period. Type 2 is represented by a gradual impairment in renal function that may or may not advance beyond moderate dysfunction. The discovery of abrupt renal failure in a cirrhotic patient that cannot be attributed to any other cause should be viewed as a marker of extreme morbidity. Median survival for type 1 hepatorenal syndrome without medical treatment is 2 weeks.¹⁶

Hepatic Encephalopathy

Hepatic encephalopathy is a poorly understood phenomenon attributed to the accumulation of nitrogenous waste products normally metabolized by the liver. Hepatic encephalopathy causes a spectrum of illness ranging from chronic fatigue or mild confusion to acute lethargy.

The development of hepatic encephalopathy suggests either that the liver is no longer able to metabolize the usual supply of nitrogenous waste or that the supply of such waste has increased. Sources of increased supply include protein loads from a large meal or from occult GI bleeding. In addition to progressive liver disease, constipation, hypo- or hyperglycemia, alcohol withdrawal, hypoperfusion states such as sepsis, and iatrogenic interventions can also compromise the liver's metabolic capacity. Hepatic encephalopathy is a common complication after **transjugular intrahepatic portosystemic shunt**, a procedure in which portal blood is shunted to the inferior vena cava, bypassing the liver. Although this procedure may succeed in reducing portal hypertension and variceal bleeding, it also slows metabolism of nitrogenous wastes by reducing hepatic blood flow. Adding or removing antibiotics from a patient's medicine regimen can also precipitate encephalopathy by changing the intestinal flora and altering the gut's ability to metabolize proteins.¹⁷

To appreciate the presence or worsening of encephalopathy, determine if there are changes in personality, worsening dementia, a decrease in levels of consciousness, or declining neuromuscular function. **Table 80–3** lists clinical stages of encephalopathy. Asterixis, which characterizes stage II, is elicited by having the patient hold the arms straight up and extending the wrists. The hands begin to flap repetitively. Another manifestation of asterixis is back-and-forth tongue movement when the tongue is extended. A patient with known encephalopathy in stage I or II who is otherwise well and has no other acute comorbidities may be managed as an outpatient after consultation with the primary care physician or gastroenterologist.

Table 80–3

Stages of Clinical Hepatic Encephalopathy

Stage	Features
I	General apathy
II	Lethargy, drowsiness, variable orientation, asterixis
III	Stupor with hyperreflexia, extensor plantar reflexes
IV	Coma

Hepatic encephalopathy is a diagnosis of exclusion. In the cirrhotic patient with altered mental status or lethargy, first exclude multiple other causes. This holds true even in the presence of an elevated serum ammonia level. Patients with end-stage liver disease are typically coagulopathic and may develop a spontaneous or traumatic subdural hematoma. Decreased hepatic gluconeogenesis and glycogen stores and poor nutritional status increase the risk of hypoglycemia and nutritional encephalopathies such as Wernicke-Korsakoff syndrome. Cirrhotic patients often are treated with diuretics and can develop hyper- or hyponatremia. Altered mental status can result from decreased hepatic clearance of drugs such as benzodiazepines and opiates, prolonging the effect and resulting in accidental overdose. Renal failure and sepsis are other considerations. Always exclude upper GI bleeding as a precipitant of hepatic encephalopathy, because the protein in the blood can translocate across the bowel of the cirrhotic patient.

Gastroesophageal varices and hemorrhage are complications of cirrhosis that are covered in [chapter 75](#), "Upper Gastrointestinal Bleeding."

HEPATIC FAILURE

Liver failure is the final common pathway for several types of liver disease. Progression to liver failure is varied and depends largely on comorbid entities, such as human immunodeficiency virus/acquired immunodeficiency syndrome, diabetes, obesity, continued injection drug use, and alcohol intake. There are roughly 2000 cases per year in the United States. Patients who develop acute liver failure have an extremely poor prognosis, with survival rates of <30%.¹⁸ Among the most common of the entities that present as acute liver failure in the United States are acetaminophen overdose (46%), indeterminate causes (14%), other drugs (11%), hepatitis B virus (7%), and autoimmune hepatitis.³

The clinical hallmarks of acute liver failure are hepatic encephalopathy, hepatorenal syndrome, and coagulopathy. The electrolyte imbalances seen in chronic liver disease can become extreme. Cerebral edema and intracranial hypertension are the most ominous complications. The catabolic nature of liver failure leads to negative nitrogen balance and immunodeficiency. Other clinical findings in acute liver failure include hypotension, hypoglycemia, and relative adrenal insufficiency. ED evaluation should include assessment for sepsis. Recognize when a patient has progressed from cirrhosis to failure or presents with acute hepatic failure, because transfer to a transplant center may be the most appropriate disposition.

GILBERT'S SYNDROME

Gilbert's syndrome is a familial liver disorder that produces occasional elevations in liver function tests and bilirubin. This syndrome does not cause cirrhosis or affect the synthetic or metabolic functions of the liver. Wilson's disease, hemochromatosis, and α_1 -antitrypsin deficiency are familial disorders that can lead to severe chronic disease and liver failure. Autoimmune hepatitis is a progressive, chronic disease that is presumably triggered by viral hepatitis or by medications. Primary biliary cirrhosis is a presumably autoimmune disorder with a chronic or chronic-degenerative course.

PRE- AND POSTHEPATIC VENOUS THROMBOSIS

Vascular diseases of the liver are rare but important, because timely diagnosis and treatment can improve outcome. **Portal vein thrombosis** affects the prehepatic portal venous system and is associated with hypercoagulable states such as polycythemia vera; with deficiencies in proteins C and S, [antithrombin 3](#), and factor V Leiden; and with abdominal trauma, sepsis, pancreatitis, cirrhosis, or hepatocellular carcinoma. The major symptom is abdominal pain; occasionally ascites can occur. Splenomegaly can occur without hepatomegaly on physical examination.¹⁹ **Hepatic vein thrombosis (posthepatic), or Budd-Chiari syndrome**, has both acute and chronic presentations, including abdominal pain, hepatomegaly, and ascites. Associated conditions include coagulopathies, polycythemia vera, paroxysmal nocturnal hemoglobinuria, and congenital webs of the vena cava.²⁰

LABORATORY EVALUATION AND IMAGING

Laboratory tests for hepatobiliary disease can be divided into four categories: (1) markers of acute hepatocyte injury or death, (2) measurements of hepatocyte synthetic function, (3) indicators of hepatocyte catabolic activity, and (4) tests to diagnose specific disease entities. Traditional liver function panels include a mix of markers of hepatocyte injury, usually including aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase, as well as indicators of hepatocyte catabolic activity (direct and indirect bilirubin). Tests that reflect hepatocyte synthetic function include prothrombin time and albumin. Ammonia reflects catabolic function of the liver. Viral hepatitis serologies are used to differentiate various types of hepatitis; acetaminophen levels can determine whether treatment for poisoning is appropriate; and various tests of ascitic fluid are used to diagnose SBP.

Bilirubin is a metabolite of heme proteins. The total level is usually reported along with the levels of conjugated (direct) and unconjugated (indirect) portions. In a functioning liver, unconjugated bilirubin is taken up by hepatocytes, conjugated, and then secreted into bile. Bilirubin is then excreted in the stool, with a small percentage being recirculated through the liver. An increased total and *indirect* bilirubin signifies either an overwhelming supply of unconjugated bilirubin to the hepatocytes (e.g., hemolytic anemia) or an injury to the hepatocytes themselves that damages their capacity to conjugate a normal supply of bilirubin (e.g., acute or chronic viral hepatitis). Total and *direct* bilirubin is increased when there is some obstruction preventing the secretion of the conjugated bilirubin that is produced by normally functioning hepatocytes (e.g., obstructing gallstone, pancreatic mass, or biliary atresia).

Transaminases (aspartate aminotransferase and alanine aminotransferase) are intracellular enzymes found in hepatocytes and some other cell types. Hepatocyte injury or necrosis releases these enzymes into the circulation. Elevations in the hundreds of units per liter suggest mild injury, or smoldering inflammation. Levels in the thousands suggest extensive acute hepatic necrosis. Less significant elevations, less than five times normal, are typical of alcoholic liver disease and NASH. Marked elevations are commonly seen with acute viral hepatitis. These enzyme levels may be near normal in end-stage liver failure, when the hepatocytes are beyond the stage of acute injury. An aspartate aminotransferase-to-alanine aminotransferase ratio of greater than 2 is common in alcoholic hepatitis because alcohol stimulates aspartate aminotransferase production.¹ Incidental findings of transaminase elevations of three to five times normal and alkaline phosphatase of up to twice normal in diabetic or obese patients suggest the presence of NASH in diabetic or obese patients.²¹ Alanine aminotransferase is a more specific marker of hepatocyte injury than aspartate aminotransferase. Aspartate aminotransferase is found not only in liver but also in heart, smooth muscle, kidney, and brain. Elevated aspartate aminotransferase can be due to medications, including acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme inhibitors, nicotinic acid, isoniazid, sulfonamides, [erythromycin](#), griseofulvin, and fluconazole.

γ-Glutamyl transpeptidase production is stimulated by alcohol consumption. It is also elevated by drugs inducing hepatic microsomal enzyme activity, such as phenobarbital and warfarin, and may rise in acute and chronic pancreatitis, acute myocardial infarction, uremia, chronic obstructive pulmonary disease, rheumatoid arthritis, and diabetes mellitus. An elevated γ-glutamyl transpeptidase in the setting of hepatitis suggests an alcoholic cause.

Alkaline phosphatase elevation is associated with biliary obstruction and cholestasis. Mild to moderate elevations accompany virtually all hepatobiliary disease, whereas elevations greater than four times normal strongly suggest

cholestasis. Alkaline phosphatase is a nonspecific marker also derived from bone, placenta, intestine, kidneys, and leukocytes. A level of up to double the expected value is normal in pregnancy.

Lactate dehydrogenase is included in most liver test panels, but it is a nonspecific marker, which limits its utility. Moderate elevations are seen in all hepatocellular disorders and cirrhosis, whereas purely cholestatic conditions cause minimal elevations. Hemolysis can produce elevation of lactate dehydrogenase and unconjugated bilirubin. The isoenzyme lactate dehydrogenase-5 is specific to the liver. Tests for lactate dehydrogenase-5 are sometimes useful although not widely available.

Ammonia is generated by hepatic metabolism of nitrogen-containing compounds. The hepatic metabolic failure seen in acute and chronic liver disease can, therefore, cause an elevated serum ammonia level. Very high ammonia levels, seen in fulminant liver failure, contribute to overall toxicity and signify poor prognosis.

Prothrombin time prolongation in liver disease reflects the decreased synthesis of the vitamin K–dependent coagulation factors II, VII, IX, and X and, as such, serves as a true measure of liver function. Prolonged prothrombin time is a common complication of advancing cirrhosis, although it also occurs in acute hepatitis and exacerbations of chronic compensated liver disease. When present in acute viral hepatitis, prolonged prothrombin time often indicates severe disease with widespread hepatocellular necrosis. There is some correlation between the extent of prothrombin time prolongation and clinical outcome in fulminant liver disease. Although prothrombin time is useful as a marker of hepatic function, abnormal values may occur in the presence of a normal liver. Vitamin K deficiency from another entity (i.e., malabsorption of fat and, therefore, of fat-soluble [vitamins](#)) can be distinguished from liver synthetic dysfunction by administration of parenteral vitamin K (phytonadione, 10 milligrams IM). A 30% reduction in prothrombin time should occur within 24 hours in vitamin deficiency states.

Albumin also reflects the liver's synthetic function. It may decrease in advancing cirrhosis or severe acute hepatitis and suggests a poor short-term prognosis. Because its half-life is approximately 3 weeks, albumin is less useful than prothrombin time in evaluating fulminant liver disease. Prothrombin time becomes prolonged in a matter of days. Serum albumin levels are also low in malnutrition, so low albumin levels do not necessarily correlate with the degree of hepatic disease in a chronically ill patient.

Viral hepatitis serologies are often grouped into screening panels by hospital laboratories. The diagnosis of specific viral hepatitis entities is complicated by phase of illness, preexisting infections, and likelihood of a given type of infection. The patient who is acutely ill with hepatitis A virus will have positive immunoglobulin M anti-hepatitis A virus antibodies. Acute clinical illness in hepatitis B virus correlates with positive hepatitis B virus surface antigen. Positive immunoglobulin M antibodies correlate to the hepatitis B virus core antigen. Diagnosis of hepatitis C virus is initiated by ordering anti-hepatitis C virus antibodies. This diagnosis is sometimes masked by the 6- to 8-week delay between infection and antibody detection as well as by the acute asymptomatic phase of the hepatitis C virus infection.²²

Ascitic fluid aspirate is tested for cell count, glucose and protein, Gram stain, and culture to identify bacterial peritonitis. The procedure for obtaining ascitic fluid, paracentesis, is explained in [chapter 86](#), "Gastrointestinal Procedures and Devices." **A total WBC count >1000/mm³ or a neutrophil count >250/mm³ diagnoses SBP.** Low glucose or high protein values suggest infection. Gram stains and culture results can be falsely negative 30% to 40% of the time, so empiric antibiotics should be started in the ED based on clinical suspicion. Culture sensitivity

increases by using 10 mL of ascitic fluid per blood culture bottle and by transferring the fluid to culture bottles at the patient's bedside. Additional studies of ascites that can help with inpatient evaluation are cytology, albumin, lactate dehydrogenase, and tumor markers.

NONHEPATIC CAUSES OF ABNORMAL LIVER TESTS

Multiple nonhepatic causes may lead to abnormal liver function tests. Abnormal liver test results occur in up to one third of those screened, and only 1% of these indicate clinically significant liver disease. Hypoalbuminemia accompanies protein-wasting enteropathies, malnutrition, and nephrotic syndrome. Alkaline phosphatase elevations occur with a variety of bone diseases, pregnancy, and malignancies. Aspartate aminotransferase elevations accompany acute myocardial infarction and rhabdomyolysis. Bilirubin elevations occur in severe hemolysis, sepsis, and syndromes involving abnormal erythropoiesis. Prothrombin time elevations occur in vitamin K deficiency, chronic antibiotic use, and warfarin therapy.^{23,24}

Urine bilirubin and urobilinogen are sometimes used as screening tests for liver disease in the ED. The sensitivity of these urine assays is 70% to 74% for identifying elevated serum bilirubin. For correlation with other liver function tests, their sensitivity is in the 43% to 53% range. Specificity for showing either bilirubin or transaminase abnormality is 77% to 87%. Blood-tinged urine will give a false-positive urobilinogen on a urine dipstick test. Taken together, these statistics do not support screening for liver disease with urine dipstick testing.²⁵

IMAGING

US and CT scanning are both useful for initial evaluation of liver disease. Bedside US can identify ascites and guide paracentesis, whereas formal US with duplex Doppler is the test of choice for identifying portal vein and hepatic vein thrombosis. Both sonogram and CT scan of the abdomen can be used to identify cancerous, vascular, or infectious lesions of the liver. CT scanning of the brain is used to identify intracranial hemorrhage in patients with liver disease and altered mental status.

TREATMENT

With the exception of acetaminophen poisoning (see [chapter 190](#)), treatment for acute hepatitis is supportive. Pay careful attention to associated conditions such as hyponatremia, alcohol or narcotic withdrawal, alcoholic ketoacidosis, and hypoglycemia. Treating chronic hepatitis in the ED means taking care of its many sequelae such as ascites, encephalopathy, coagulopathy, and variceal bleeding. Chronic hepatitis infection is typically treated by gastroenterologists in an outpatient setting. Liver failure requires critical care in the ED and consultation with a liver transplant center for disposition, including transfer if needed.

ASCITES

Mild- to moderate-volume ascites can be managed with a salt-restricted diet and diuretics, both of which create a negative sodium balance and encourage loss of ascitic fluid. Recommended diuretics include spironolactone, 50 to 200 milligrams per day, and amiloride, 5 to 10 milligrams per day. Furosemide can be problematic because it can lead to overdiuresis.⁵ To facilitate monitoring for adverse side effects, diuretics for the cirrhotic patient should be prescribed in collaboration with his or her outpatient physician.

Paracentesis is recommended therapy for large-volume ascites. There are several important considerations when performing paracentesis on a cirrhotic patient. First, the patient's prothrombin time/INR is likely to be elevated. Second, the amount of fluid that can be removed without infusion of albumin to prevent intravascular collapse is controversial. For any tap, guidelines from the American Association for the Study of Liver Diseases state that paracentesis should be considered safe from a bleeding perspective unless there is evidence of fibrinolysis (i.e., three-dimensional bruising, oozing from IV start sites) or overt disseminated intravascular coagulation. For therapeutic paracentesis, American Association for the Study of Liver Diseases guidelines recommend the use of albumin, 6 to 8 milligrams/L of fluid removed, for amounts greater than 4 L.⁵ One safe approach is to perform diagnostic paracentesis in the ED and defer large-volume therapeutic taps to the inpatient setting or the ED observation unit.

SPONTANEOUS BACTERIAL PERITONITIS

SBP is the most common life-threatening complication of ascites, classically presenting with fever and diffuse abdominal pain and tenderness. However, any or all of these features may be absent. In patients with known ascites, the 1-year incidence of SBP is 29%. Recurrence of SBP is as high as 44%, and survival in patients with a first episode of SBP is low (68.1% at 1 month and 30.8% at 6 months), probably a result of acute infection in the setting of advanced liver disease.¹⁵

Initial treatment is empiric antibiotic therapy to cover typical enteric flora. The most common isolates in SBP are *Escherichia coli*, *Klebsiella pneumoniae*, and *Streptococcal pneumoniae*. Empiric antibiotic treatment recommendations from the most recent (2012) guideline from the American Association for the Study of Liver Diseases are shown in [Table 80–4](#).⁵ Although there is no conclusive evidence proving that cefotaxime is superior to other choices, it is a widely accepted first-line parenteral treatment for SBP. Oral therapy with broad-spectrum quinolones is an option in patients with mild, uncomplicated disease and close follow-up.²⁶ Patients may have had prior infections with resistant organisms, so review microbiologic sensitivities from prior admissions, if available. The addition of IV albumin (1.5 grams/kg at diagnosis, 1 gram/kg on day 3) to antibiotic therapy may reduce renal failure and hospital mortality in patients with SBP.²⁷

Table 80–4

Diagnosis and Treatment of Spontaneous Bacterial Peritonitis

Diagnosis	Ascitic fluid, obtain 50 cc for cell count, Gram stain, and culture (transfer blood to culture bottles at the bedside for best results)
	WBC count $>1000/\text{mm}^3$
	or
	Polymorphonuclear leukocytes $>250/\text{mL}$
	or
	Bacteria on Gram stain
Empiric treatment	Cefotaxime or other third-generation cephalosporin
	or
	IV fluoroquinolone (ineffective in patients who have received prophylactic quinolone treatment)
	or
	Oral fluoroquinolone in a very mild case with close follow-up

HEPATIC ENCEPHALOPATHY

To address hepatic encephalopathy, first consider other entities that could cause altered mental status, such as infection, intracranial hemorrhage, or hyponatremia. Once hepatic encephalopathy is diagnosed, treatment is aimed at reducing the production of nitrogenous wastes by reducing protein intake and suppressing the metabolic activity of intestinal bacteria.

Lactulose is the current mainstay of therapy for hepatic encephalopathy. Lactulose is a synthetic disaccharide containing one molecule of galactose and one of fructose. It is minimally absorbed into the bloodstream. In the colon, it degrades primarily into **lactic acid**. In the acidified environment, ammonia is trapped and excreted in the stool. Blood ammonia levels can decrease up to 50% using lactulose therapy. Lactulose also inhibits glutamine-dependent ammonia production in the gut wall. Lactulose is given PO or PR. The oral dose is 20 grams diluted in a glass of water, fruit juice, or carbonated drink. For rectal administration, dilute 300 mL of syrup with 700 mL of water or normal saline. The enema should be retained for 30 minutes.

Coagulopathy needs to be treated if the patient has uncontrolled bleeding or is scheduled to undergo a procedure with potential bleeding complications. Vitamin K deficiency can be treated with vitamin K, 10 milligrams IV or PO. Fresh frozen plasma can be given in doses appropriate for the patient's prothrombin level. Finally, decreased or malfunctioning platelets should be replaced with pooled donor platelets. Specific treatments for variceal bleeding are addressed in [chapter 75](#).

METABOLIC AND RESPIRATORY FAILURE

Treatment of fulminant liver failure in the ED involves care of the patient's respiratory status, blood pressure, and encephalopathy; correction of electrolyte derangements; identification of cerebral edema or intracranial hemorrhage; attention to active bleeding; and careful disposition, ensuring that the patient will be assessed for liver transplant in a timely fashion.

Patients with respiratory failure due to ascites, effusions, or decreased alertness require intubation. Bilevel positive airway pressure is not typically an option in these cases because patients are too somnolent and at risk for aspiration. Blood pressure at this stage of liver disease is typically low due to malnutrition, bleeding, vomiting, diarrhea, and third spacing of fluid. Treat with judicious fluids, blood products, and vasopressors, as needed. Altered mental status at this stage can be from encephalopathy, metabolic abnormalities, intracranial bleeding, or brain edema with increased intracranial pressure. In the case of intracranial hemorrhage, treat coagulopathy. Consult neurosurgery or refer to a facility with neurosurgical services if the patient could benefit from hematoma evacuation or intracranial pressure monitoring. [Mannitol](#) is appropriate as a temporizing measure in cases of increased intracranial pressure caused by cerebral edema.⁶

DISPOSITION AND FOLLOW-UP

The disposition of a patient with acute or chronic hepatitis is complex and requires careful planning with the patient and caretakers. Discussion with the primary care physician and gastroenterologist can clarify a vague clinical picture. Patients with acute hepatitis require supportive treatment with pain management, antiemetic medication, and fluid resuscitation. Consider admission for high-risk patients, including the elderly and pregnant women, and patients who do not respond adequately to supportive care. Admit those who have a bilirubin ≥ 20 milligrams/dL, prothrombin time 50% above normal, hypoglycemia, low albumin, or GI bleeding, which requires further evaluation to determine the presence of varices.²⁸

In patients with chronic hepatitis, admission may be indicated for patients with ascites if they have significant respiratory compromise or abdominal pain. In addition, admit the patient with fever, acidosis, or leukocytosis and for evaluation and treatment of SBP.²⁹ New-onset or worsening hepatic encephalopathy, hepatorenal syndrome, and coagulopathy with bleeding are also strong indications for admission.³⁰ Patients with severe hyponatremia and severe hyper- or hypovolemia should also be managed in the hospital.³¹

Consider patient safety in the disposition of patients with advanced cirrhosis. Weakness, muscle wasting, and mild encephalopathy are serious risks for falls, and coagulopathy is a risk for cerebral bleed. Patients must be stable on their feet or have supervised assistance for discharge to home.

Discharge planning should include follow-up care by a gastroenterologist or transplant specialist. Patients and family members can be referred to Alcoholics Anonymous, Al-Anon, or support groups for transplant or other special needs. Discharge medications may include antibiotics, diuretics, lactulose, antiemetics, and pain medications.

SPECIAL CONSIDERATIONS

PAIN CONTROL IN PATIENTS WITH HEPATIC DISEASE

It can be difficult to decide on appropriate pain medications and sedatives for patients with compromised liver function. Avoid NSAIDs in patients with chronic hepatitis and cirrhosis due to GI toxicity and possible potentiation of renal dysfunction. Acetaminophen has traditionally been avoided in patients with any type of liver disease, but there are several trials indicating it to be safe for short-term use, at a reduced dose of 2 grams total per day. Gabapentin and pregabalin are safe options for neuropathic pain. Avoid opioids whenever possible, because opioids are metabolized by the liver and their sedative effects can be unpredictable in patients with compromised liver function. Opioids are contraindicated in patients with a history of encephalopathy or substance use. If absolutely necessary, fentanyl and tramadol at reduced doses and increased dosing intervals are possible choices in select patients because they lack the toxic metabolites of traditional opioids.³² When sedation or pain control is required for the critically ill patient with liver failure, a titratable infusion of a nonbenzodiazepine medication with a short half-life and no toxic metabolites is useful. Propofol has been well studied in the setting of endoscopy and is safe at least in the short term for patients with cirrhosis.³³ Fentanyl provides pain relief and some degree of sedation.

PREGNANCY

Pregnant women can present with various hepatic or cholestatic disorders not specific to pregnancy. HELLP syndrome (hemolysis, elevated liver enzymes, low platelets), however, stands apart as a life-threatening process that must not be missed in the ED. HELLP occurs as part of the pre-eclampsia–eclampsia spectrum in the late third trimester or in the postpartum period. It can present with symptoms resembling viral illness—headache, malaise, nausea, and vomiting. Hypertension, headache, and proteinuria are other associated findings. Eighty percent to 90% of patients present with relative hypertension, and proteinuria is present 85% to 100% of the time. Headache, usually considered a mainstay of the pre-eclampsia diagnosis, is not a sensitive or specific finding.³⁴

Perinatal mortality in cases where HELLP complicates a pregnancy before 29 weeks can be as high as 20%. Check liver function studies, CBC, and lactate dehydrogenase in those who present with even vague symptoms of illness in their third trimester and in any third-trimester patient with relative hypertension. Definitive treatment in pregnancies later than 34 weeks is immediate delivery, whereas patients who are mildly ill with HELLP at <34 weeks of gestation may sometimes be managed expectantly. ED disposition of patients with elements of HELLP syndrome is admission to the obstetrics inpatient service.³⁴ Further discussion of HELLP is provided in [chapter 100](#), "Maternal Emergencies after 20 Weeks of Pregnancy and in the Postpartum Period."

LIVER TRANSPLANT PATIENT

Liver transplant patients can develop a variety of illnesses, most commonly abdominal, infectious, and metabolic in nature. Febrile patients should be pan cultured, and broad-spectrum antibiotics should be initiated pending further inpatient evaluation. Metabolic derangements can include hyper- or hypoglycemia, sodium imbalance, and hypo- or hyperkalemia. Rejection of the transplant should be a concern even in the absence of abdominal pain and tenderness. Symptoms of rejection can be vague and can include nausea, vomiting, malaise, anorexia, abdominal pain, vomiting, and jaundice. In one series of 290 liver transplant patient visits to the ED, 69% resulted in hospitalization.³⁵ Further discussion is provided in the section on Special Situations in [chapter 297](#), "The Transplant Patient."

NONALCOHOLIC FATTY LIVER DISEASE

NAFLD deserves particular mention in the discussion of chronic liver disease. It affects up to 30% of the U.S. population by some estimates and is now thought to be the third most common reason for transplantation after hepatitis C virus infection and alcoholic liver disease. Exact figures are unclear because NAFLD often goes undiagnosed through the phases of steatosis (fatty deposits in the liver) and steatohepatitis (fatty deposits with inflammation, also identified by the acronym NASH), and is often categorized as idiopathic cirrhosis by the time of diagnosis and consideration for transplantation. NAFLD is associated with obesity, type 2 diabetes, and hyperlipidemia. Many patients will have fatty liver seen incidentally on abdominal imaging, and few of these patients will go on to develop cirrhosis.²¹ There is no specific treatment for NAFLD. The mainstays of treatment are weight loss and exercise, which have been shown to reduce fat deposition and inflammation of the liver parenchyma, but not fibrosis. The efficacy of diabetic medications and statins has not been well studied, but these are also used in the treatment of NAFLD. Patients with NAFLD found even incidentally during ED evaluation should be advised to avoid further injury by abstaining from alcohol.²¹

TRAVELERS AND GLOBAL CITIZENS

Travelers who have been outside the United States who present with abdominal pain, vomiting, diarrhea, or fever are at risk for having liver disease caused by parasitic infection. **Schistosomiasis** is a waterborne parasite that infects >200 million people worldwide and can cause portal hypertension by invading the portal venules. *Echinococcus* species cause multiple liver cysts. Ascariasis causes hepatobiliary obstruction. *Entamoeba histolytica* infects roughly 10% of the world's population and causes parasitic liver abscesses.³⁶ For further discussion, see [chapter 161](#), "Global Travelers."

VENO-OCCLUSIVE DISEASE

Veno-occlusive disease of the liver is a potentially fatal adverse effect of herbal remedies, chemotherapy, or bone marrow transplant. It is associated with abdominal pain, the presence of hepatomegaly, ascites, weight gain, and jaundice in a patient with concerning history.³⁷

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REFERENCES

1. www.who.int/immunization/topics/hepatitis/en/ (*Immunization, vaccines, and biologicals. Hepatitis.* World Health Organization.) Accessed June 23, 2014.

2. Singal AK, Anand BS: Recent trends in the epidemiology of alcoholic liver disease. *Clin Liver Dis.* 2013; 2: 53.

3. Ichai P, Samuel D: Epidemiology of liver failure. *Clin Res Hepatol Gastroenterol.* 2011; 35: 610.
[PubMed: 21550329]

4. Mammen EF: Coagulation defects in liver disease. *Med Clin North Am.* 1994; 78: 545.
[PubMed: 8170258]

5. Runyon BA: AASLD practice guideline: management of adult patients with ascites due to cirrhosis: update 2012. *Hepatology.* 2013; 57: 1651.
[PubMed: 23463403]

6. Khan SA, Shah N, Williams R, Jalan R: Acute liver failure: a review. *Clin Liver Dis.* 2006; 10: 239.
[PubMed: 16971260]

7. Abdualmjid RJ, Sergi C: Hepatotoxic botanicals: an evidence-based systematic review. *J Pharm Pharm Sci.* 2013; 16: 376.
[PubMed: 24021288]

8. Russo MW, Hoofnagle JH, Gu J, et al. Spectrum of statin hepatotoxicity: experience of the drug-induced liver injury network. *Hepatology.* 2014; 60: 679.
[PubMed: 24700436]

9. <http://aapredbook.aappublications.org.une.idm.oclc.org/site/news/vaccstatus.xhtml> (Redbook Online. American Academy of Pediatrics Committee on Infectious Diseases vaccination recommendations.) Accessed April 24, 2014.

10. <http://www.cdc.gov.une.idm.oclc.org/hepatitis/Statistics.htm> (Centers for Disease Control and Prevention: Viral hepatitis topics.) Accessed March 25, 2009.

11. Bondesson JD, Saperston AR: Hepatitis. *Emerg Med Clin North Am.* 1996; 14: 695.
[PubMed: 8921765]

12. Russo MW, Galanko JA, Shrestha R, et al. Liver transplantation for acute liver failure from drug induced liver injury in the United States. *Liver Transpl.* 2004; 10: 1018.
[PubMed: 15390328]

13. O'Shea RS, McCullough AJ: Treatment of alcoholic hepatitis. *Clin Liver Dis.* 2005; 9: 103.
[PubMed: 15763232]

14. Lucey MR, Mathurin P, et al. Medical progress: alcoholic hepatitis. *N Engl J Med*. 2009; 360: 2758.
[PubMed: 19553649]
-
15. Franca AV, De Souza JB, Silva CM, Soares EC: Long-term prognosis of cirrhosis after spontaneous bacterial peritonitis treated with ceftriaxone. *J Clin Gastroenterol*. 2001; 33: 295.
[PubMed: 11588542]
-
16. Salerno F, Gerbes A, Gines P, et al. Diagnosis, prevention and treatment of the hepatorenal syndrome in cirrhosis: a consensus workshop of the International Ascites Club. *Gut*. 2007; 56: 1310.
[PubMed: 17389705]
-
17. Als-Nielsen B, Gluud LL, Gluud C: Benzodiazepine receptor antagonists for hepatic encephalopathy (review). *Cochrane Database Syst Rev*. 2004; 2: CD002798.
[PubMed: 15106178]
-
18. Stravitz RT, Kramer AH, Davern T, et al. Intensive care of patients with acute liver failure: recommendations of the U.S. Acute Liver Failure Study Group. *Crit Care Med*. 2007; 35: 2498.
[PubMed: 17901832]
-
19. Tsochatzis EA, Senzolo M, Germani G, et al. Systematic review: portal vein thrombosis in cirrhosis. *Aliment Pharmacol Ther*. 2010; 31: 366.
[PubMed: 19863496]
-
20. Kim-Schluger L: Budd–Chiari syndrome. *Mt Sinai Expert Guides Hepatol* 294–300, 2014.
-
21. Charlton MR, Burns J, Pederson R, et al. Frequency and outcomes of liver transplantation for nonalcoholic steatohepatitis in the United States. *Gastroenterology*. 2011; 141: 1249.
[PubMed: 21726509]
-
22. <http://depts.washington.edu.une.idm.oclc.org/hepstudy/index.html> (Marazzo J, Spach D: Hepatitis Web study. March 31 , 2009.) Accessed April 26, 2009.
-
23. Kamath PS: Clinical approach to the patient with abnormal liver test results. *Mayo Clin Proc*. 1996; 71: 1089.
[PubMed: 8917295]
-
24. Aranda-Michel J, Sherman KE: Tests of the liver: use and misuse. *Gastroenterologist*. 1998; 6: 34.
[PubMed: 9531115]
-
25. Kupka T, Binder LS, Smith DA, et al. Accuracy of urine urobilinogen and bilirubin assays in predicting liver function test abnormalities. *Ann Emerg Med*. 1987; 16: 1231.
[PubMed: 3662182]
-
26. Chavez-Tapia NC, Soares-Weiser K, Brezis M, Leibovici L: Antibiotics for spontaneous bacterial peritonitis in cirrhotic patients. *Cochrane Database Syst Rev*. 2009; 1: CD002232.

[\[PubMed: 19160207\]](#)

27. Sort P, Navasa M, Arroyo V, et al. Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. *N Engl J Med*. 1999; 341: 403.

[\[PubMed: 10432325\]](#)

28. Berenguer M, Wright TL: Acute hepatitis and liver failure, in Wachter RM, Goldman L, Hollander H,(eds): *Hospital Medicine*, 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins, 2005:809.

29. Cheruvattath R, Balan V: Infections in patients with end-stage liver disease. *J Clin Gastroenterol*. 2007; 41: 403.

[\[PubMed: 17413611\]](#)

30. Han MK, Hyzy R: Advances in critical care management of hepatic failure and insufficiency. *Crit Care Med*. 2006; 34: S225.

[\[PubMed: 16917427\]](#)

31. Lin M, Liu SJ, Lim IT: Disorders of water imbalance. *Emerg Med Clin North Am*. 2005; 23: 749.

[\[PubMed: 15982544\]](#)

32. Chandok N, Watt, KDS: Pain management in the cirrhotic patient: the clinical challenge. *Mayo Clinic Proc*. 2010; 85: 451.

[\[PubMed: 20357277\]](#)

33. Sharma P, Singh S, Sharma B, et al. Propofol sedation during endoscopy in patients with cirrhosis, and utility of psychometric tests and critical flicker frequency in assessment of recovery from sedation. *Endoscopy*. 2011; 43: 400.

[\[PubMed: 21547878\]](#)

34. Sibai BM: Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. *Obstet Gynecol*. 2004; 103: 981.

[\[PubMed: 15121574\]](#)

35. Savitsky EA, Votey SR, Mebust DP, et al. A descriptive analysis of 290 liver transplant patient visits to an emergency department. *Acad Emerg Med*. 2000; 7: 898.

[\[PubMed: 10958130\]](#)

36. Hoffner RJ, Kilagblian T, Esekogwu VI, et al. Common presentations of amebic liver abscesses. *Ann Emerg Med*. 1999; 34: 351.

[\[PubMed: 10459092\]](#)

37. Chen H, Wang X, Fan T, et al. A case of veno-occlusive disease following liver transplantation. *Exp Ther Med*. 2014; 7: 141.

[\[PubMed: 24348779\]](#)

USEFUL WEB RESOURCES

1a. Centers for Disease Control and Prevention: Viral hepatitis—

<http://www.cdc.gov.une.idm.oclc.org/hepatitis/index.htm>

2a. Drug-Induced Liver Injury Network—<https://dilin.dcri.duke.edu/>

3a. Redbook Online: American Academy of Pediatrics Committee on Infectious Diseases Vaccination

Recommendations—<http://aapredbook.aappublications.org.une.idm.oclc.org/site/news/vaccstatus.xhtml>

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