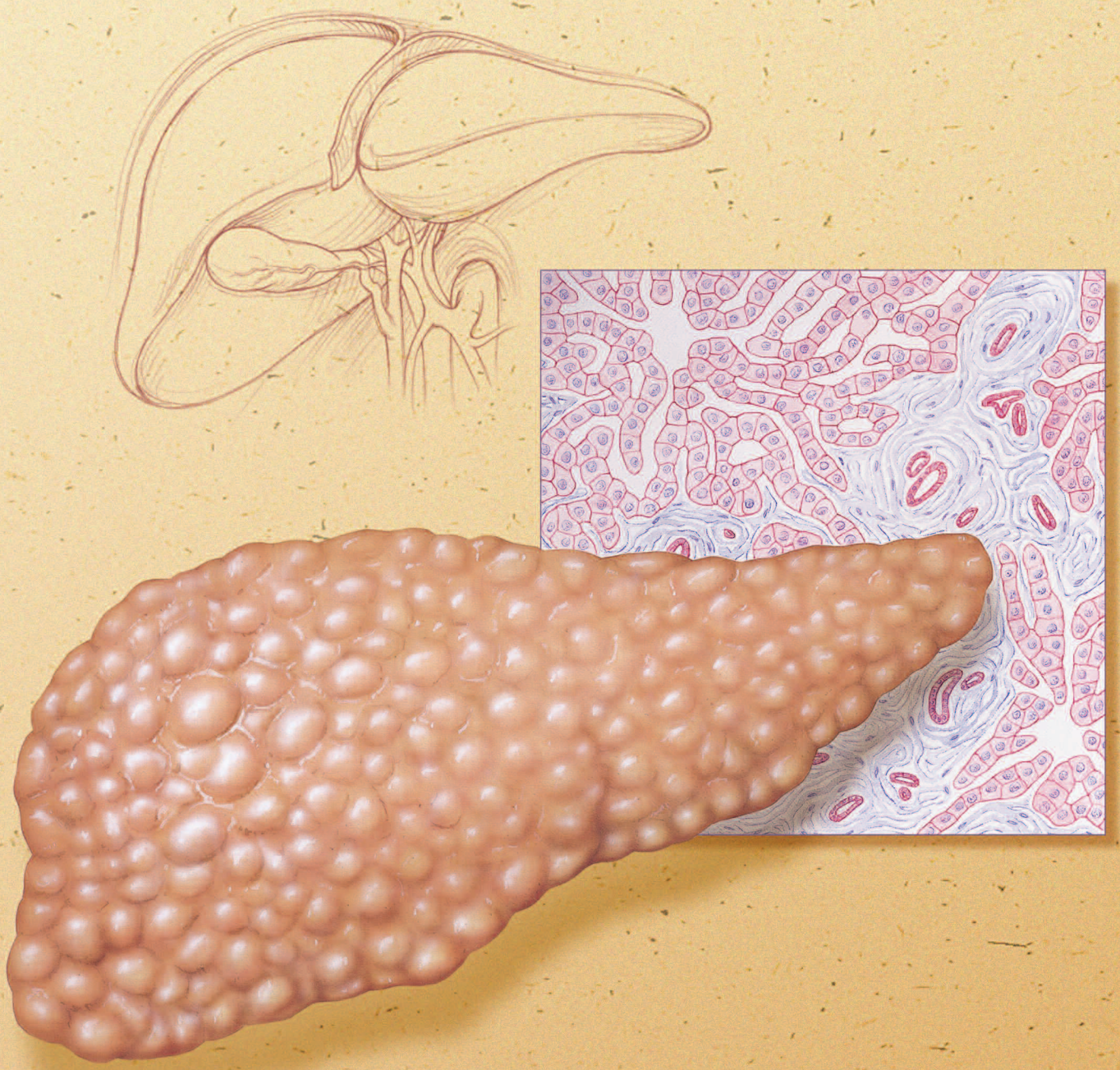
Cirrho



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CE 2.5 CONTACT HOURS Rx 0.5 PHARMACOLOGY

SIS

Caring for Patients with End-stage Liver Failure

By Lynn A. Kelso, RN, APRN,BC, MSN, FCCM

Caring for patients with end-stage liver disease can be very challenging for NPs. Cirrhosis, the final stage of liver injury, occurs when there is fibrosis and nodular regeneration within the liver tissue.[1] Every year in the United States, complications from cirrhosis lead to over 400,000 hospitalizations and 27,000 deaths (making it the 10th leading cause).[2,3] Without liver transplantation, cirrhosis is usually fatal and patients with cirrhosis who are admitted to ICUs have a greater than 50% mortality rate.[1]

There are many conditions that can lead to the development of cirrhosis, including excessive alcohol intake, viral infections, chronic heart failure, and metabolic disorders such as Wilson's disease (overabundance of copper) and hemochromatosis (overabundance of iron). Biliary disorders, such as primary biliary cirrhosis or sclerosing cholangitis, can also lead to cirrhosis. Medications such as isoniazid, herbal supplements such as germander, and toxins such as arsenic can also cause liver damage, which results in cirrhosis.

These liver disorders can be classified as either hepatocellular or cholestatic. Hepatocellular disorders cause damage to the hepatocytes (functional cells of the liver) and lead to elevations in alanine and aspartate aminotransferase levels (ALT, AST). Viral hepatitis, alcohol ingestion, and drug-induced liver dysfunction are considered hepatocellular. Cholestatic liver diseases—including biliary stones, malignancy, or primary biliary cirrhosis—are related to obstruction of the biliary tree and lead to elevations of the canalicular enzymes alkaline phosphatase and gamma glutamyl transpeptidase (GGT).[4] (see *Interpretation of Liver Function Tests*.)

Pathophysiology

Regardless of the underlying cause, cirrhosis leads to dysfunction of hepatic cells, portosystemic shunting of blood, and portal hypertension.[4] The many functions of the liver include storage, manufacturing, and cleansing of the blood. As the liver fails it can no longer function properly, which leads to the complications we see in our patients (see *Hepatic Cell Changes in Cirrhosis*).

The liver is responsible for storage of many nutrients including vitamins A, D, E, K, and B_{12}, and trace minerals such as iron and copper. As the liver becomes more diseased, the storage of nutrients can be affected.

The liver manufactures bile, albumin, and all of the clotting factors except von Willebrand's. Bile is necessary for fat digestion and absorption of fat-soluble vitamins, including vitamin K; when adequate bile is not produced, or is not excreted normally into the intestine, absorption cannot take place. Without adequate vitamin K, dependent clotting factors II, VII, IX, and X can not be produced. This can lead to an increased risk of bleeding and a prolongation of both the prothrombin time (PT) and international normalized ratio (INR). To differentiate the cause of prolonged PT, patients can be given subcutaneous or I.V. vitamin K. If the problem is with absorption of vitamin K, the PT and INR should correct within 24 to 48 hours; if the problem stems from production of clotting factors, parenteral vitamin K won't change the PT or INR. Decreased production of albumin can decrease the oncotic pressure within the vasculature. This can lead to the development of peripheral edema and ascites.[3]

The liver is also responsible for cleansing the blood of

both toxins and bacteria. The liver receives 75% of its blood supply from the portal vein, which enables it to detoxify blood from the splanchnic bed. As blood is shunted from the portal circulation into the systemic circulation, toxins and organisms are no longer removed from the blood. Also, as hepatocytes fail, the Kupffer cells that are responsible for cleansing blood no longer function properly and do not adequately detoxify the blood that flows through the liver. This can lead to the development of hepatic encephalopathy (HE) and an increased risk of infection.

When the liver becomes nodular and fibrotic, blood can no longer pass easily through the liver and backs up into the portal vein. Normal portal pressures are between 5 and 10 mmHg. When pressures increase past 10 mmHg, portal hypertension can lead to the development of varices in the esophagus, stomach, and rectum. As the pressure continues to increase, patients are at greater risk of variceal rupture and life-threatening hemorrhage.[4]

While there are many complications related to end-stage liver disease, those that will most commonly lead to ICU admission include hepatic encephalopathy (leading to an inability to protect the airway), variceal bleeding, and infection.

Hepatic Encephalopathy

The exact cause of HE is unknown but is thought to be caused by a build up of circulating toxins such as ammonia, an increase in levels of γ-aminobutyric acid (GABA) or endogenous benzodiazepines, or an increase in levels of false neurotransmitters.[5]

The most popular theory is the increase in circulating levels of ammonia, which is related to the liver's inability to detoxify the blood and shunting of portal blood to the systemic circulation.[5] It is important to understand, however, that ammonia levels do not necessarily correlate with the severity or grade of HE, and correct assessment of the patient is paramount.[5]

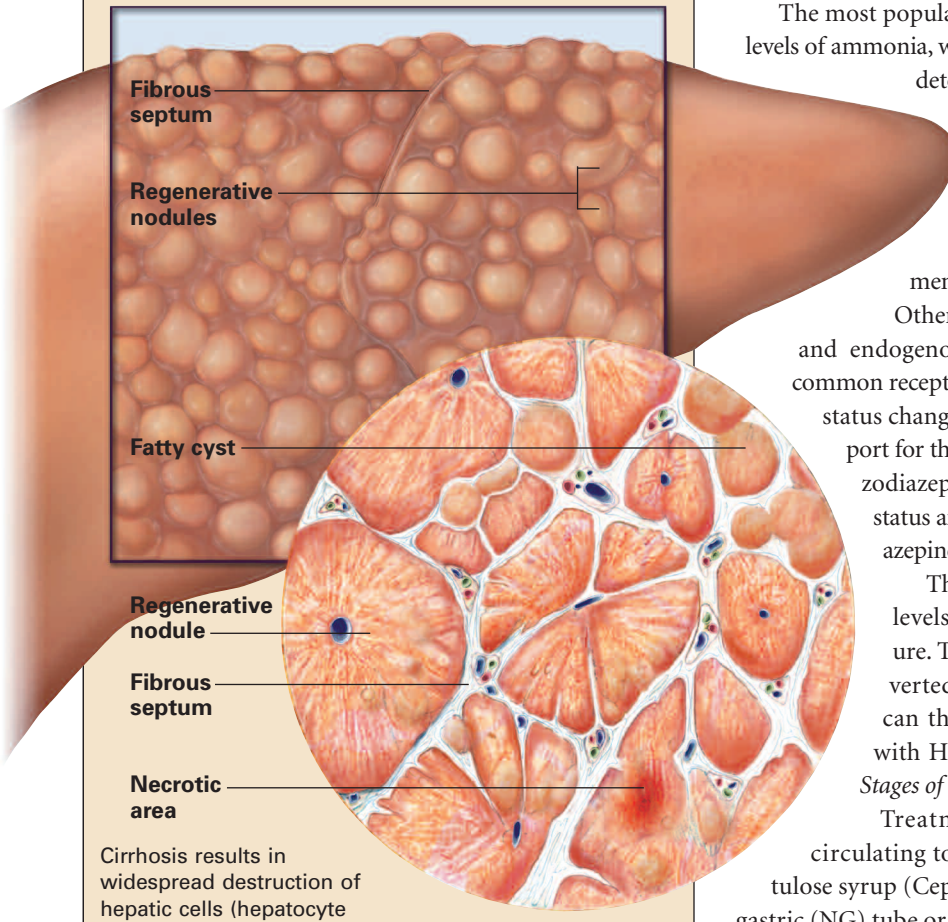
Others believe that increased levels of GABA and endogenous benzodiazepines, which share a common receptor in the brain, may lead to the mental status changes seen in patients with HE. The support for this theory is related to the fact that benzodiazepine antagonists may improve mental status and that the administration of benzodiazepines may lead to the development of HE.[5]

The final theory is related to the increased levels of aromatic amino acids in liver failure. These can enter the brain and be converted into false neurotransmitters, which can then lead to the symptoms associated with HE.[5] There are four stages of HE (see *Stages of Hepatic Encephalopathy*).

Treatment of HE focuses on decreasing circulating toxin levels, especially ammonia. Lactulose syrup (Cephulac) can be administered via nasogastric (NG) tube or enemas. Once a patient's stool begins to soften or loosen, the dose can be titrated to an average of three to four stools per day. Neomycin sulfate can also be administered via NG tube to decrease intestinal flora that can contribute to the formation of ammonia.

Related to the GABA/benzodiazepine theory of HE, flumazenil (Romazicon) may be administered I.V. (push or infusion) to assess a patient's underlying mental status and

Hepatic Cell Changes in Cirrhosis



Cirrhosis results in widespread destruction of hepatic cells (hepatocyte necrosis), which are replaced by fibrotic cells. Regeneration nodules form and the liver parenchyma undergo extensive and irreversible changes. The disease alters normal liver structure and vasculature, impairs blood and lymphatic flow, and ultimately causes hepatic insufficiency.

Source: Fenimore GS, Manno MS. Control cirrhosis complications. *Men in Nursing.* 2007;2(1):40.

Interpretation of Liver Function Tests

Laboratory test	Normal value (adults)
Bilirubin, total	0.3 to 1.0 mg/dL
Direct	0.4 mg/dL
ALT	10 to 35 units/L*
AST	20 to 48 units/L*
Alkaline phosphatase	50 to 120 units/L*
GGT	1 to 24 units/L*

Hepatocellular disorders: assess total bilirubin, ALT (more specific than AST), AST

Cholestatic disorders: assess total bilirubin, direct bilirubin, alk phos, GGT

*Normal levels higher in males

Sources: Whiteman K, McCormick C. When your patient is in liver failure. *Nursing.* 2005;35(4):58-63.
Jacobs DS, et al. *Laboratory Test Handbook.* Hudson, Ohio: Lexi-Comp.;1996.

to possibly prevent the need for intubation while waiting for other treatment strategies to begin working. Because it is so short acting, a continuous infusion of flumazenil may be necessary to maintain the effect while mental status improves. Evaluation of the literature related to the use of flumazenil in HE has shown that there may be short-term improvement in mental status, but there is no significant change in outcome.[7]

Esophageal Variceal Bleeding

Upper gastrointestinal (GI) bleeding can be life threatening and can also be the presenting symptom in up to 25% of patients with cirrhosis.[1] Bleeding is most frequently caused by esophageal varices, but can also be related to gastric varices or portal hypertensive gastropathy.

Variceal bleeding occurs in up to 50% of patients with cirrhosis.[8] Airway protection and volume resuscitation must occur quickly in these patients, and then definitive therapy to control the bleeding must be undertaken. There should be a very low threshold for intubating patients with a variceal bleed. They require sedation for an endoscopic procedure and are at high risk for aspiration.

Volume resuscitation should be performed with normal saline, blood, and blood products. Patients with an elevated INR require fresh frozen plasma and should also be given vitamin K by either subcutaneous or I.V. route. Platelets should be transfused if the platelet count is less than 50,000/mm^3.

Octreotide (Sandostatin) may be given by I.V. infusion to decrease portal blood flow by vasoconstriction of splanchnic vessels.[4] An endoscopy should also be performed so that variceal bleeding can be controlled by either banding or sclerosing of visible varices. When both endoscopic bleeding control and an octreotide infusion are used, patients have better outcomes.[8]

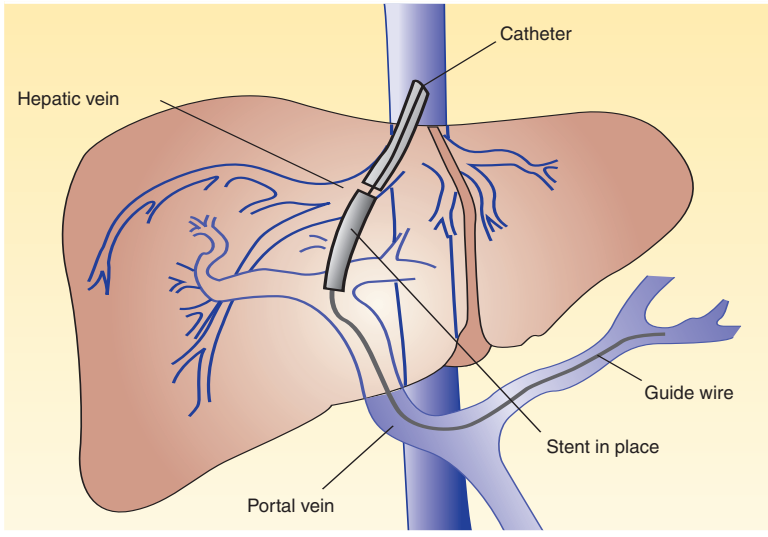
Patients who have experienced two or more variceal bleeds, or who's bleeding is not controlled by endoscopy and medication, may be candidates for a transjugular intrahepatic portosystemic shunt (TIPS) procedure. While bleeding can be controlled in up to 90% of patients undergoing a TIPS procedure, the mortality rate approaches 40%. A TIPS procedure involves placing a shunt between the portal vein and

Stages of Hepatic Encephalopathy

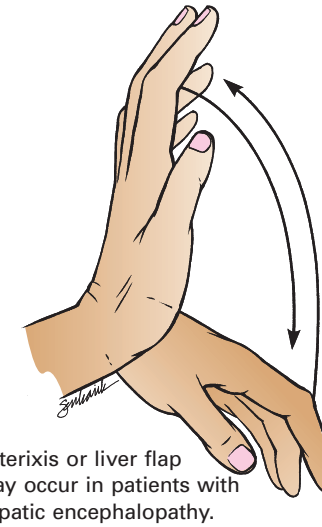
Listed below are common signs and symptoms for the patient with hepatic encephalopathy. Stage 4 patients have the highest mortality rate.[5,6]

Stage	Clinical signs and symptoms
1	Mild confusion, personality changes, and altered sleep/wake cycles, but no visible asterixis. Loss of calculating function (can be assessed by asking the patient to continually subtract the number 7 from 100 until no longer able to correctly calculate the difference. In order to use this assessment method, the patient must be able to perform simple mathematical functions).[5,6] Intubation for airway protection is usually not necessary; however, the patient should be closely monitored for any signs of deterioration that could quickly lead to respiratory compromise.[5,6]
2	Severe personality changes, disorientation, possible incontinence, and asterixis. Intubation for airway protection is usually not necessary; however, the patient should be closely monitored for any signs of deterioration that could quickly lead to respiratory compromise.[5,6]
3	Stuporous but are still arousable with incoherent speech, marked confusion, and noticeable asterixis. May require intubation and mechanical ventilation because frequently unable to protect own airway.[5,6]
4	Encephalopathic coma and may or may not respond to noxious stimuli and may posture. Require intubation for airway protection and mechanical ventilation.[5,6]

Transjugular Intrahepatic Portosystemic Shunt



Asterixis



Asterixis or liver flap may occur in patients with hepatic encephalopathy.

the hepatic vein, thereby decompressing the portal system and the varices associated with portal hypertension (see *Transjugular Intrahepatic Portosystemic Shunt*). Because blood from the GI track is shunted around the liver and back into the systemic circulation, there is an increase in circulating toxins and patients are at greater risk for developing HE. There is also a risk of stenosis or thrombosis of the TIPS, which increases the risk for rebleeding.[8]

Mechanical tamponade can be accomplished with either a Minnesota or Sengstaken-Blakemore tube, and may be necessary for patients who are unable to undergo endoscopy or TIPS procedure. Because the majority of variceal bleeds occur in the distal portion of the esophagus, control can frequently be obtained by placing traction on the inflated gastric balloon. This can control bleeding in up to 90% of patients but the risk of rebleeding approaches 50%.[8,9] There is no exact volume of air necessary for inflation of the gastric balloon, although 300 mL is average.[9] If the esophageal balloon is necessary, it should be inflated to no more than 40 mmHg and monitored using a pressure manometer.[9]

Prior to tamponading a variceal bleed, patients should be intubated and placed on mechanical ventilation in order to protect their airways. Patients should be closely monitored for any sign of airway obstruction, which can occur if the tube migrates out of position. Patients are also at risk for developing tissue breakdown or perforation of the stomach or esophagus if the balloon is left inflated for too long a period of time. On average, the esophageal balloon is left inflated for no longer than 24 hours, and may be deflated intermittently to decrease the pressure placed on the esophagus. The gastric balloon is left inflated for an average of 24 to 48 hours.[9]

Once the bleeding has been controlled and the patient is hemodynamically stable, treatment should be focused on decreasing the portal vein pressure. If a TIPS procedure cannot be performed, patients can be placed on a beta-adrenergic blocker. Propranolol or nadolol can be used to decrease portal hypertension.[8]

Fighting Infection

Patients with end-stage liver disease are at greater risk of developing infection for multiple reasons. First, as the liver fails, the Kupffer cells fail to detoxify blood from the splanchnic bed. This means that bacteria from the intestinal tract can enter the systemic circulation.[4] Patients are also frequently malnourished, which can affect their ability to fight off infection. Patients should be closely monitored for signs of infection, and there should be a very low threshold for starting antibiotics, as infections can easily lead to sepsis.

Spontaneous bacterial peritonitis (SBP) develops in up to 30% of patients with ascites.[10] When a patient with cirrhosis develops fever or abdominal tenderness, SBP should be suspected. Portal hypertension and low oncotic pressure, secondary to the decreased production of albumin, lead to the collection of ascites. Translocation of bacteria from the intestinal tract into the peritoneum can cause infection. The most common organisms seen in SBP include *Escherichia coli, Klebsiella pneumoniae, Streptococcus pneumoniae,* and enterococcus species.[11]

A paracentesis should be performed whenever SBP is suspected. Either a diagnostic tap or a large volume para-

centesis can be performed depending upon the amount of ascites present. An abdominal ultrasound can be helpful in locating the fluid.

Ascitic fluid should be sent for cell count with differential to assess the white blood cell (WBC) count and the percentage of polymorphonuclear neutrophils (PMNs). When WBCs number greater than 500 cells/mm^3, or PMNs greater than 250 cells/mm^3 or 75% of WBCs, bacterial infection should be suspected.[10] Ascitic fluid should also be sent for Gram stain (although it is frequently insensitive) and culture, which can yield better results if sent in blood-culture bottles. If SBP is suspected, antibiotic therapy should be started immediately after obtaining cultures.

If a large volume paracentesis is completed (more than 4 liters removed) the patient should receive albumin to replace protein. Ten grams of albumin for every liter of ascites drained should be I.V. administered.[10]

Further Difficulties

Although these three complications—HE, variceal bleeding, and infection—can lead to ICU admission, other complications of end-stage liver disease can make treating patients more difficult. Kidney failure can result from actual damage to the kidneys or can develop secondarily to liver failure. Patients with hepatorenal syndrome will frequently have oliguria unresponsive to fluid or diuretics, hyponatremia, and low urine sodium. It is important to remember that urine sodium must be sent for testing prior to giving diuretics, as they may artificially increase sodium excreted into the urine. Transplant candidates may require dialysis to support renal function. Patients who are not candidates for liver transplantation may not be candidates for dialysis.

Respiratory failure can result from altered mental status or an inability to breathe effectively. Patients with a large amount of ascites may not be able to properly expand their lungs. Pleural effusions are also common with ascites, especially right-sided effusions, which can also affect a patient's ability to breathe. Draining fluid from the pleural space or peritoneal cavity can improve ventilatory function. A small fraction of patients can develop hepatopulmonary syndrome. This occurs in chronic liver disease when the alveolar-arterial gradient increases or an intrapulmonary shunt develops. Supplemental oxygen may help, but patients may require embolization of dilated pulmonary vessels or administration of methylene blue I.V. which can counteract the effects of nitric oxide.[3]

Preventing skin breakdown can be very challenging for nurses. Patients are frequently malnourished and have fragile skin that can easily tear. Bruising is common in patients who have coagulopathy. Peripheral edema can also make it difficult to maintain skin integrity.

Monitoring Patients

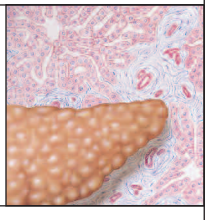
It is important to closely monitor patients with end-stage liver disease. Daily laboratory values, including complete blood count and comprehensive metabolic profile, should be calculated. Care should be taken to correct any electrolyte abnormalities. If a patient has anemia or thrombocytopenia, blood or blood products may be needed. Coagulation studies should be done frequently, especially PT and INR. Patients who have a prolonged PT/INR, and are either actively bleeding or at high risk for bleeding, may require either continuous or timed fresh frozen plasma transfusions.

While surveillance cultures are not necessary in chronic liver failure, cultures should be obtained whenever a patient is febrile or there is an unexplained increase or decrease in the WBC count. If a patient is hemodynamically unstable, antibiotics may be started even without culture confirmation of infection. Once the culture results are known, the provider should make sure the antibiotic regimen covers the pathogens.

A daily chest X-ray can help to monitor for pleural effusions. An abdominal ultrasound may be performed to assess for ascites. If a patient has undergone a TIPS procedure, ultrasound can also determine if the shunt is patent.

A computed tomography scan of the head may be necessary for patients with stage 4 encephalopathy, especially if they begin to posture. Although cerebral edema is not common in patients with chronic liver failure, it is important to rule out an intracerebral bleed.

If a patient is not a candidate for transplantation, end-of-life issues must be addressed with the patient and family.



Psychosocial Care

End-stage liver disease is irreversible without a liver transplant. If a patient is not a candidate for transplantation, end-of-life issues must be addressed with the patient and family, especially if a life-threatening complication or a sudden decompensation of liver function develops. Patients who have had liver disease for a long period of time may have already discussed this with their families. End-of-life discussions can be very difficult, particularly depending upon the underlying cause of the liver disease. There may be unresolved anger or fear in the family of a patient who developed cirrhosis be-

cause of alcohol ingestion, drug use, or viral hepatitis, for example.

Families must also understand that their loved ones may not be candidates for all treatment measures. For example, patients who are not transplant candidates may not be started on dialysis if they develop kidney failure. This can be difficult for families to accept.

Even patients who are candidates for transplantation may not survive to transplant. This can be especially difficult for a family who had the hope of a cure for their loved one.

Patients who survive their ICU stays must learn how to prevent or recognize complications, including the signs and symptoms of infection. To prevent hepatic encephalopathy, they should understand the precipitating causes, such as a high-protein meal. Patients and families should learn to recognize early signs of deterioration in function (such as mood changes, mild confusion, changes in sleeping habits, musty sweet odor of breath, and drowsiness) and know when to seek medical attention.

Take the Challenge

Management of patients with end-stage liver disease can be challenging. Patients can deteriorate very rapidly and require close, vigilant monitoring. The goal is to help patients return to their previous states of health so that they can either return home or survive until transplantation. If transplantation is not an option, the goal may change to helping both patients and their families transition to end-of-life care. NP

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