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# Variceal Hemorrhage
## from Esophageal Varices Associated with Alcoholic Liver Disease

Learn how to recognize and treat this life-threatening complication.

**Overview:** Esophageal varices occur in about half of all people with alcoholic cirrhosis. About one-third of these will experience variceal hemorrhage, a life-threatening event. This article describes alcoholic cirrhosis and its complications, discusses the etiology of esophageal varices and the risk factors for hemorrhage, and addresses emergent treatment. Further treatment options, including endoscopic variceal ligation, endoscopic injection sclerotherapy, balloon tamponade, and transjugular intrahepatic portosystemic shunt placement, are also discussed.

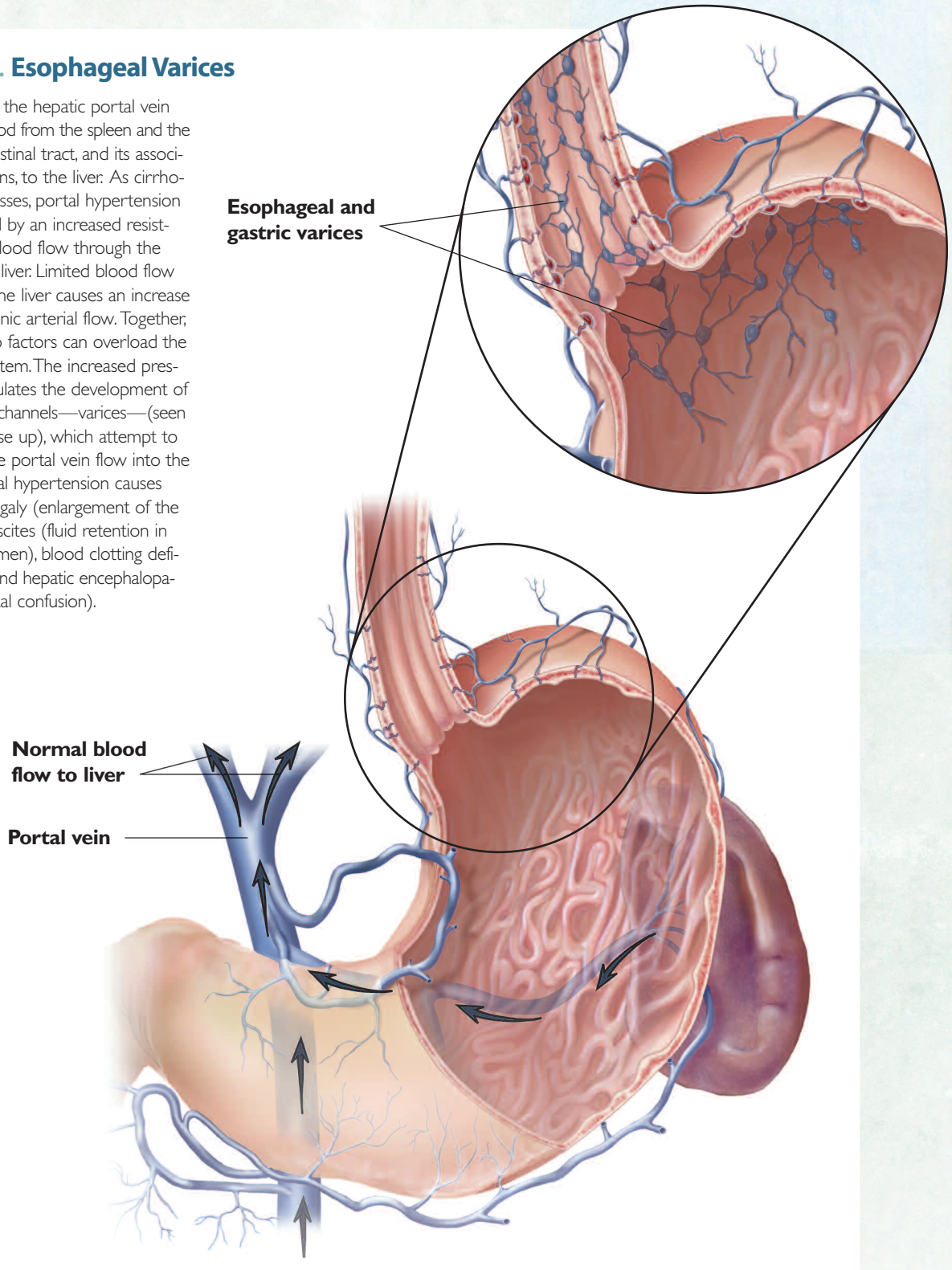
Marie Barth, a 63-year-old woman, was admitted to the ICU from the ED with hepatic encephalopathy caused by alcoholic cirrhosis. (This case is a composite based on my experience.) She was confused and disoriented, and a review of her medical records indicated long-term alcohol abuse. Her vital signs on admission were as follows: heart rate, 80 beats per minute; respiration, 24 breaths per minute; blood pressure, 116/64 mmHg. Physical assessment revealed cachexia, jaundice, jugular vein distension, and a distended, tender abdomen with shifting dullness. Laboratory results indicated an elevated serum ammonia level of 230 micrograms per deciliter. Paracentesis of the abdomen revealed cloudy ascitic fluid suggestive of spontaneous bacterial peritonitis, and a specimen was sent for laboratory testing. A lactulose (Chronulac and others) enema was ordered to quickly lower her serum ammonia level.

Two days after admission the patient was alert and oriented, and her ammonia level was within the normal range. But while being prepared for transfer to the medical–surgical unit, Ms. Barth vomited a large amount of bright red blood and blood clots. Because of this patient's history of alcohol abuse, the team suspected bleeding esophageal varices as the likely cause of her hematemesis (see Figure 1).

The nurse immediately turned the patient onto her side and raised the head of the bed to a high Fowler position to protect her airway. Vital signs were as follows: heart rate, 124 beats per minute; respiration, 28 breaths per minute; blood pressure, 90/52 mmHg. The cardiac monitor revealed sinus tachycardia. Pulse oximetry revealed an oxygen saturation level of 86% on room air. The physician ordered an immediate transfusion of two units of packed red blood cells. A nurse initiated oxygen through a nonrebreather mask to help correct the hypoxemia. Once the patient was stable and the oxygen saturation level reached 94%, low-flow oxygen was administered via nasal cannula, with an order to adjust the flow as necessary to maintain oxygen saturation at 94%. A Yankauer suction catheter was readily available in case intervention was needed to prevent aspiration. In an effort to control the bleeding, an initial bolus of octreotide (Sandostatin) 50 micrograms IV was administered, followed by a continuous infusion of 50 micrograms per hour.

## Figure 1. Esophageal Varices

Normally, the hepatic portal vein brings blood from the spleen and the gastrointestinal tract, and its associated organs, to the liver. As cirrhosis progresses, portal hypertension is induced by an increased resistance to blood flow through the damaged liver. Limited blood flow through the liver causes an increase in splanchnic arterial flow. Together, these two factors can overload the portal system. The increased pressure stimulates the development of collateral channels—varices—(seen in the close up), which attempt to bypass the portal vein flow into the liver. Portal hypertension causes splenomegaly (enlargement of the spleen), ascites (fluid retention in the abdomen), blood clotting deficiencies, and hepatic encephalopathy (mental confusion).



## Gender, Level of Alcohol Intake, and Relative Risk of Liver Disease

A large prospective study in Denmark investigated the relationship between self-reported alcohol intake and the risk of developing liver disease, surveying more than 13,000 adults and following them for 12 years.[1] The researchers found that, at an intake of 28 to 41 alcoholic beverages weekly, the relative risk of developing cirrhosis was 7% for men and 17% for women, and that, at any level of intake, women had a significantly higher risk of developing cirrhosis than men. The reasons for this aren't fully understood. Ely and colleagues point out that women generally have a lower volume of body water than men, resulting in a higher blood alcohol level per amount consumed; gender differences in how alcohol is metabolized are also thought to play a role.[2] Others have hypothesized that estrogens increase gut permeability and portal endotoxin levels, leading to greater injury to the liver.[3]

The consulting gastroenterologist recommended endoscopic treatment as soon as hemostasis was achieved. Orders were also given for immediate and then daily liver function tests, as well as for a complete blood count and prothrombin time test. Initial laboratory results revealed a hemoglobin level of 7.3 g/dL and a hematocrit value of 23%. The physician ordered a transfusion of three more units of packed red blood cells. Prothrombin time was elevated at 25 seconds.

### ALCOHOLIC CIRRHOSIS: AN OVERVIEW

The pathogenesis of alcoholic liver disease isn't fully understood. But it's known that in the liver ethanol oxidizes into acetaldehyde, which appears to be the principal agent for various toxic effects. As acetaldehyde and its metabolite acetate accumulate, numerous metabolic processes are disrupted; one result is the development of fatty liver—a condition in which lipid vacuoles form inside the liver cells, resulting in cell degeneration and death. If the patient abstains from alcohol, fatty liver damage is often, though not always, reversible. But if alcohol consumption continues, liver damage can progress to alcoholic hepatitis or cirrhosis or both. Alcoholic hepatitis is characterized by fibrosis and inflammation; necrosis (often focal) may also occur. Alcoholic cirrhosis is characterized by extensive fibrosis associated with the formation of nodules that disrupt liver structure (see Figure 2). (For more on alcoholic liver disease, see *Gender, Level of Alcohol Intake, and Relative Risk of Liver Disease*.[1-3])

Cirrhosis leads to several severe complications. The extensive fibrosis compromises blood flow within the liver, inhibiting perfusion and resulting in *portal hypertension*. Blood backs up into the veins of the stomach and esophagus, resulting in *gastrointestinal and esophageal varices*. Other complications contribute to the likelihood of variceal bleeding. Portal hypertension contributes to *ascites*, the accumulation of fluid in the peritoneal cavity. In some patients with cirrhosis and ascites, the renin-angiotensin-aldosterone system is activated, resulting in sodium and total body water retention.[4] Patients with cirrhosis and ascites are at higher risk for bacterial infections, including *spontaneous bacterial peritonitis* (bacterial peritonitis in the absence of an abscess or other intraabdominal source of infection).[5,6] The cirrhotic liver's inability to process toxins causes them to build up in the bloodstream, leading to *hepatic encephalopathy*; the buildup of toxins can also increase portal pressure, making variceal hemorrhage more likely.[7] In some patients liver failure leads to renal failure (*hepatorenal syndrome*). There's evidence that this is "a relatively frequent event" in patients with cirrhosis and upper-gastrointestinal hemorrhage.[8]

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**Signs and symptoms of alcoholic liver disease.** Presentation will depend on disease severity. In a patient still able to compensate, signs and symptoms can be vague and might include intermittent mild fever, unexplained epistaxis (nosebleed), morning indigestion, spider angiomas, palmar erythema, ankle edema, abdominal pain, hepatomegaly, and splenomegaly.[6] As the disease progresses, the patient can no longer compensate. Signs and symptoms result from both impaired liver function and portal hypertension. Those associated with impaired liver function include jaundice, muscle wasting, weight loss, weakness, spontaneous bruising, epistaxis, and purpura (the last three are indications of coagulopathy). Those

associated with portal hypertension include variceal hemorrhage, ascites, hepatic atrophy, hepatic encephalopathy, and hypotension. Continuous mild fever, white nails, clubbing of fingers, sparse body hair, and gonadal atrophy may also be present.[6, 9]

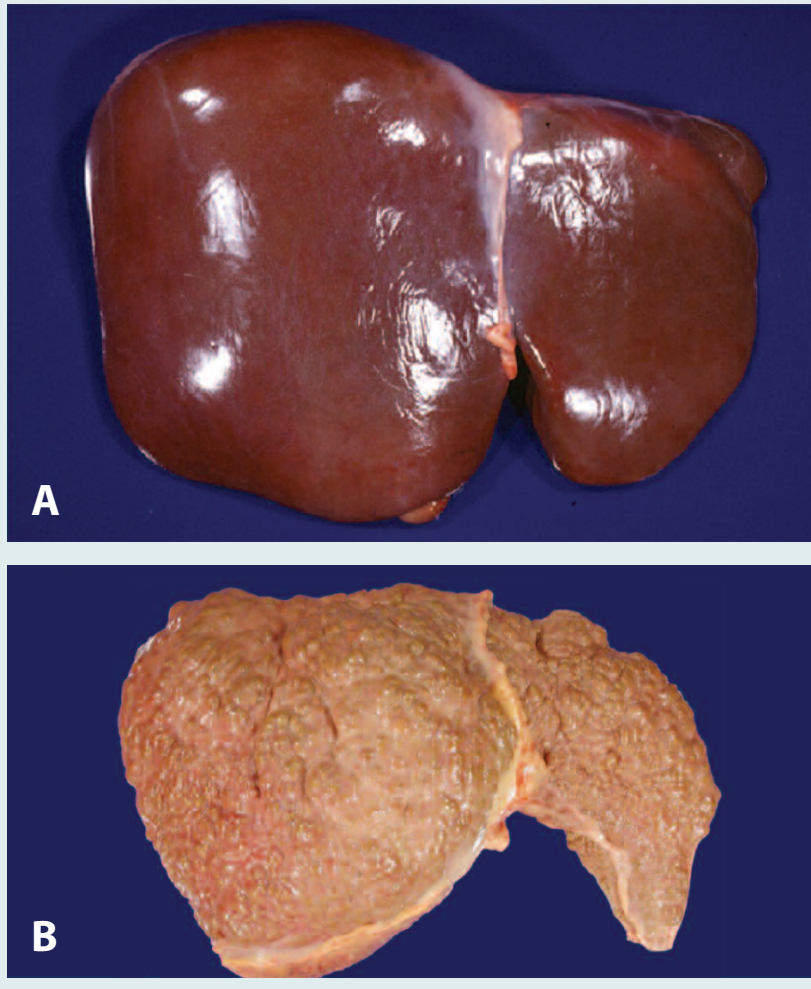
## ESOPHAGEAL VARICES: PREVALENCE AND RISK FACTORS

Esophageal varices occur in about half of people with cirrhosis; indeed, one comprehensive review states that "if followed long enough, most cirrhotics eventually develop" the condition.[10] Hemorrhage occurs in about one-third of people with varices and is life threatening. Each bleeding event carries a 20% to 30% risk of death; up to 70% of patients who aren't treated die within one year of the initial event.[10]

Factors associated with an increased risk of initial variceal hemorrhage include larger variceal size (diameter greater than 5 mm); the presence of red spots or wales on the varices; more severe portal hypertension, with risk increasing at hepatic venous pressures above 12 mmHg; and more severe cirrhosis, with or without ascites.[10, 11] (Cirrhosis is sometimes evaluated according to the Child-Pugh scoring system, which incorporates factors such as serum albumin and bilirubin levels, prothrombin time, and the presence or absence of ascites and encephalopathy. Patients with Child-Pugh Class C cirrhosis—the

**Figure 2. Liver Changes with Cirrhosis**

A. Normal liver. B. Cirrhosis. Note the small size of the cirrhotic liver.



poorest prognosis—are at higher risk for variceal bleeding than are those with less severe disease.[12])

Factors associated with increased risk of rebleeding include those above plus more severe initial hemorrhage, being older than 60 years of age, the presence of bacterial infection, and renal failure.[10] (See *Factors Associated with Increased Risk of Variceal Hemorrhage*.[10-12])

## EMERGENT TREATMENT

Immediate treatment of variceal hemorrhage includes protecting the airways to prevent aspiration, providing hemodynamic support, treating coagulopathy, and reducing portal pressure.[13, 14]

**Protect the airway.** To prevent aspiration, patients should be turned to one side and the head of the bed raised to a high Fowler position. Patients with massive hemorrhage should be intubated.[15] A Yankauer suction catheter should be readily available in the event that intervention is needed to prevent aspiration.

**Provide hemodynamic support.** Both normal saline and blood components are typically given. Current guidelines for treating acute variceal hemorrhage state that one goal of blood transfusions is to maintain the hemoglobin level at about 8 g/dL.[11] (Alternatively, the goal can be to maintain hematocrit at 24% to 30%.[16, 17]) It's important to remember that, in patients with portal hypertension, excessive transfusion can increase portal pressure and lead to further bleeding.

Patients who receive "significant" transfusions are at risk for hypocalcemia and hyperkalemia.[15] And normal saline infusion increases the risk of hypernatremia. Thus serum potassium, calcium, and sodium levels must be closely monitored.

**Treat coagulopathy.** A cirrhotic liver is incapable of synthesizing vitamin K, which is necessary for coagulation; thus if coagulopathy is present, parenteral vitamin K and fresh frozen plasma may be ordered.[13] The goals of treatment are not only to control the initial bleed but also to prevent rebleeding, which occurs within hours to days or weeks in about 50% of patients.[18, 19] However, one review cautioned that the safety and efficacy of vitamin K administration in this population hasn't been demonstrated.[20]

**Reduce portal pressure.** Octreotide is the drug of choice in the management of acute variceal bleeding. An analogue of the peptide somatostatin, it works by inhibiting the release of vasodilatory hormones such as glucagon, which indirectly causes vasoconstriction of the viscera and decreased portal vein flow. Although regimens vary, one review found that an initial bolus of 50 micrograms IV achieved "the maximum hemodynamic effect," followed by a continuous infusion of 25 to 50 micrograms hourly for up to five days to control bleeding.[21] Possible adverse effects of this regimen include dizziness, orthostatic hypotension, palpitations, nausea, and hypoglycemia.

Vasopressin (Pitressin) is also effective, but it's used less often because it's "extremely potent" and can have serious adverse effects.[14, 21] Typically an initial dose of 0.2 units per minute IV is given, with the dosage increasing by 0.2 to 0.4 units every hour (to a maximum of 0.9 units per minute) until the bleeding is controlled; the dosage is then lowered by 0.1 to 0.2 units per minute every 12 hours. Vasopressin constricts mesenteric arterioles and decreases portal flow, thereby lowering portal pressure. One large review concluded that hemostasis was achieved in 70% to 85% of cases; however, early rebleeding occurred in 30% to 50%.[10] Some experts think vasopressin may actually increase mortality because of its vasoconstrictive effects on other organs such as the heart and intestines.[15] But studies have shown that concomitant administration of nitroglycerin (Nitro-Bid and others) reduces this effect.[10] Shah and Kamath recommend administering nitroglycerin through a patch, with doses adjusted to blood pressure readings.[14] Unfortunately, neither octreotide nor vasopressin increases survival rate.[15]

*Treatment of variceal hemorrhage includes protecting the airways, providing hemodynamic support, treating coagulopathy, and reducing portal pressure.*

Once hemostasis has been achieved, definitive treatment by endoscopy can be performed.

## ENDOSCOPIC TREATMENT

Therapeutic endoscopy is considered the definitive treatment for active variceal hemorrhage. **Endoscopic variceal ligation (EVL)** is the preferred therapy, with **endoscopic injection sclerotherapy (EIS)** an alternative if ligation proves technically difficult.[16] The technique is performed using an endoscope with a banding device mounted at its tip. The varix is drawn into the suction chamber of the endoscope

and an elastic band is applied at or just distal to the bleeding point. This causes vessel thrombosis, necrosis, and fibrosis, destroying the varix. It's recommended that a multiband ligator be used to minimize the need for reintubation.[22] Repeat procedures are required every one to two weeks, until all varices have been eliminated.[11] Complications include bleeding ulcers and esophageal perforation; systemic complications are rare.[10, 11] (To see a video of this procedure, go to http://bit.ly/31jSB5.)

In EIS, a catheter with a retractable needle is passed through the endoscope. The needle is inserted directly into the varix and a sclerosant such as sodium morrhuate or sodium tetradecyl is injected. The sclerosant and edema serve to stop the acute hemorrhage. The procedure is typically repeated one week later and then at three-week intervals, until the resulting thrombosis and fibrosis destroy the varix.[10] Complications include bleeding ulcers, esophageal perforation, stricture formation, and pleural effusions; systemic complications such as aspiration pneumonia and spontaneous bacterial peritonitis have also been reported.[10, 15]

One large review concluded that, compared with EIS, EVL resulted in faster variceal elimination, fewer complications, and fewer rebleeding episodes.[10] But EVL also had a higher rate of variceal recurrence. It's unclear whether the concomitant administration of octreotide with EVL or EIS improves patient outcomes.[10]

Both EVL and EIS are performed using moderate (conscious) sedation. During either procedure, two nurses should be present: one to monitor the patient's vital signs (including oxygen saturation level) and protect the patient's airway, another to assist the gastroenterologist. Because sclerosants are quite caustic, during an EIS procedure it's also important to protect the patient's and clinicians' eyes.

## BALLOON TAMPONADE

When endoscopy isn't available to treat variceal hemorrhage, balloon tamponade can be used. It can also be used as an adjunct to pharmacotherapy and EVL or EIS, especially when bleeding is difficult to control.[23, 24] The device used most often is the Sengstaken–Blakemore tube (SBT), which has both esophageal and gastric balloons; when inflated, these compress the varices and decrease esophageal blood flow. To reduce the patient's risk for aspiration, the stomach might be lavaged with sterile saline to remove blood before insertion[25]; however, there's an increased risk of additional bleeding due to trauma from the nasogastric tube. Although balloon tamponade controls acute hemorrhage in more than 80% of cases, rebleeding upon deflation is common.[12] Complications include esophageal ulceration and perforation, aspiration pneumonia, and airway obstruction caused by SBT migration into the larynx; mortality rates of up to 20% have been reported.

Before SBT insertion, the nurse should inspect and inflate all balloons to check for leaks, then deflate them and label each port. Because insertion can induce projectile vomiting and further deterioration of the patient's condition, clinicians should be prepared to clear the patient's airway and to resuscitate if necessary. Following insertion, the esophageal balloon is inflated to the specified pressure and tube placement is radiographically confirmed. To maintain correct position, the tube is then securely taped to the side of the face. If the applied force, known as skin traction, isn't adequate to stop the bleeding, a weighted traction apparatus can be applied; however, this may increase the risk of tube migration.[26]

Because of the risk of airway obstruction from tube migration, the tube's position should be clearly marked so that any displacement can be quickly recognized[27]; scissors should be readily available to cut the tube if the airway becomes compromised. Because of the risk to the esophageal mucosa of pressure necrosis, the physician might order balloon deflation for 30 to 60 minutes every eight hours.[25] Upon deflation, rebleeding occurs in as many as 50% of cases, and clinicians must be prepared with contingency measures.[28]

## SALVAGE THERAPY: TIPS PLACEMENT

Salvage therapy refers to final available treatment for a given condition, when prognosis is poor and the patient hasn't responded to or can't tolerate other treatments. The goal is to effect cure or improve the patient's quality of life.

### Factors Associated with Increased Risk of Variceal Hemorrhage[10-12]

#### *Initial hemorrhage*

Risk increases with the following:

- larger variceal size (diameter > 5 mm)
- presence of red spots or wales on the varices
- more severe portal hypertension (hepatic venous pressure > 12 mmHg)
- more severe cirrhosis, with or without ascites (Child-Pugh Class C cirrhosis)

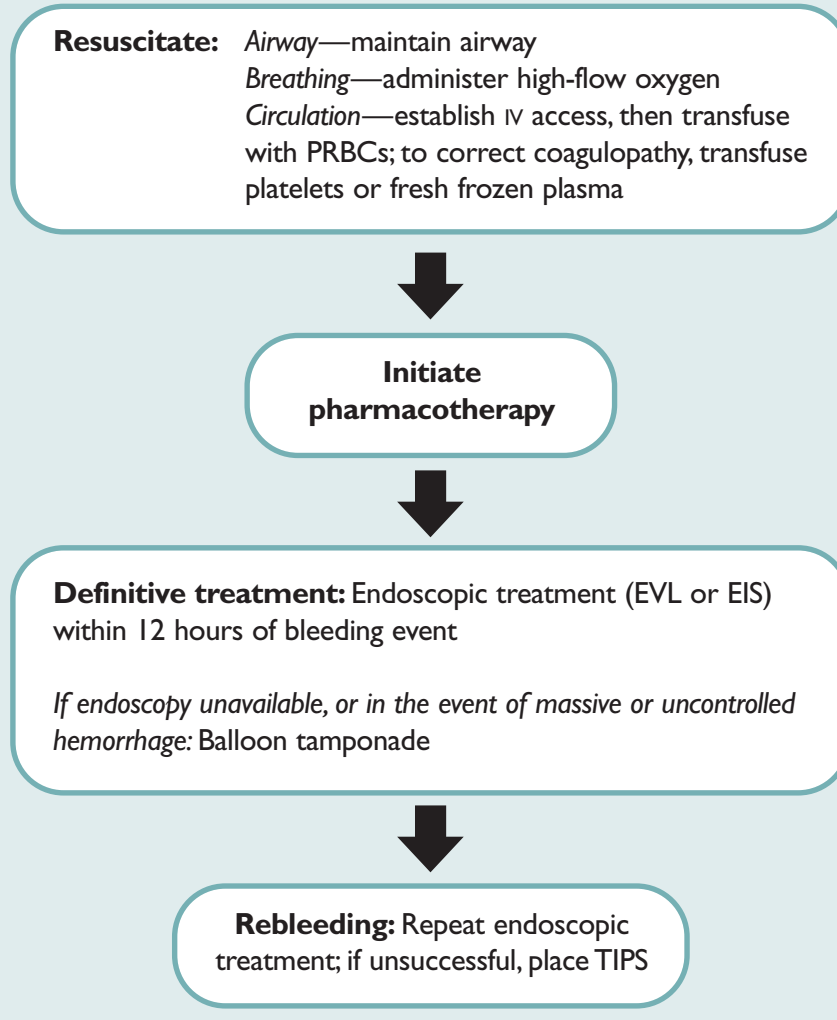
#### *Recurrent hemorrhage*

Risk increases with all of the above, and with the following:

- severity of initial bleed
- age > 60 years
- bacterial infection
- renal failure
- active alcoholism

For variceal hemorrhage associated with alcoholic liver disease, salvage therapy usually involves placement of a **transjugular intrahepatic portosystemic shunt (TIPS)**.[14] The procedure is performed by an interventional radiologist. Angiography is used to create a shunt between the hepatic and portal veins, which is then maintained by placement of a fenestrated metal stent. Although patients who undergo TIPS placement are less likely to bleed than are those undergoing endoscopic therapy, their chances of survival aren't improved and may be worse.[15] Procedure-related complications include hematomas, liver capsule rupture, and pulmonary edema; long-term complications include encephalopathy, liver failure, hemolysis, and TIPS stenosis. Another option is creation of a surgical shunt through an anastomosis between the portal vein and the vena cava. However, surgical shunts carry a significantly increased risk of death compared with endoscopic therapy.[15] Following either procedure, the patient's vital signs must be closely monitored to ensure that bleeding has been effectively controlled; serum ammonia level

**Figure 3. Treatment of Variceal Hemorrhage**




EIS = endoscopic injection sclerotherapy; EVL = endoscopic variceal ligation; PRBC = packed red blood cell; TIPS = transjugular intrahepatic portosystemic shunt

and level of consciousness should also be periodically reassessed.

For a quick guide to treatment for variceal hemorrhage, see Figure 3.

## CASE REVISITED

Over the next two days, two EVL procedures were performed and octreotide continued to be infused. In addition to the five units of packed red blood cells already given to Ms. Barth, she also received two units of fresh frozen plasma. But 44 hours after the first variceal hemorrhage, rebleeding occurred; the patient again vomited blood and her condition deteriorated.

A polymorphonuclear leukocyte count of 310 $cm^2$ was indicative of spontaneous bacterial peritonitis, and Ms. Barth was started on a five-day course of cefotaxime (Claforan) 6 g IV per day. Because antibiotic treatment failure isn't unusual with this complication, she required close monitoring. (Indications of such failure include rapid deterioration with developing shock within the first hour of initiating therapy, or less than a 25% reduction in polymorphonuclear leukocyte count on follow-up paracentesis two days after initiating therapy.) Lactulose enemas were repeated to quickly lower her serum ammonia level. But on her fifth day in the ICU, Ms. Barth again became encephalopathic and her kidneys began to fail. Despite salvage therapy, her condition continued to deteriorate and, a week later, she died. ▼

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