Diagnosing and Managing Portal Hypertension, Ascites and Variceal Hemorrhage

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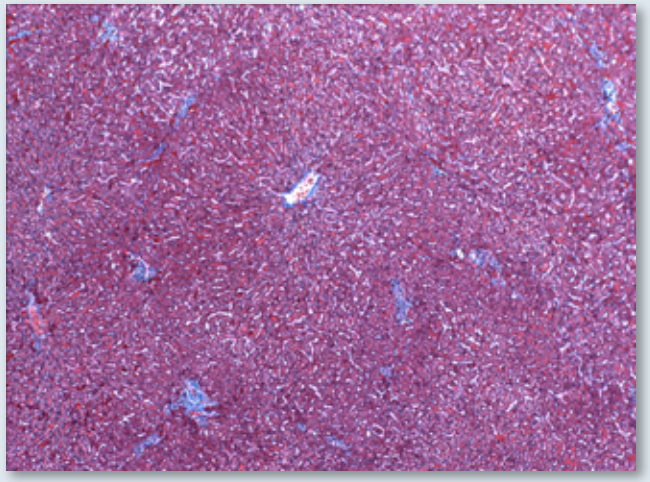
Gross and Microscopic Image of a Normal and a Cirrhotic Liver

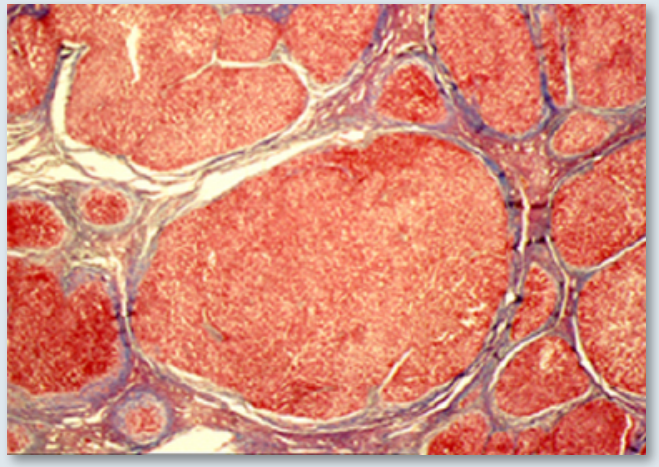
Normal

Nodules

Cirrhosis

Irregular surface





Nodules surrounded by fibrous tissue

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Prevalence of Cirrhosis

- The prevalence of cirrhosis, both worldwide and in the US, is unknown[1]
  - Cirrhosis is an outcome of a variety of causes; underlying cause is commonly used for surveillance purposes[2]
  - Compensated cirrhosis often goes undetected for prolonged periods of time[1]
- Experts estimate that 5.5 million people in the United States have cirrhosis[3]

1. Schuppan D, Afdhal NH. *Lancet* 2008;371(9615):838-851
2. Available at http://pubs.niaaa.nih.gov/publications/surveillance83/Cirr05.htm.
3. Khungar V, Poordad F, *Clin Liver Dis* 2012;16:73-89

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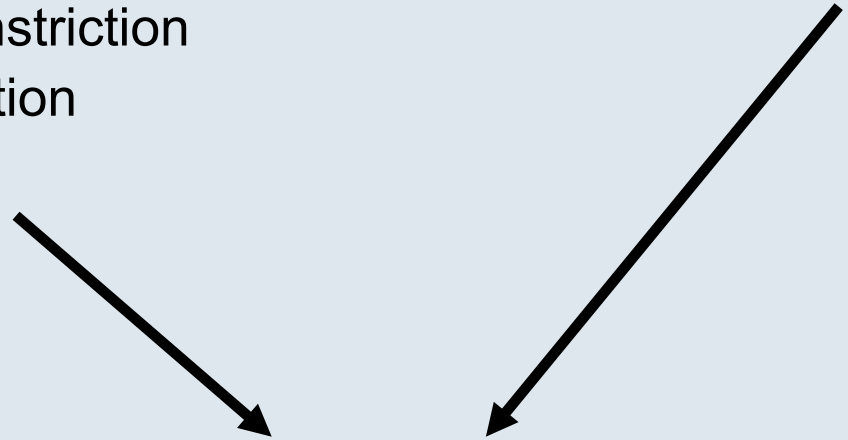
Portal Hypertension

Increased Resistance

(Architectural changes secondary to fibrous tissue formation; active vasoconstriction due to decrease in formation of endogenous NO)

Increased Blood Flow

(Splanchnic arteriolar vasodilation_)



Increased Portal Pressure

- Shunting (encephalopathy)
- Increased salt and water retention (ascites)
- Variceal formation (bleeding)

Adapted from Garcia-Tsao G, et al. *Hepatology*. 2007;46:922-938.

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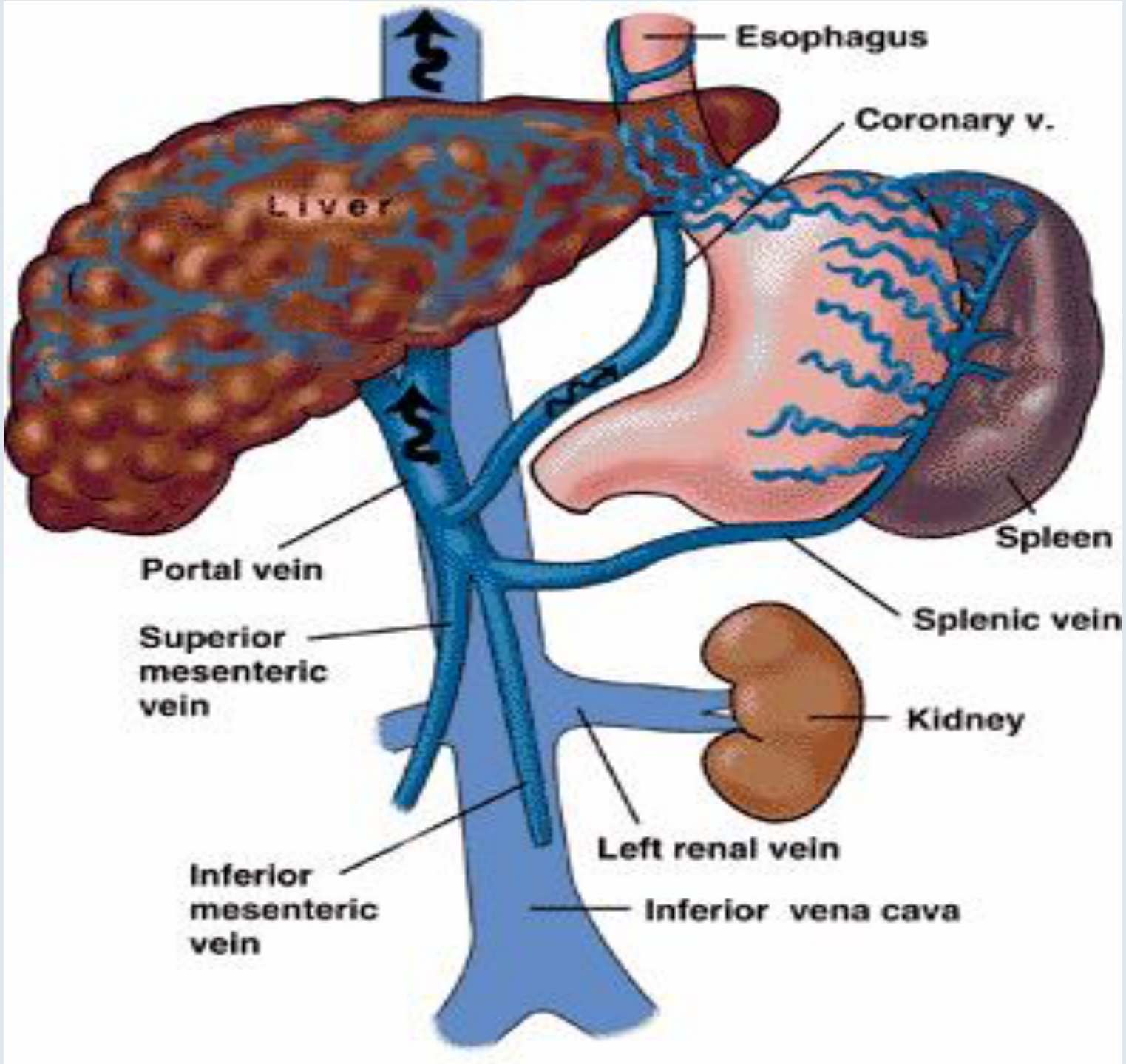

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Portal Hypertension

- Consequences of portal hypertension produce symptoms:
  - Gastroesophageal varices
  - Ascites
  - Enlarged spleen
  - Hepatic encephalopathy

From: http://www.merck.com/mmhe/sec10/ch135/ch135d.html. Accessed 09/09/15

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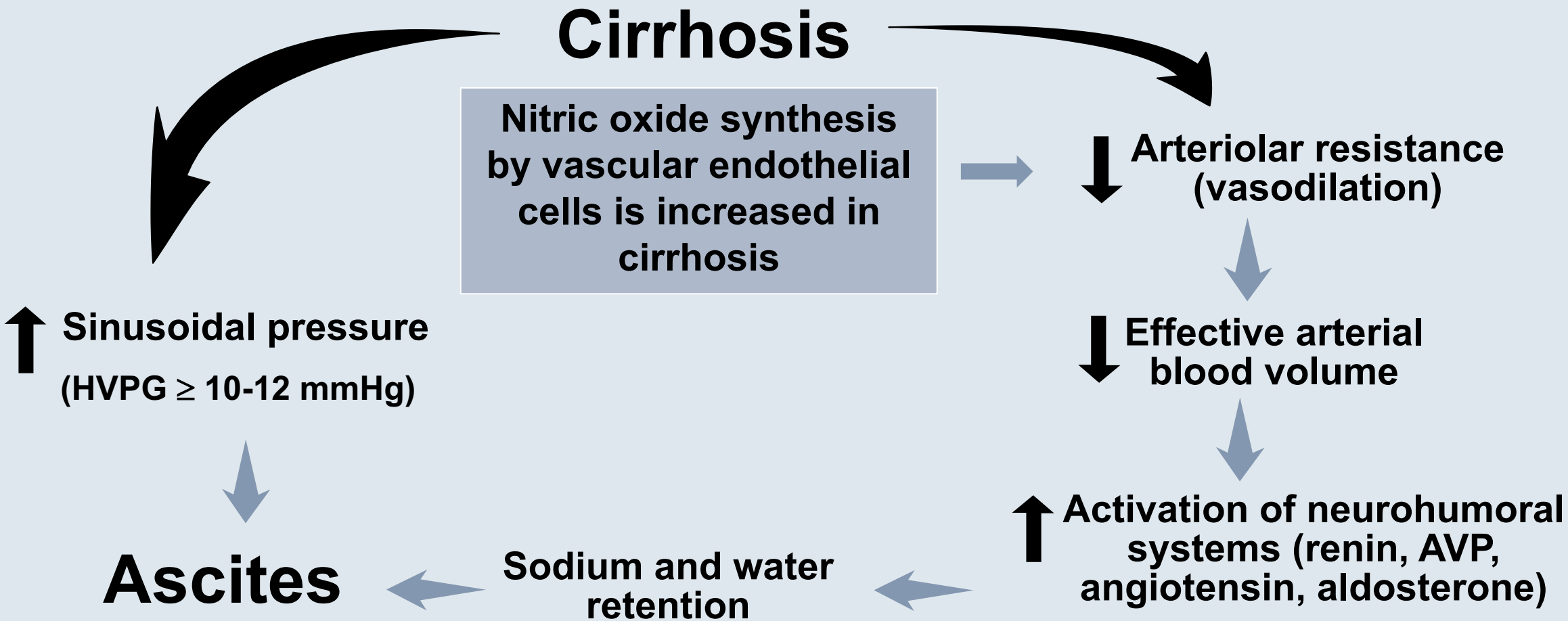
Pathogenesis of Ascites



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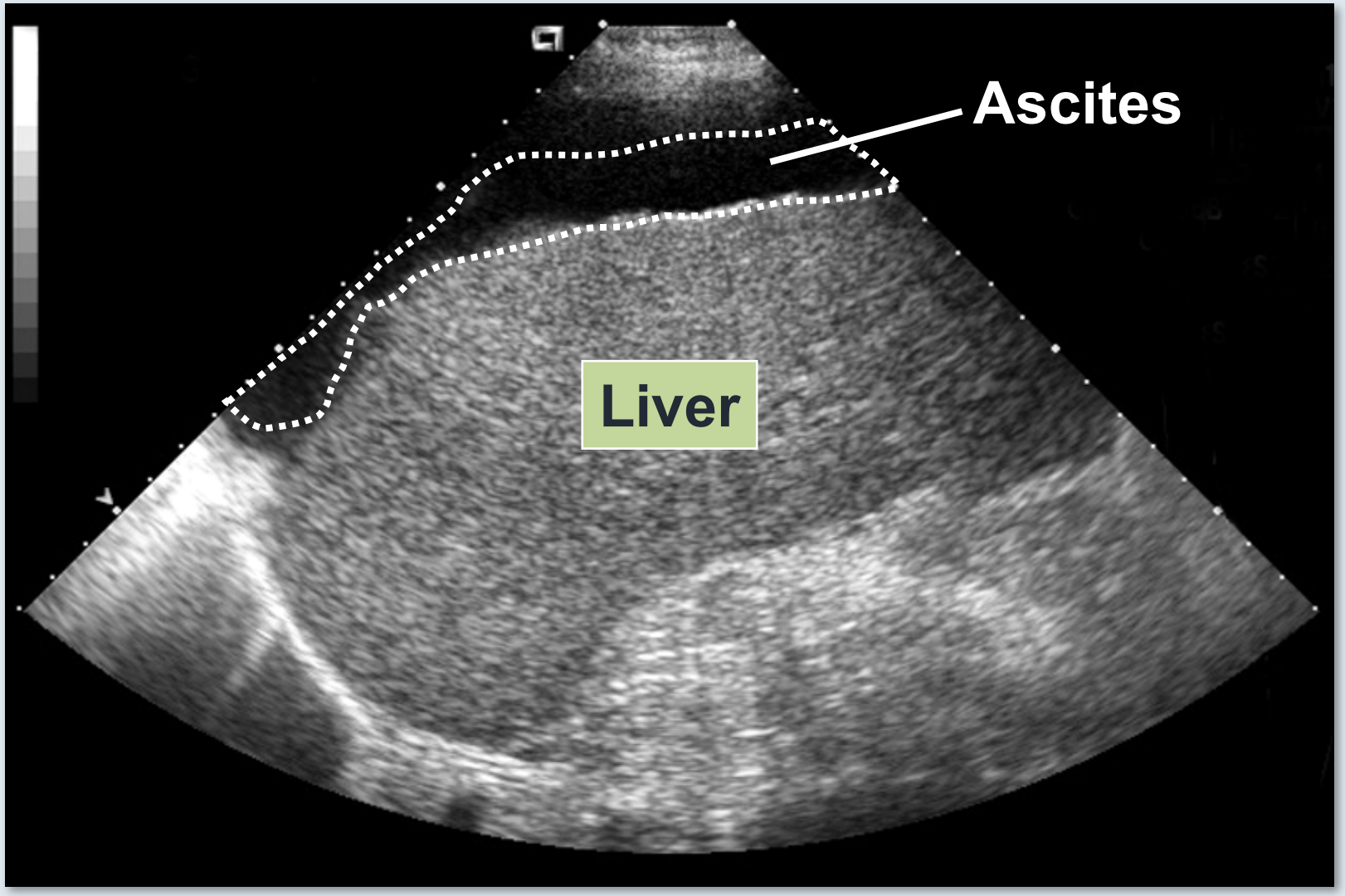
Ultrasound is the Most Sensitive Method to Detect Ascites



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Diagnostic Paracentesis

- Indications
  - New-onset ascites
  - Admission to hospital
  - Symptoms/signs of SBP
  - Renal dysfunction
  - Unexplained encephalopathy
- Contraindications
  - None: Can be done at any INR or platelet count

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Management of Uncomplicated Ascites

Diuretic Therapy

- Dosage (initial ratio 5:2)
  - Spironolactone 100-400 mg/day
  - Furosemide (40-160 mg/d) for inadequate weight loss or if hyperkalemia develops
- Increase diuretics if weight loss <1 kg in the first week and <2 kg/week thereafter
- Decrease diuretics if weight loss >0.5 kg/day in patients without edema and >1 kg/day in those with edema
- Side effects
  - Renal dysfunction, hyponatremia, hyperkalemia, encephalopathy, gynecomastia

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Refractory Ascites

- Diuretic-intractable ascites
  - Therapeutic doses of diuretics cannot be achieved because of diuretic-induced complications
- Diuretic-resistant ascites
  - No response to maximal diuretic therapy (400 mg spironolactone + 160 mg furosemide/day)
- Prophylactic TIPS
  - 6 trials of 390 patients
  - Concluded survival benefit based on urine sodium, bili, and portal pressure reduction (OR 0.45;95% CI, 0.24-0.81)

Chen RP, et al. *J Clin Gastroenterol* 2014;48(3):290-9

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Ascites

- Ascites is the most common of the 3 major complications of cirrhosis
- Occurs when portal hypertension has developed
- 50-60% of patients with “compensated” cirrhosis, i.e., without having developed one of these complications, develop ascites during 10 years of observation
- 50% mortality rate within 3 years
- Patients should generally be considered for liver transplantation referral

Arroyo V, Colmenero J. *J Hepatol*. 2003;38:S69-S89; European Association for the Study of the Liver. *J Hepatol*. 2010;53:397-417.

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Esophageal Varices

- Gastroesophageal varices present in ~50% of patients with cirrhosis
  - Presence correlates with severity of liver disease
  - 40% of Child A patients have varices
  - 85% of Child C patients have varices
- Cirrhotic patients without varices develop them at a rate of 8% per year
  - Patients with small varices develop large varices at a rate of 8% per year

Garcia-Tsao G, et al. *Hepatology.* 2007;46:922-938.

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Esophageal Variceal Hemorrhage

- Occurs at a yearly rate of 5% to 15%
- Most important predictor of hemorrhage is size of varices
- Other predictors of hemorrhage are:
  - Decompensated cirrhosis (Child B/C)
  - Endoscopic presence of red wale marks
- Associated with a mortality of ≥20% at 6 weeks
- Bleeding ceases spontaneously in ≤40% of patients

Garcia-Tsao G, et al. *Hepatology.* 2007;46:922-938.

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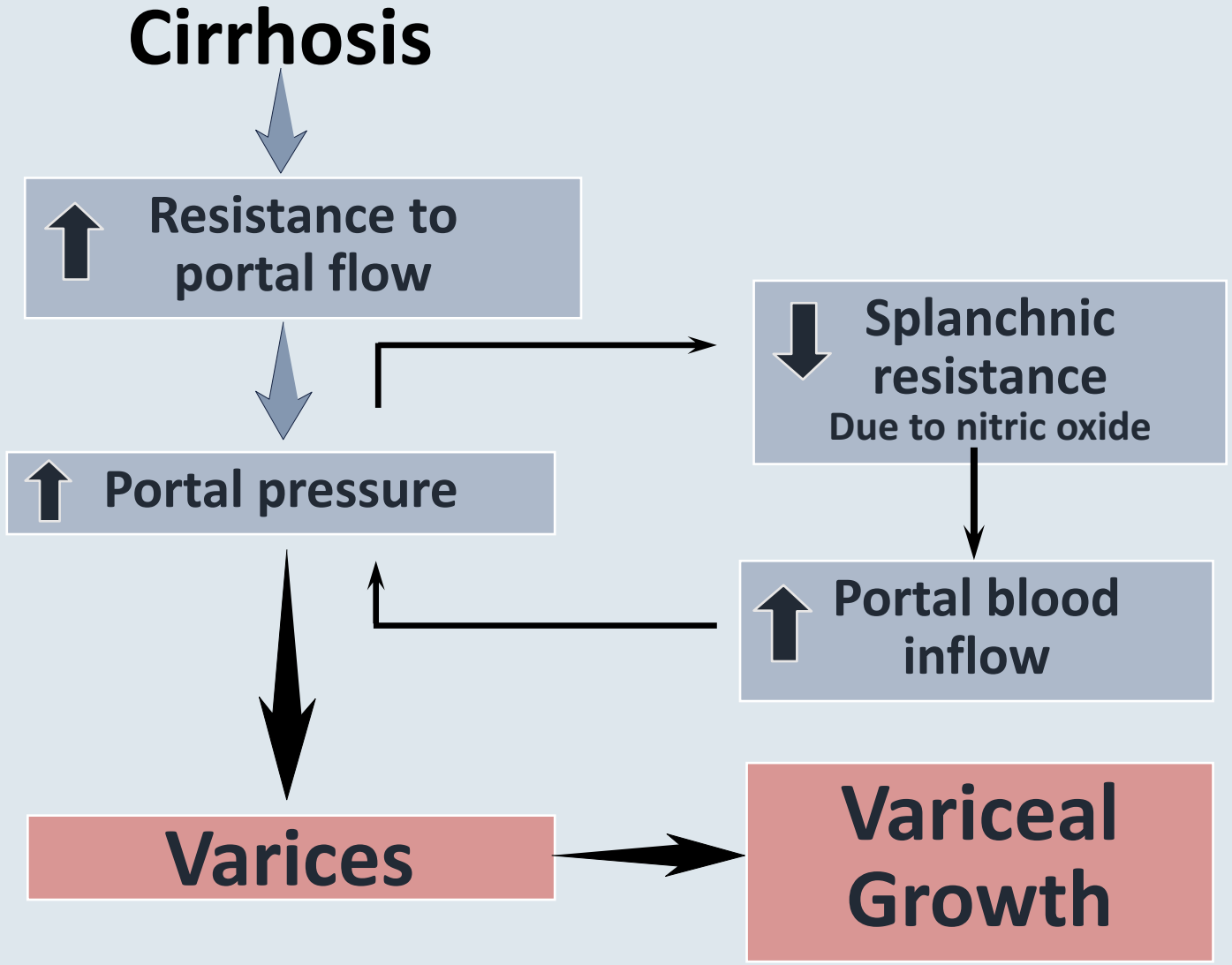
Varices and Variceal Hemorrhage



Varices present in 40-60% of cirrhotic patients

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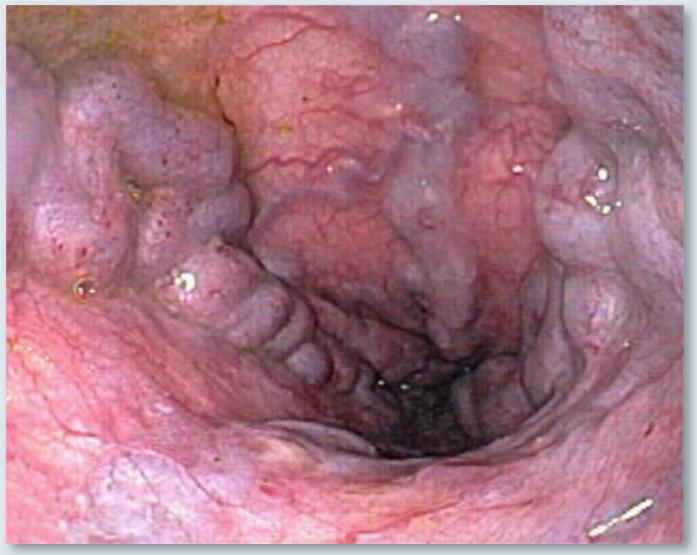
Varices Increase in Diameter Progressively

No varices

Small varices

Lower risk of bleeding



Large varices

Higher risk of bleeding

7-8%/year

7-8%/year

Merli et al. *J Hepatol* 2003;38:266

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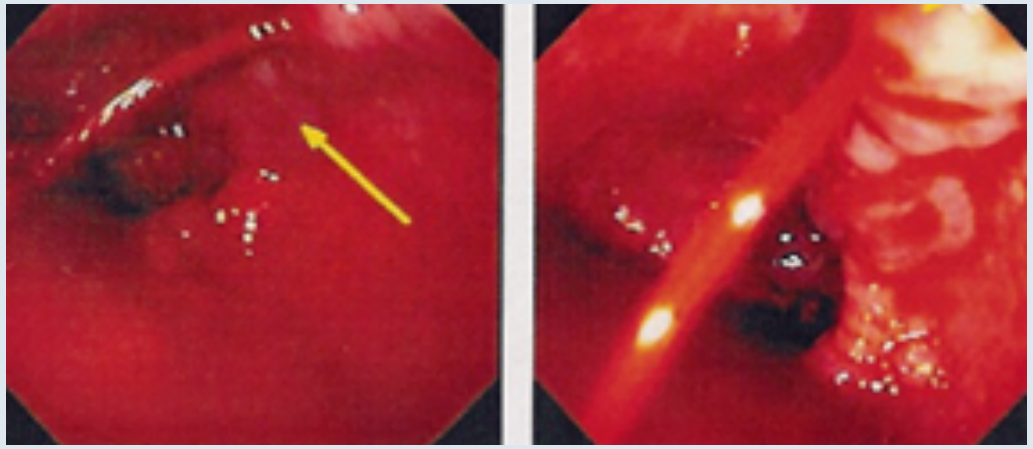
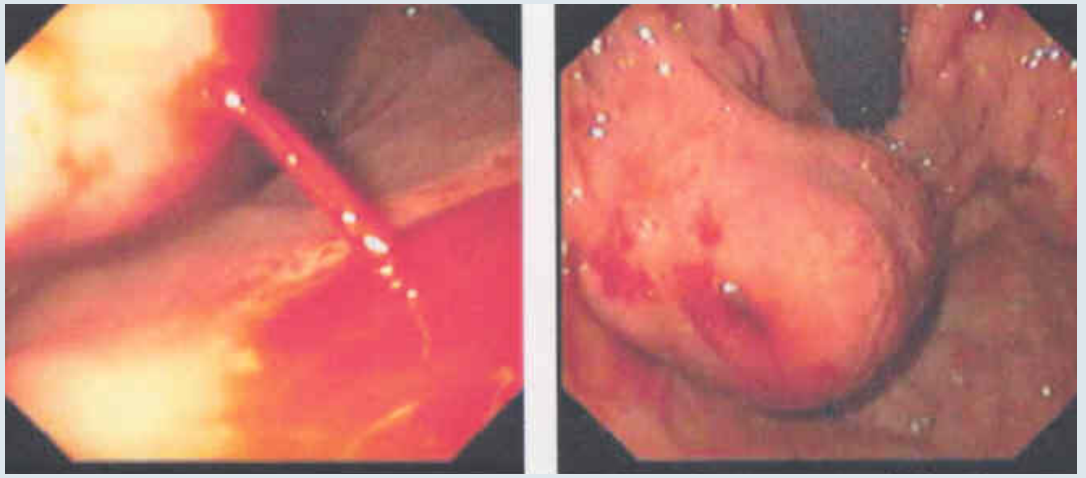
Bleeding Esophageal Varices

- Risk factors:
  - Large varices
  - Childs score C
  - Cherry red/red wale markings (endoscopic red signs)
  - HVPG > 12mm HG
- 20% mortality with initial bleed



Bleeding Gastric Varix

- 10% of variceal hemorrhages
- Do not respond well to EBL
- Rule out splenic vein thrombus



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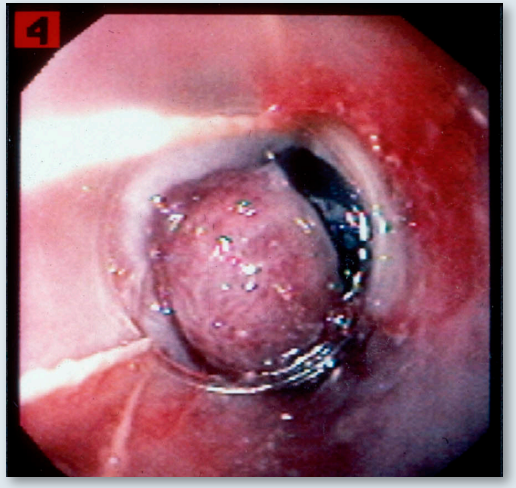
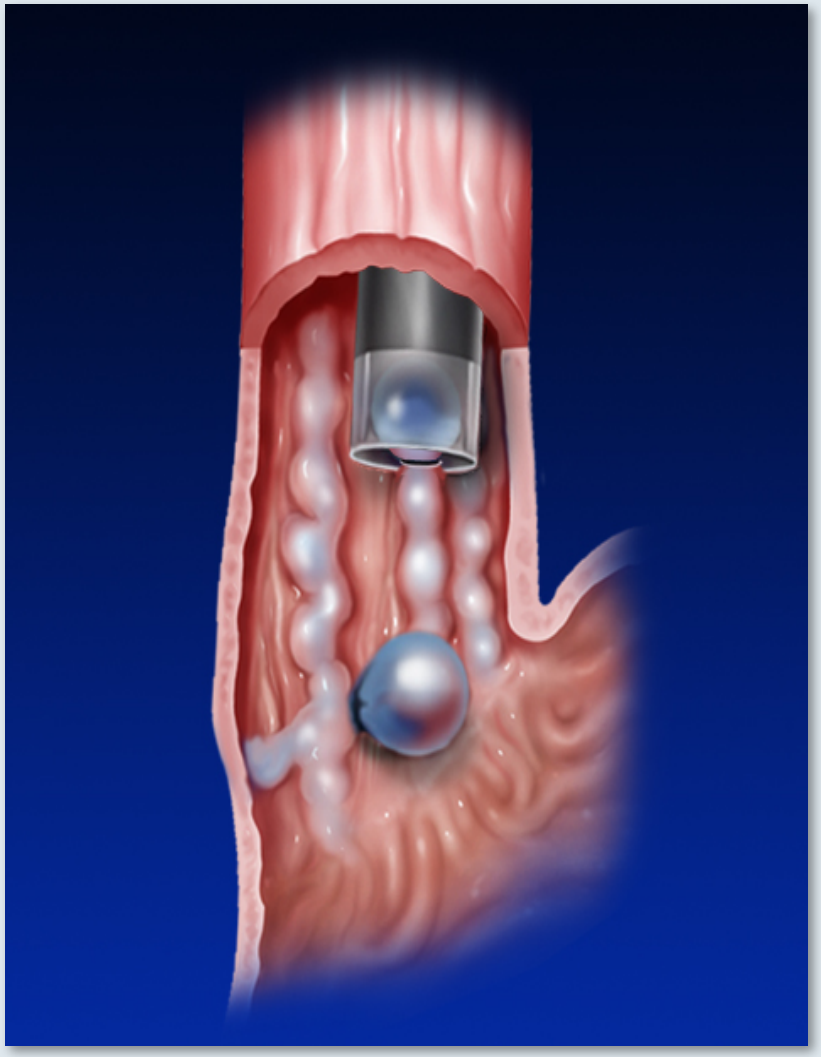
Endoscopic Variceal Band Ligation: Current Gold Standard for Bleeding Varices

- Bleeding controlled in 90%
- Antibiotics are standard of care
- Rebleeding rate 30%
- Compared with sclerotherapy:
  - Less rebleeding
  - Lower mortality
  - Fewer complications
  - Fewer treatment sessions



Ligated Esophageal Varix



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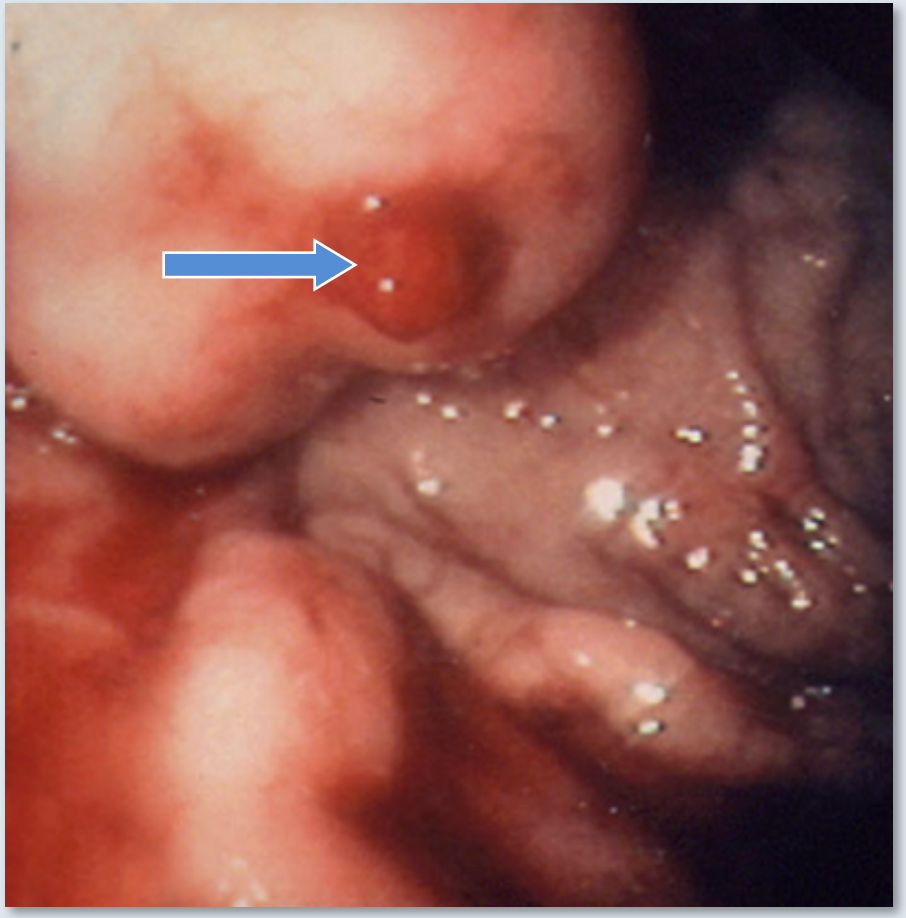
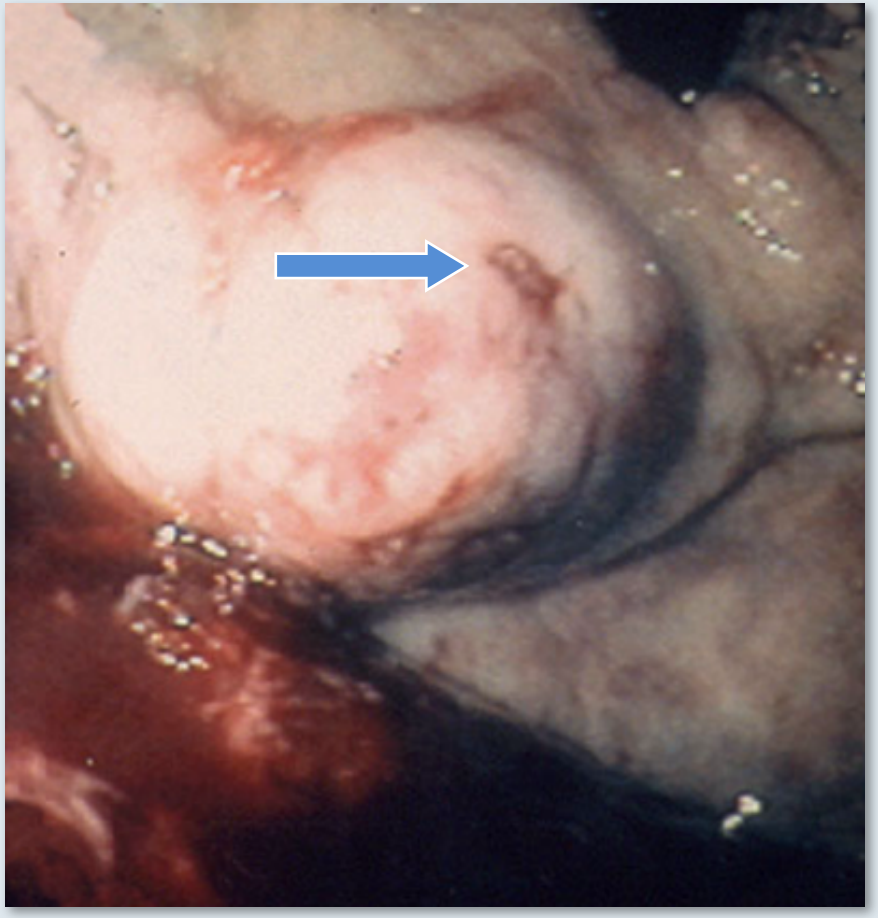
Gastric Varices



Pretreatment cyanoacrylate



Post-treatment cyanoacrylate

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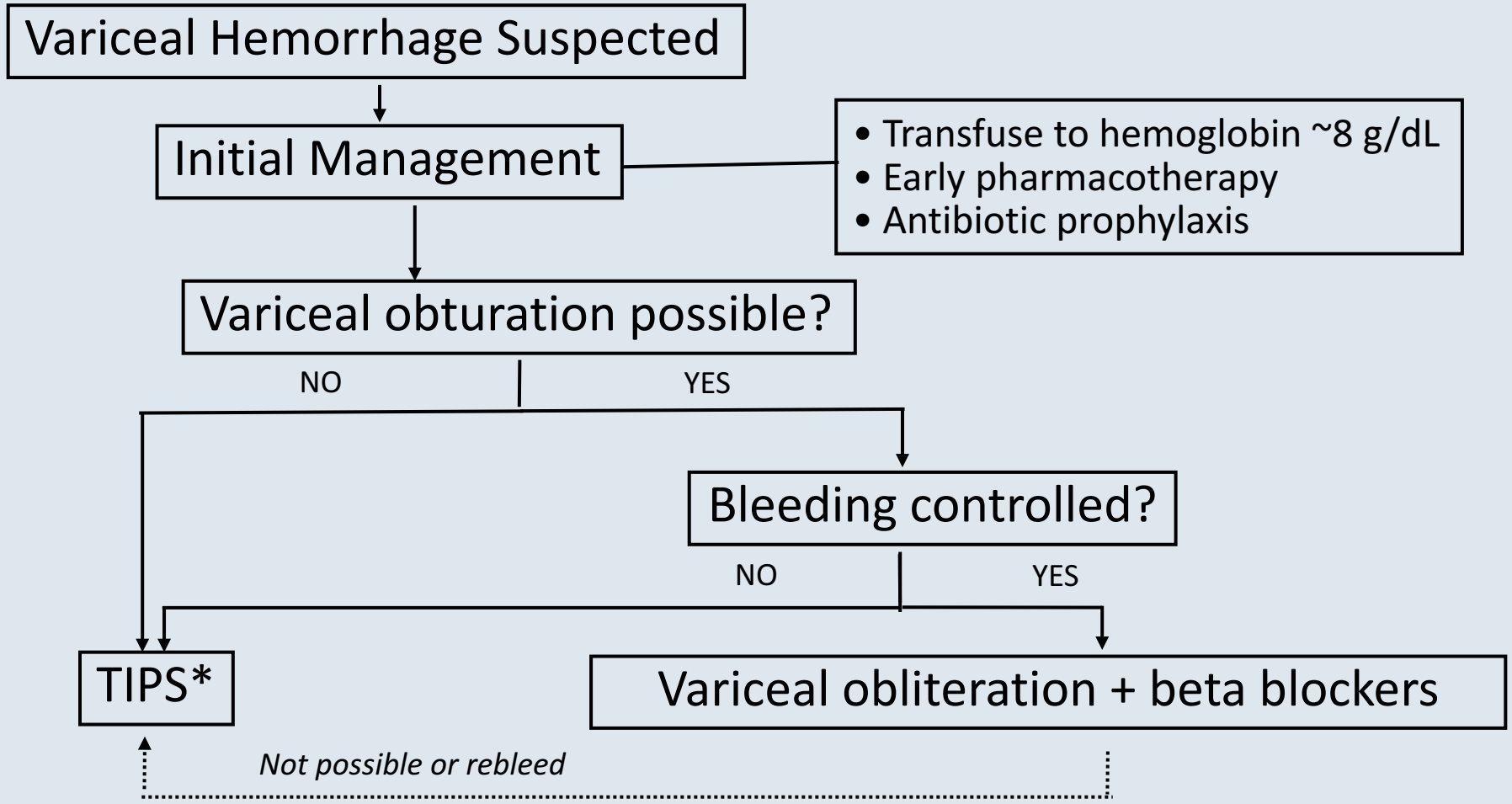
Management of Acute Gastric (Fundal) Variceal Bleeding



*Surgical shunt may be considered for Child's Class A

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Comparative Outcome Probabilities for Various Complications of Cirrhosis

Complication	Survival at 1 Year	Survival at 3 Years
Varices (Non-Bleeding) w/o Ascites[1]	97%	NA
Ascites ± Varices[1,2]	80%	50%
Bleeding Varices ± Ascites[1]	43%	NA
Hepatic Encephalopathy[3]	42%	23%

NA=Not Available.

1. Adapted from D'Amico G, et al. *J Hepatol.* 2006;44:217-231;
2. Arroyo V, Colmenero J. *J Hepatol.* 2003;38:S69-S89;
3. Adapted from Bustamante, et al. *J Hepatol.* 1999;30:890-895.

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Summary

- Cirrhosis and the development of portal hypertension can result in decompensation as manifest by HE, ascites and variceal bleeding.
- Patients with decompensated liver disease should be treated with the goal to reduce portal pressures and manage the complications to improve patient comfort and reduce risk.
- Decompensation is a signal for marked increase risk of morbidity and mortality and appropriate patients should be referred for consideration of liver transplantation

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