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Acute Complications of Cirrhosis

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Denver Health Medical Center

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Objectives

- Discuss the etiology, classification, and pathophysiology of cirrhosis
- Review complications of cirrhosis
- Examine treatment modalities for complications of cirrhosis

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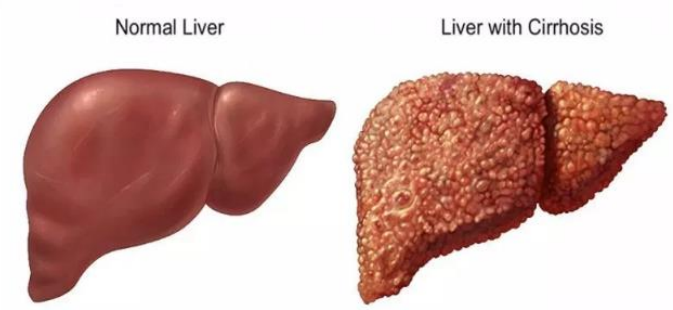
Background

- Severe, chronic, progressive fibrosis due to chronic injury, leading to liver failure and associated complications
- 11th leading cause of death of adults in the United States in 2020
  - 4.5 million adults diagnosed with liver disease (1.8% of the population)
  - Likely an underestimation of the burden of disease



wonder.cdc.gov. Accessed Feb 11th, 2022.
Starr SP, et al. Am Fam Physicians. 2011.
Ge PS, et al. Treatment of Patients with Cirrhosis. N Engl J Med. 2016.

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Epidemiology & Health Disparities

Race	• Non-Hispanic Black Americans • Mexican Americans
Income	• Below poverty level
Education	• 12th grade or less
Comorbidities	• Diabetes • Elderly

Scaglione, S, et al. The epidemiology of cirrhosis in the US. Clin J Gastroenterol. 2015.

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Causes

- Most common causes in the US:
  - Alcohol Use Disorder
  - Viral Hepatitis (Hepatitis B and C)
  - Fatty Liver Disease
    - Nonalcoholic steatohepatitis (NASH)
    - Nonalcoholic fatty liver disease (NAFLD)
- These causes account for approximately 80% of the patients on the liver transplant waitlist between 2003-2014
    - Second longest organ waitlist in the United States (second to kidney transplantation)

https://optn.transplant.hrsa.gov/data/. Accessed February 11th, 2022.
Ge PS, et al. Treatment of Patients with Cirrhosis. N Engl J Med. 2016.

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Additional Causes

- Infection
- Autoimmune
- Hemochromatosis
- Medications

Heidelbaugh JJ, et al. Am Fam Physicians. 2006.

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Categorizing Cirrhosis

Compensated

- No clinical s/sx of cirrhosis
- May be unaware of diagnosis

Decompensated

- Portal hypertension
- Ascites
- Spontaneous bacterial peritonitis
- Etc.

Ge PS, et al. Treatment of Patients with Cirrhosis. N Engl J Med. 2016.

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Mortality

- Much higher in those with cirrhosis
  - 26.4% per two-year interval in those with cirrhosis versus 8.4% in propensity matched controls
- Significant differences when comparing compensated and decompensated cirrhosis
  - Risk of death:
    - Compensated: 4.7 times higher than the general population
    - Decompensated: 9.7 times higher than the general population
  - Life expectancy:
    - Compensated: 10-13 years
    - Decompensated: as little as 2 years

Ge PS, et al. Treatment of Patients with Cirrhosis. N Engl J Med. 2016.
Scaglione, S, et al. The epidemiology of cirrhosis in the US. Clin J Gastroenterol. 2015.

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Financial Burden

- Continuing to rise due to cirrhosis and associated complications requiring hospitalization
  - Estimated direct and indirect costs to be in the billions
  - As hospitalizations go up, so does the cost burden on the healthcare system
- Extended length of stay, medications, and need for emergent procedures all increase cost in this patient population
- Chronic liver disease patients have also been shown to have
  - Longer admissions
  - More readmissions
  - Less access to care than other disease states

Desi A, et al. Increasing economic burden of patients with cirrhosis. Clin and Translational Gastro. 2019.
Hirode G, et al. Trends in the Burden of Chronic Liver Disease Among Hospitalized US Adults. JAMA Netw Open. 2020.
Asrani SK, et al. Increasing healthcare burden of chronic liver disease compared to other chronic diseases. Gastro. 2018.

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Diagnostics & Screening

- Appropriate screenings for unhealthy alcohol use, binge drinking, and alcohol use disorder
  - Alcohol Use Disorders Inventory Test (AUDIT)
  - AUDIT-C (questions 1-3 of AUDIT)
- Biomarkers of alcohol use can be found in urine, hair, or blood
  - NOT recommended to use as tools to "catch" people → open the floor for discussion
  - Patients should always consent to testing

Crabb, et al. Diagnosis and Treatment. AASLD. 2019.

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Laboratory Values

Liver Related Enzymes		
Laboratory Test	**Description**	**Key Points**
Aminotransferases (AST/ALT)	- Produced in hepatocytes - Indicates hepatocellular injury - Rapidly changing	- Inadequate to establish alcohol use - AST:ALT ratio > 1 may indicate cirrhosis 2/2 alcohol
Gamma-glutamyl transferase (GGT)	- Enzyme found in cell membranes in spleen and liver tissues	- Frequently elevated in heavy drinking - Greater sensitivity than AST for cirrhosis - Not specific for alcohol use
Bilirubin	- Created through degradation of several heme-containing proteins - Non-specific to liver disease	- Elevations occur in 1later disease, and may indicate more severe cirrhosis

Ruiz, et al. Bilirubin in liver disease. Advances in laboratory medicine. 2021.
Crabb, et al. Diagnosis and Treatment. AASLD. 2019.

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Laboratory Values

Additional Labs

Laboratory Test	Description	Key Points
Albumin	- Produced by the liver in hepatocytes, accounts for 10% of liver protein production daily - Provides oncotic pressure in plasma - Indicator of nutritional status	- Lower albumin carries an overall negative prognosis (cirrhosis + other disease states) - Should not be supplemented externally (ALBIOS, ATTIRE) for sake of repletion
INR	- Prothrombin time compared to a laboratory normative prothrombin time - Designed with vitamin-k antagonists in mind	- NOT an indication of bleed risk - Patients may be in a hypercoagulable state despite elevated INR
Platelets	- Synthesized by the liver - Improved prognostic factor for bleeding when compared to INR	- Can be used as a biomarker for cirrhosis severity, not validated, taking trend and baseline into account

Crabb, et al. Diagnosis and Treatment. AASLD. 2019.
Harrison. Western J Em Med. 2018.

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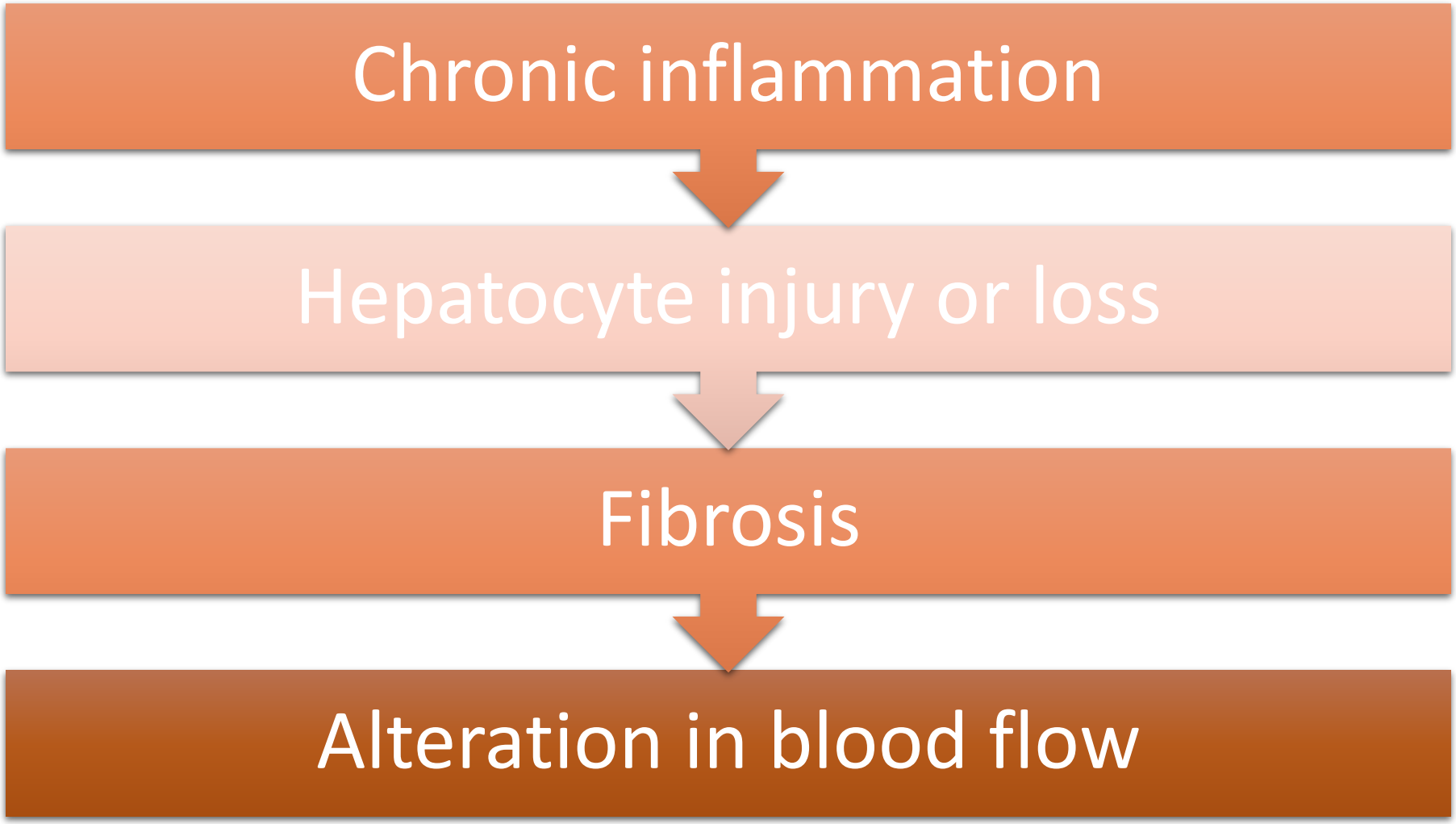
Pathophysiology Overview



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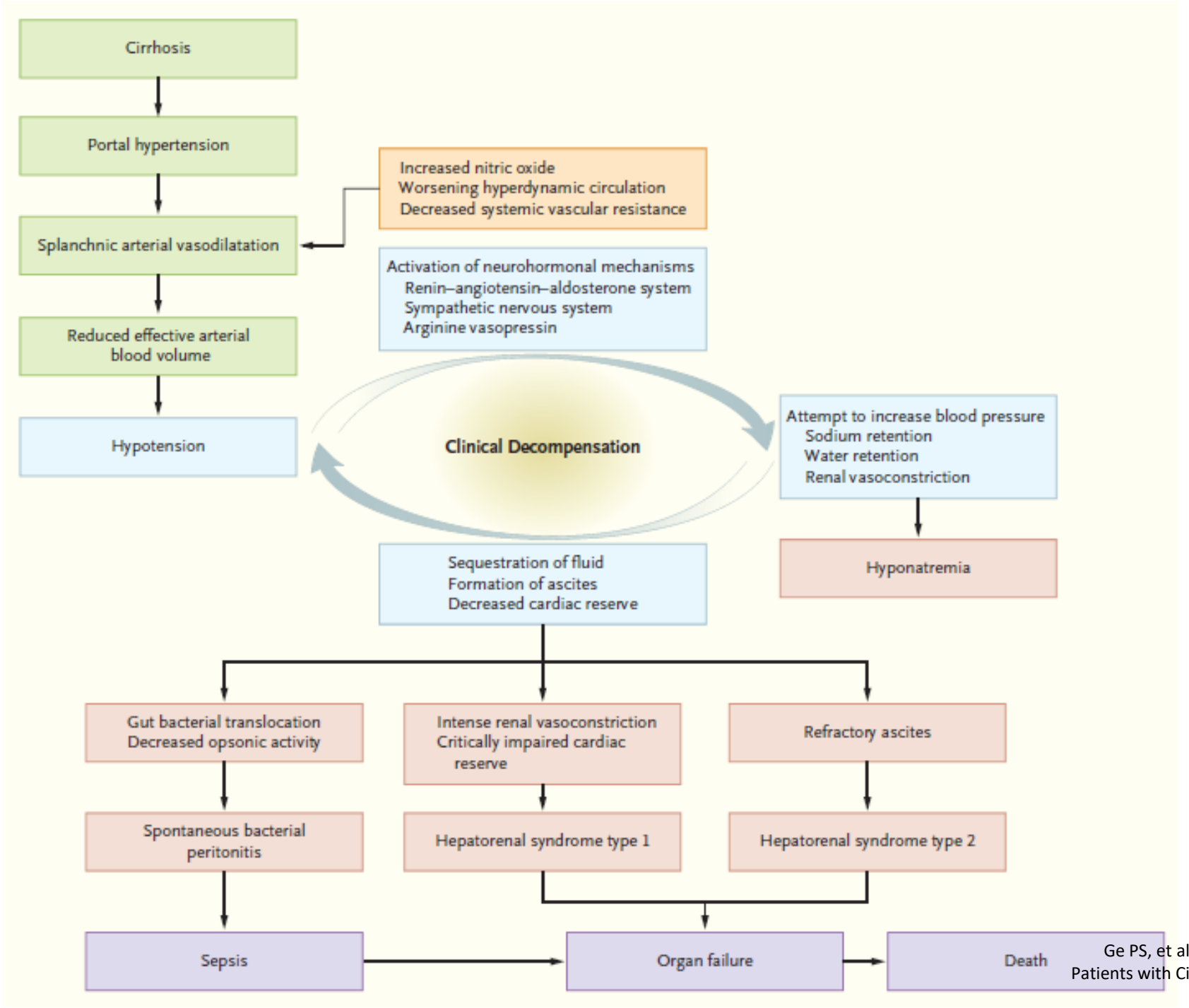

Ge PS, et al. Treatment of Patients with Cirrhosis. N Engl J Med. 2016.

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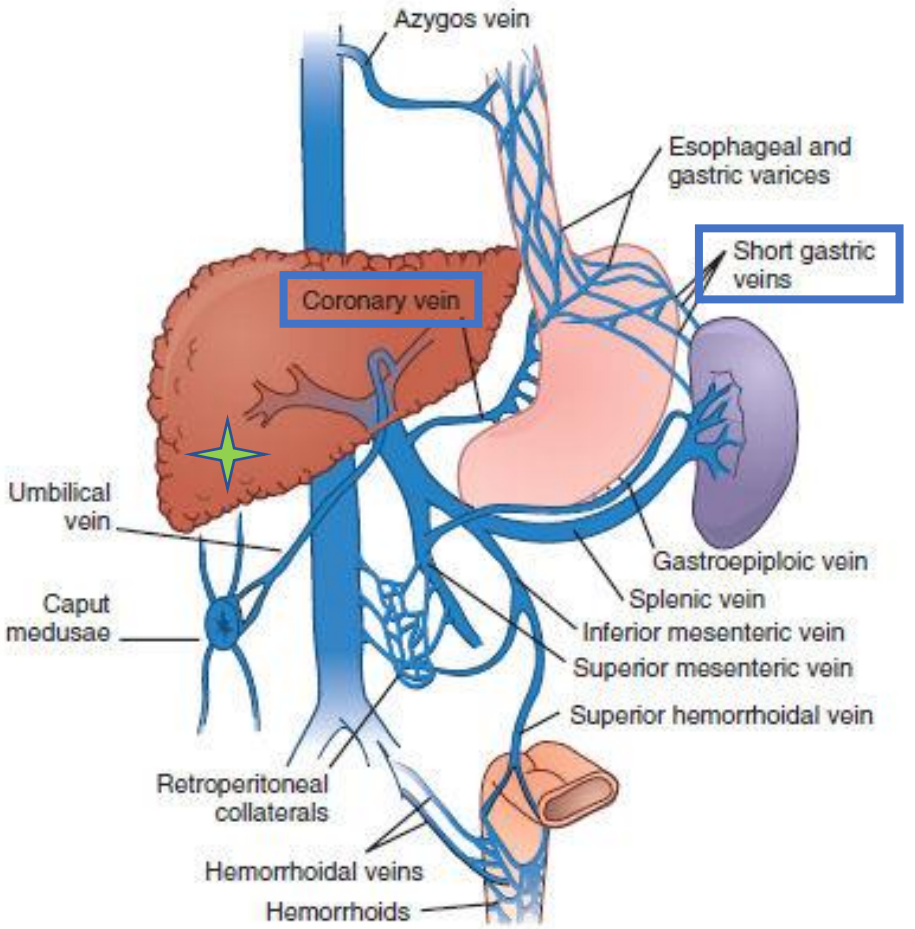
Portal Hypertension

- Increased structural resistance
  - Fibrous tissue
  - Vascular distortion
- Intrahepatic vasoconstriction
  - Decreased nitric oxide bioavailability
- Splanchnic arterial vasodilation



http://www.surgicalcore.org

Portosystemic collaterals

Garica-Tsao G, et al. Hepatology 2007; 46;3: 922-938.

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Predictive Models

Child-Pugh Classification

Model for End Stage Liver Disease (MELD)

Starr SP, Raines D. Am Fam Physicians 2011.

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Cirrhosis Severity

Child Pugh Classification	
Includes: encephalopathy, ascites, INR, albumin, bilirubin	
Score	**Interpretation**
5-6	A – least severe liver disease
7-9	B – moderately severe liver disease
10-15	C – most severe liver disease
Model for End Stage Liver Disease (MELD)	
Includes: creatinine/need for dialysis, bilirubin, sodium, and INR	
Score	**Interpretation**
9-40	Predicts 3 month mortality Worsens with increasing score Consider listing for transplant ~15-17

Durand, F. et al. *Hepatology* 2005;42:S100-S107.

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Clinical Presentation

- Anorexia
- Weight loss
- Weakness
- Fatigue
- Osteoporosis
- Jaundice

- Pruritus

- Gastrointestinal bleeding
- Coagulopathy
- Easy bruising
- Increasing abdominal girth
- Mental status changes

Starr SP, et al. Am Fam Physicians. 2011.

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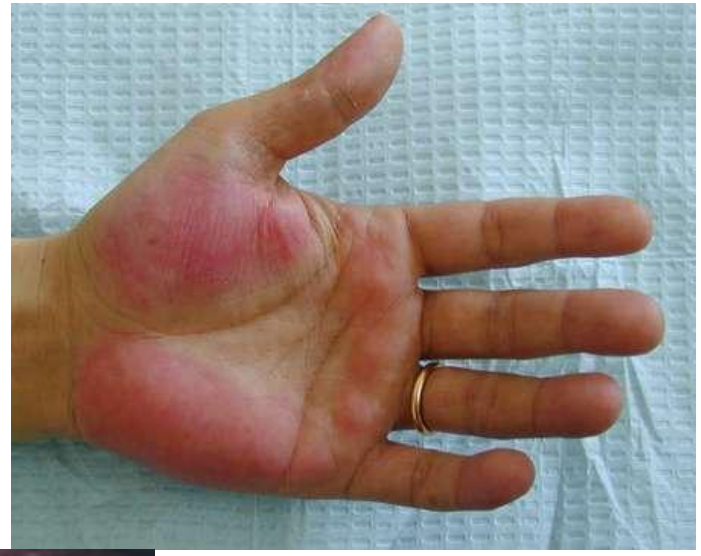
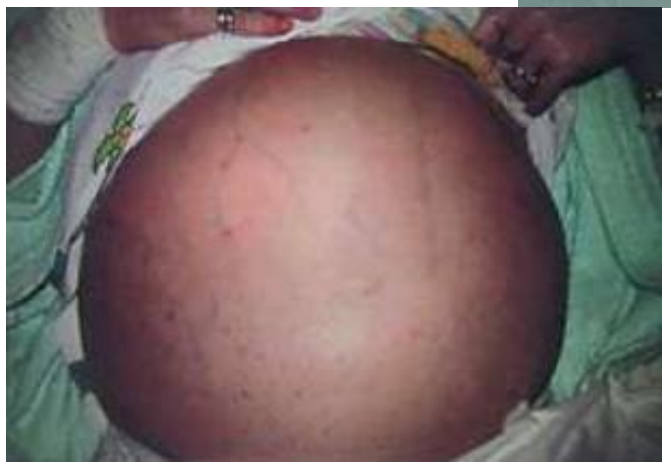
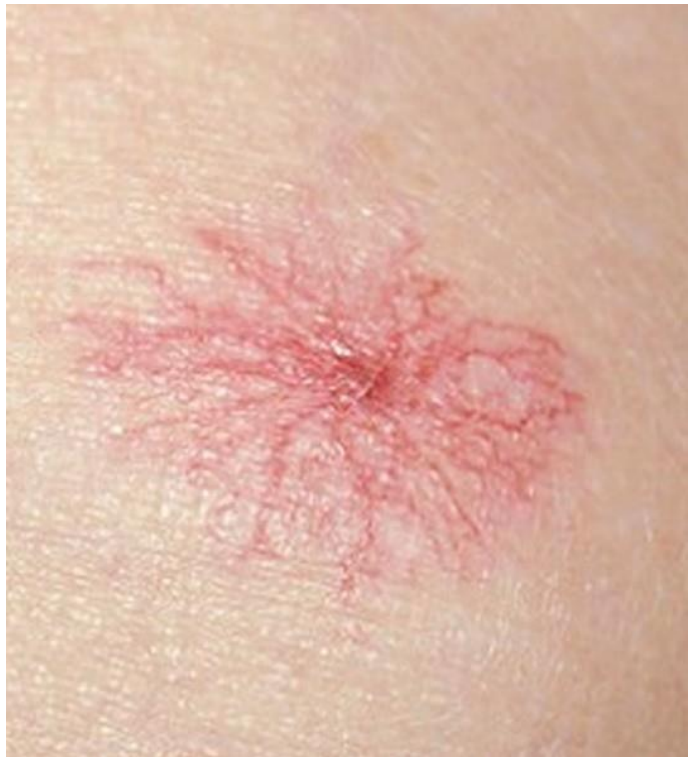
Physical Exam Findings







Starr SP, Raines D. Am Fam Physicians 2011.

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Physical Exam

- Decreased blood pressure
- Spider angiomas
- Palmar erythema
- Sweet, pungent breath
- Gynecomastia
- Peripheral edema
- Hepatomegaly
- Splenomegaly
- Asterixis
- Ascites

Starr SP, Raines D. Am Fam Physicians 2011.

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Treatment Overview

- As mentioned, cirrhosis is progressive and non-reversable
- Treatment of cirrhosis is currently focused on mitigating complications that commonly arise

Portal Hypertension

Hepatorenal Syndrome

Ascites

Hepatic Encephalopathy

Spontaneous Bacterial Peritonitis

Variceal Hemorrhage

Esophageal Varices

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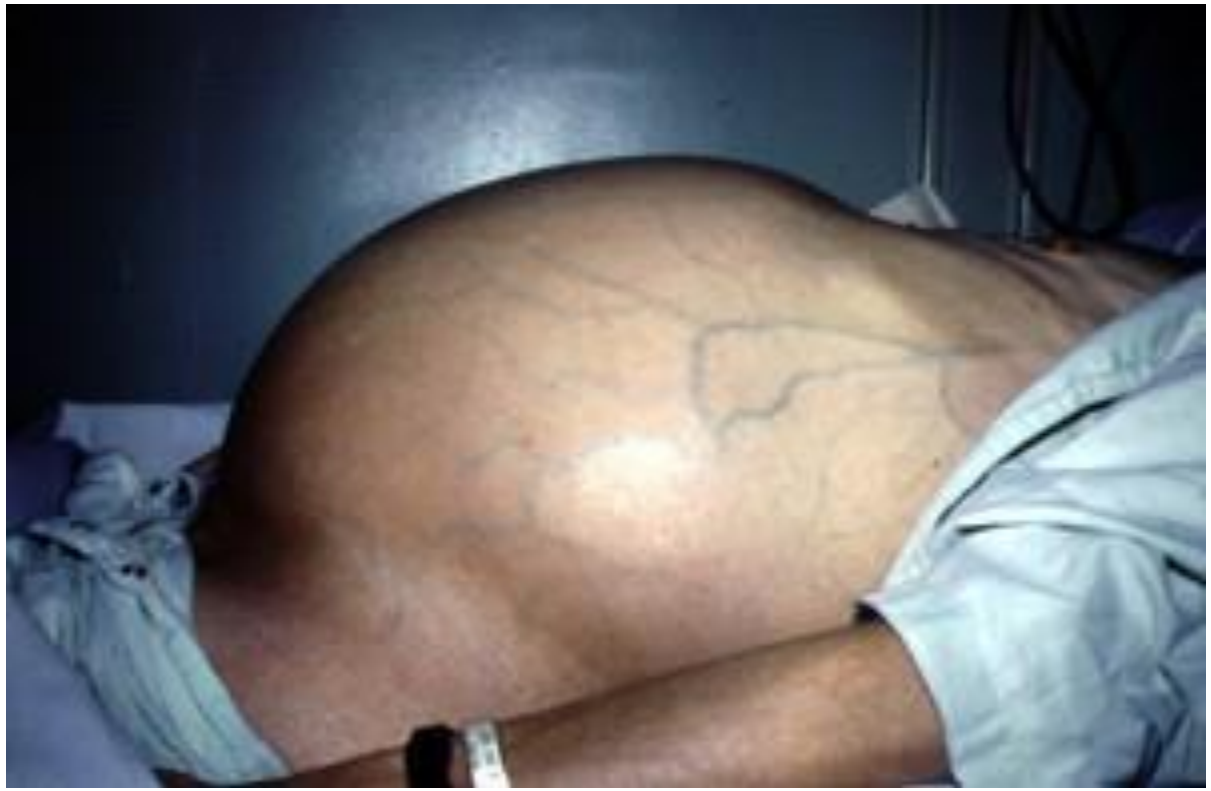
Ascites



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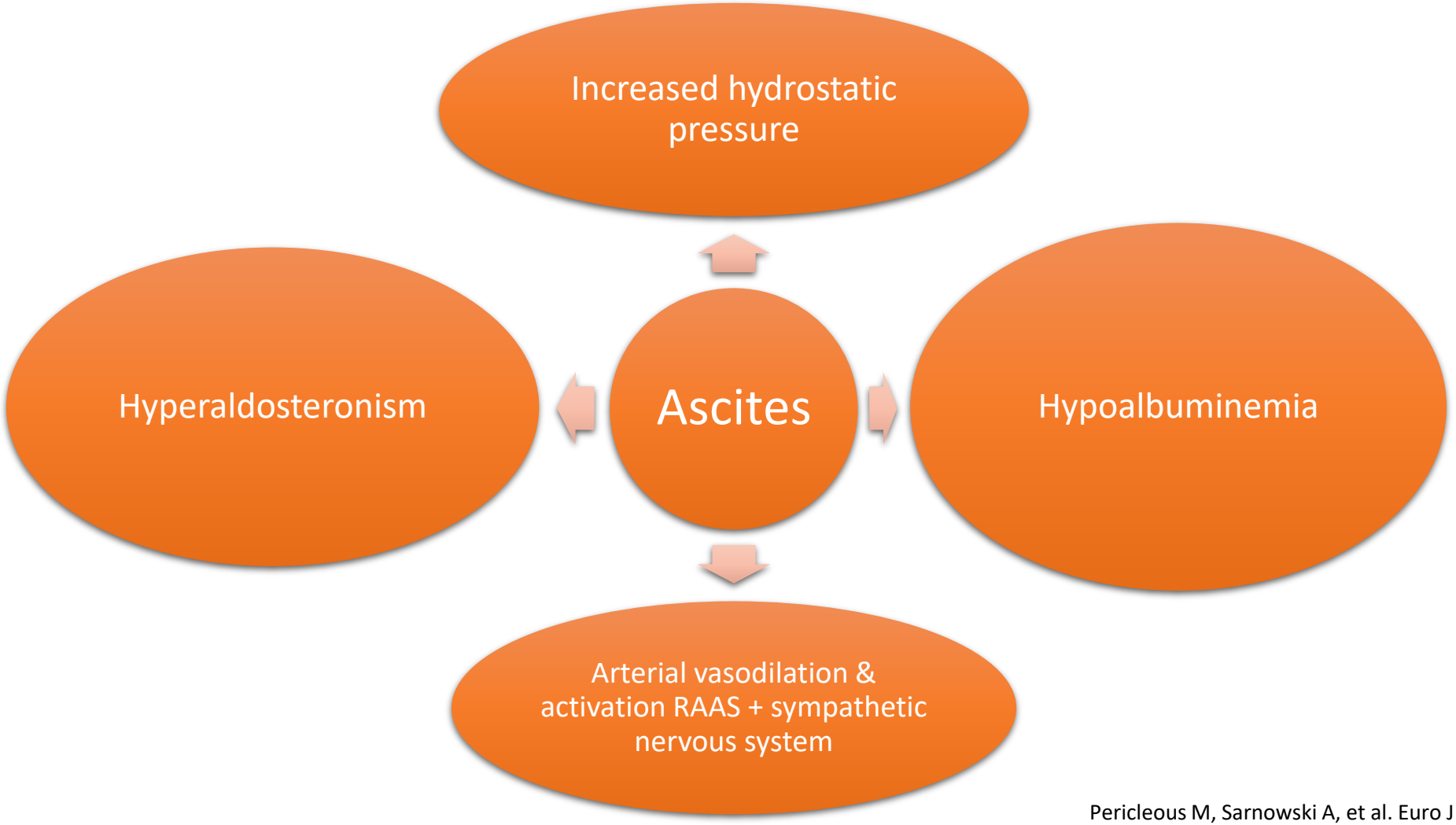
Ascites: Pathophysiology



Pericleous M, Sarnowski A, et al. Euro J Gastroenter Hept 2016

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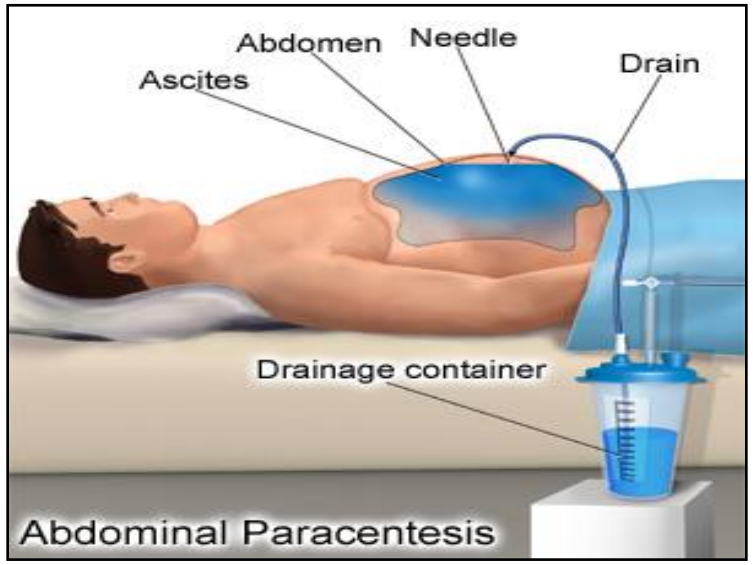
Ascites: Evaluation

- Paracentesis



- Serum albumin ascites gradient (SAAG)
  - SAAG = $Albumin_{serum} - Albumin_{ascitic\ fluid}$
  - SAAG ≥ 1.1g/dL implies portal hypertension is present

Hou W, Sanyal AJ. Med Clin N Am 2009

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Ascites Treatment

1ST LINE	
Alcohol Cessation	Treat underlying cause
Sodium Restriction	2000 mg per day
Diuretics	Spironolactone & Furosemide: • Ratio of 100:40 • Max Dose: 400 mg spironolactone, 160 mg furosemide
2ND LINE	
Paracentesis	Albumin: • ≤ 5 L - None • > 5 L - 6 to 8 g per liter removed
BP Medication Adjustments	Discontinuation of ACE-I, ARB, BB • MAP > 82 mmHg
Midodrine	Add to diuretics in hypotensive patients: • Dosing: 7.5 mg TID
Refractory	
Serial Therapeutic Paracentesis, TIPS, Peritoneovenous Shunts, Transplant	

Ge PS, Runyon BA. Treatment of Patients with Cirrhosis. *N Engl J Med* 2016;327:767-77.

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Ascites: Treatment

Agent	Dose	MOA	Onset of Effect	Dose Limiting Effects
Spironolactone	Initial: 12.5-100 mg Max: 400 mg	- Aldosterone antagonist - Decreases aldosterone effect in distal tubules	3-5 days	- Gynecomastia - Hyperkalemia
Furosemide	Initial: 40 mg Max: 160 mg	- Loop diuretic - Blocks reabsorption of Na+ in Loop of Henle, ↑ Mg 2+ and Ca 2+ excretion	3-5 days	- Hypotension - Intravascular dehydration

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Spontaneous Bacterial Peritonitis (SBP)

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SBP

- Bacterial infection of ascitic fluid without an obvious source
- Mortality rate can be greater than 20%
- Usually signifies advanced disease
- Organisms:
  - Enteric - E.coli, K. pneumoniae
  - S. aureus
  - Hospital acquired infections have increased risk of resistance

Biggins, et al. 2021 Practice Guidance. Hepatol 2021.

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SBP Specific Symptoms

- Abdominal pain
- Tenderness on palpation
- Ileus
- BUT
  - Up to 1/3 of patients may be asymptomatic
  - Present with AMS and/or AKI
- A diagnostic paracentesis should be obtained to evaluate ascitic fluid even in the absence of infectious symptoms

Biggins, et al. 2021 Practice Guidance. Hepatol 2021.

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Diagnostic Paracentesis

- Evaluation of ascitic fluid:
  - Cell count:
    - Polymorphonuclear leukocyte (PMN) count ≥ 250 cells/mm^3 indicative of SBP
  - Cultures:
    - Ideally isolate organism to guide antibiotic therapy
    - Difficult, even more so after antibiotics have been given
      - ALWAYS obtain paracentesis prior to initiating therapy
    - Also recommended to obtain blood cultures
    - If PMN count < 250 cells/mm3 with positive cultures but no s/sx of infection → no antibiotics

Biggins, et al. 2021 Practice Guidance. Hepatol 2021.

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Spontaneous Bacterial Peritonitis

TREATMENT	
Antibiotics	•**3rd Generation cephalosporin for 5 days**: • Cefotaxime 2g q8h • Ceftriaxone 1g q12h •**Alternate**: • Ofloxacin 400mg BID
Albumin	Reduce risk of renal failure: •Day 1: 1.5 mg/kg within 6 hours of presentation •Day 3: 1 mg/kg Also give when: •Scr > 1 mg/dl •BUN > 30 •Total bilirubin > 4

Biggins, et al. 2021 Practice Guidance. Hepatol 2021.

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Monitoring for Improvement

- Though not routinely done in practice, you can assess for empiric antibiotic response with repeat paracentesis
  - 2 days after antibiotic initiation
  - Expect a 25% decrease in PMN from baseline
- Lack of PMN decrease may indicate antibiotic failure, and broader antibiotic therapy may be needed

Biggins, et al. 2021 Practice Guidance. Hepatol 2021.

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Prevention of Recurrent SBP

- Once a patient with cirrhosis has developed SBP, they are at increased risk for redevelopment (secondary prevention)
- Individuals who have had an episode of SBP should be provided prophylactic antibiotics to prevent the development of an additional episode

"SECONDARY" PREVENTION	
Antibiotics	•Norfloxacin (no longer available in US), Ciprofloxacin, or Bactrim •Bactrim: 1 DS tablet daily •Ciprofloxacin: 500mg daily
Monitoring	•Bactrim: renal function, hyperkalemia, DDI's •Ciprofloxacin: renal dose adjustments, QTc monitoring

Biggins, et al. 2021 Practice Guidance. Hepatol 2021.

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Varices

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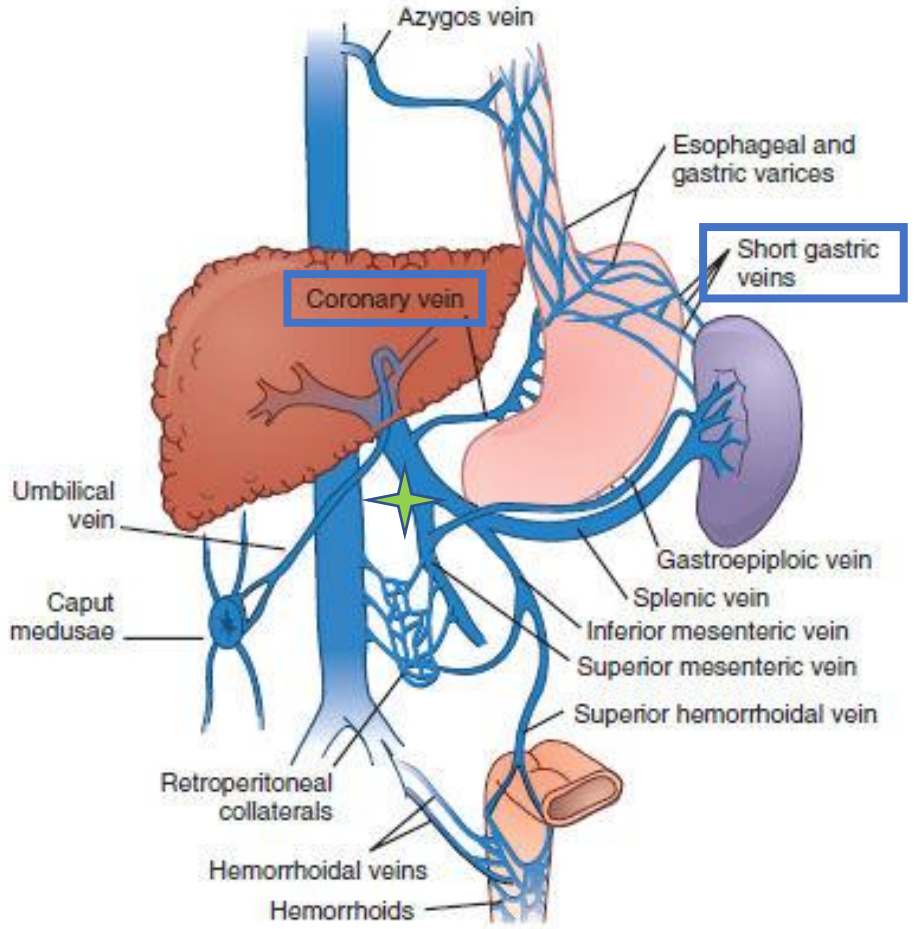
Portal Hypertension Revisited

- Increased structural resistance
  - Fibrous tissue
  - Vascular distortion
- Intrahepatic vasoconstriction
  - Decreased nitric oxide bioavailability
- Splanchnic arterial vasodilation



http://www.surgicalcore.org

Portosystemic collaterals

Garcia-Tsao G, et al. Am J Gastroenterol 2017.

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Varices: Pathophysiology

Portal hypertension causes resistance to drainage

Superficial vessels (varices) develop to accommodate overload

Varices are weak and easily disrupted

Garcia-Tsao G, et al. Am J Gastroenterol 2017.

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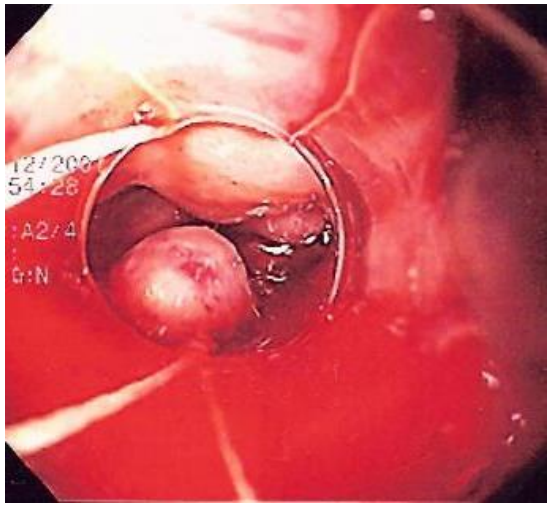
Risk of Variceal Bleed

- Varices can be categorized into high verus low risk
  - High risk includes:
    - Medium and large varices
    - Small varices with red wale marks (indicating high risk of bleed)



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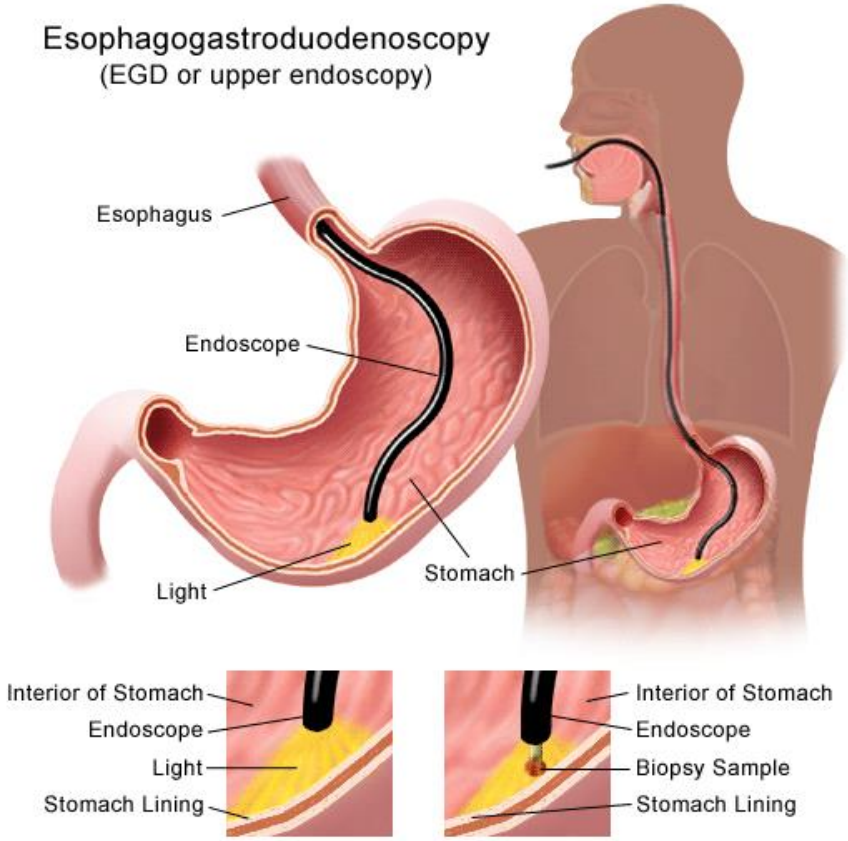
Esophagogastroduodenoscopy



- Abbreviated EGD
- Identifies presence of varices
  - Will also be used to identify sources of gastric bleeding
- Can be used to preemtively eliminate varices, as well as treat those that are bleeding

Garcia-Tsao G, et al. Am J Gastroenterol 2017.

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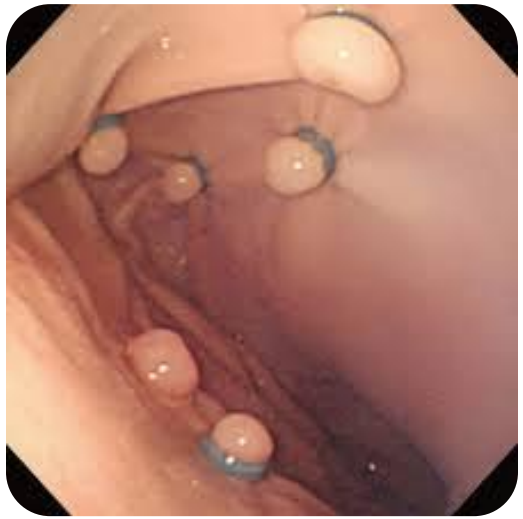
Primary Prevention of a Bleed

- Recommended for patients with medium/large varices at high risk for bleeding
  - First line → nonselective β-blockers
  - Alternative → endoscopic variceal ligation (EVL)



Garcia-Tsao G, et al. Am J Gastroenterol 2017.

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Primary Prevention of Variceal Hemorrhage

Therapy	Dosing	Goals
Propranolol	• No ascites = Max 320 mg • Ascites = Max 160 mg	HR of 55-60 Stop if SBP < 90
Nadolol	• No ascites = Max 160 mg • Ascites = Max 80 mg	HR of 55-60 Stop if SBP < 90

Carvedilol	• Regardless of Ascites:
	  • Max = 6.25 mg BID
	  *Unless hypertensive
		Stop if SBP < 90

OR		
EVL	• Every 2-8 weeks until elimination of varices	Variceal eradication

Garcia-Tsao G, et al. *Hepatology* 2017;65(1):310-335.
Ge PS, Runyin BA. Treatment of Patients with Cirrhosis. *N Engl J Med* 2016;327:767-77.

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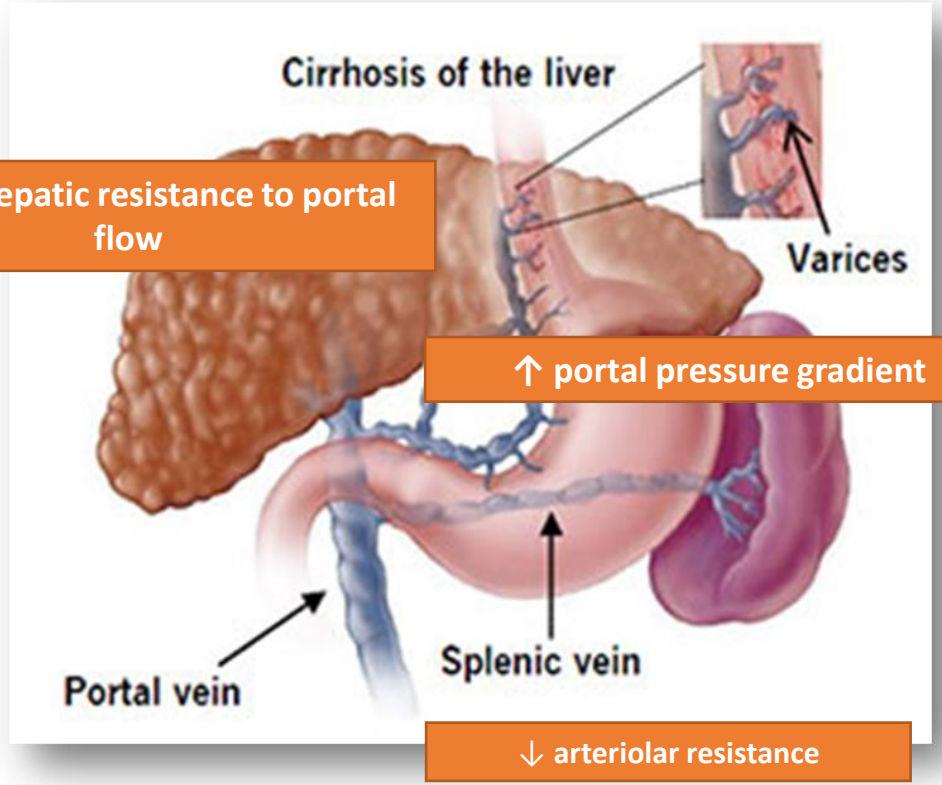
Recap of Mechanisms

Non- selective β blockers

- **β1 blockade:**
  - ↓ cardiac output and splanchnic blood flow
- **β 2 blockade:**
  - prevent splanchnic vasodilation mediated by β2 receptors, allowing unopposed α adrenergic effects
  - ↓ portal blood flow and ↑ vasoconstriction of splanchnic vascular bed

↑ intrahepatic resistance to portal flow

↑



↑ portal pressure gradient

↓ arteriolar resistance

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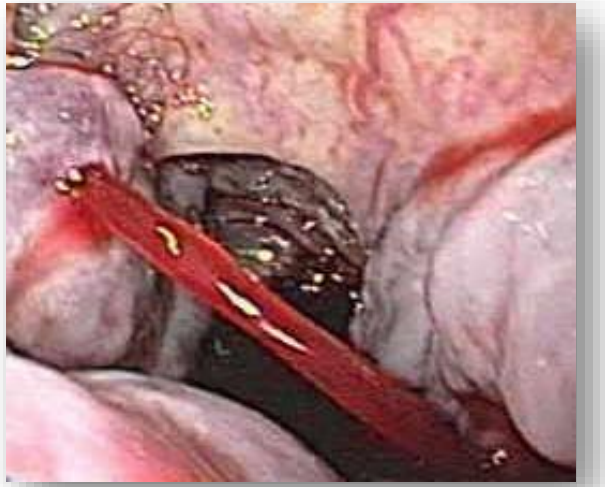
Acute Variceal Hemorrhage (VH)

- Goals:
  - Control bleeding
  - Maintain hemodynamic stability
  - Prevent rebleed
  - Prevent acute complications



Garcia-Tsao G, et al. Am J Gastroenterol 2017.

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Management of Acute Variceal Bleed

- Protect airway to prevent aspiration
- STAT EGD
  - Blakemore/tamponade if needed
- Modest blood transfusions & fluid resuscitation
  - Goal Hgb >7g/dL
  - Too much can increase portal pressure, ascites, and risk of hemorrhage
- Hold inappropriate home medications
  - Beta blockers
  - Anti-hypertensives
  - NPO if severe bleed
- Start appropriate pharmacotherapy

Garcia-Tsao G, et al. Am J Gastroenterol 2017.

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Pharmacotherapy for VH

- Octreotide
- Antibiotics
- IV PPI

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Octreotide

- Local splanchnic vasoconstrictor
  - Decreases blood to the variceal bleed by “clamping down” the vasculature
- Associated with lower 7-day mortality, but limited data

Agent	Dose	Duration	Monitoring
Octreotide	- 50 mcg bolus (can be repeated x1) - 50 mcg/hr continuous infusion	- 24-72 hours after bleeding has stopped - Maximum 5 days	NA

Garcia-Tsao G, et al. Am J Gastroenterol 2017.

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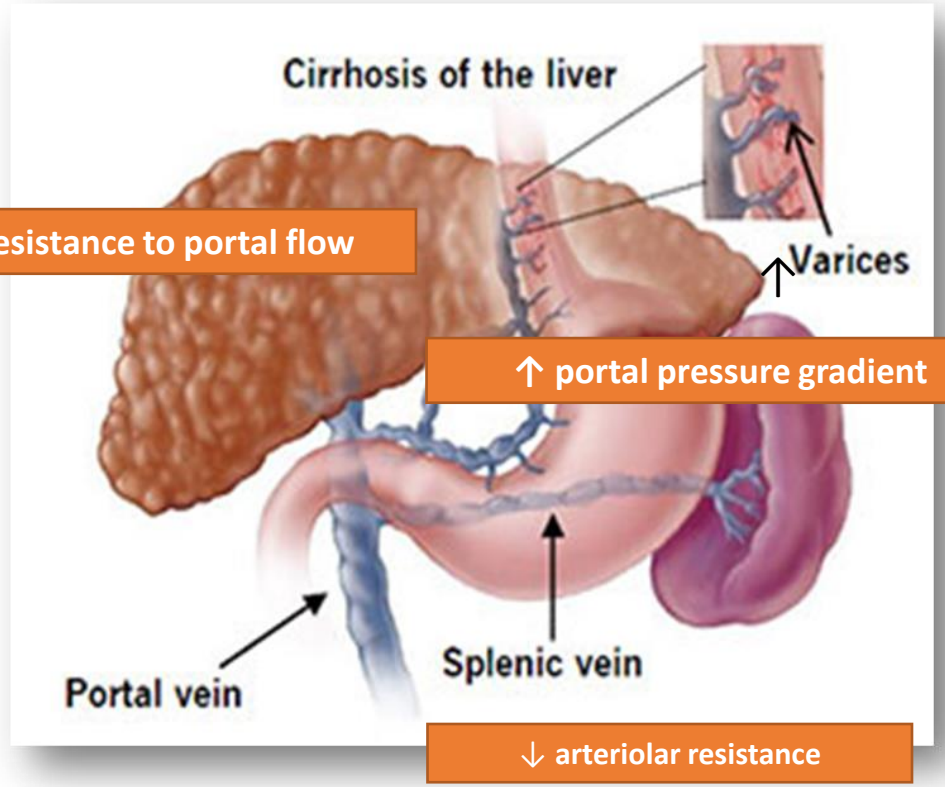
Recap of Mechanisms

↑ intrahepatic resistance to portal flow



↑ portal pressure gradient

↓ arteriolar resistance

Octreotide

- ↑ vasoconstriction of splanchnic bed
- ↓ portal venous pressure
- ↓ splachnic blood flow

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Antibiotics

- With high pressure bleed → increased risk of bacterial infection
  - Use of prophylactic antibiotics to prevent infection in the setting of VH
  - Decreased risk of infection, recurrent hemorrhage, and death
- Given bleeding, IV route is preferred
  - Antibiotics: Ceftriaxone 1g q24 hours
  - Duration: Maximum of 7 days
- Ceftriaxone dosing for infection prevention (1g q24 hours) is different than that of SBP treatment (2g q24 hours)
- Once patients have recovered from a bleed, there is a need to prevent recurrent bleed

Garcia-Tsao G, et al. Am J Gastroenterol 2017.

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Secondary Prevention of Variceal Hemorrhage (Preventing Rebleed)

Therapy	Dosing	Goals
Propranolol	• No ascites = Max 320 mg • Ascites = Max 160 mg	HR of 55-60 Stop if SBP < 90
Nadolol	• No ascites = Max 160 mg • Ascites = Max 80 mg	HR of 55-60 Stop if SBP < 90
WITH		
EVL	• Every 1-4 weeks until elimination of varices	Variceal eradication Prevention of VH

Garcia-Tsao G, et al. Am J Gastroenterol 2017.

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The Beta Blocker Controversy in Patients with Cirrhosis

- Initially found to be beneficial, thought to decrease risk of bleed as well as rebleed after recovery from a variceal hemorrhage
- Conflicting evidence emerged in the 2000's
  - Are we doing harm with beta blockers in patients with cirrhosis?
- Piecing out the evidence

Garcia-Tsao G, et al. Am J Gastroenterol 2017.

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Propranolol for prevention of recurrent gastrointestinal bleeding in patients with cirrhosis - A controlled study

Design	• Randomized controlled trial • Propranolol arm (n=38); placebo arm (n=36)
Population	• Cirrhosis, admitted for GI bleed and stabilized
Results	• Propranolol group = 96% free of recurrent GI bleed at 1 year • Placebo group = 50% free of recurrent GI bleed at 1 year • $P < 0.0001$
Conclusion	• Propranolol is effective in preventing recurrent GI bleeding in patients with cirrhosis

Lebrec, D. et al. *N Eng J Med* 1981;305:1371–1374.

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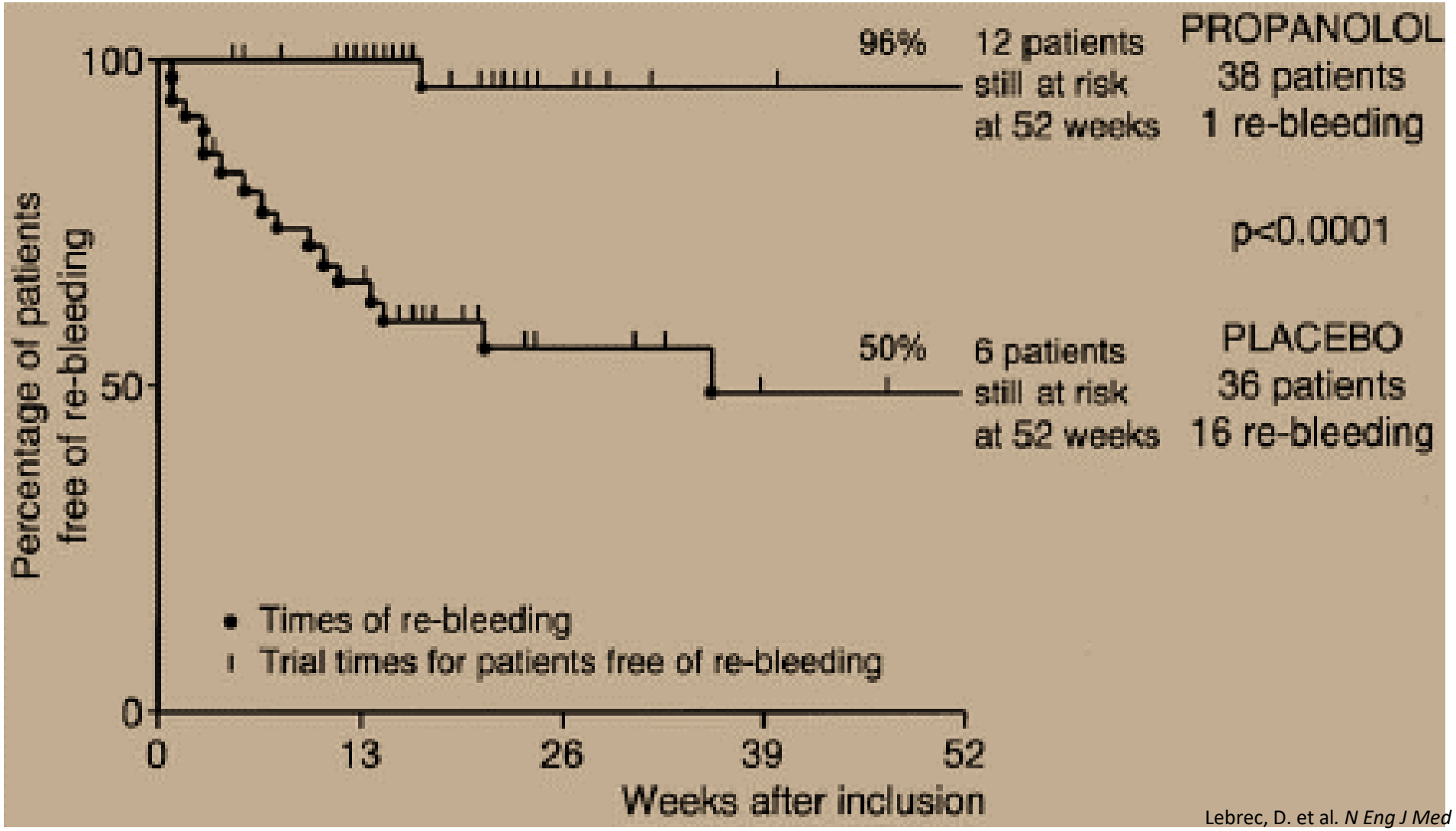
Lebrec et al.



Lebrec, D. et al. *N Eng J Med* 1981;305:1371–1374.

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Harm With Beta Blockers

Author	Patients	Design	Outcome	Results
Serste 2010	Refractory ascites (n=151)	Case-control	1 year survival	19% propranolol vs 64% no propranolol, NNH = 2
Serste 2011	Refractory ascites (n=10)	Crossover	Paracentesis induced circulatory dysfunction (PICD)	8 patients developed PICD on propranolol, 1 patient developed PICD after propranolol discontinued
Mandorfer 2014	Patients receiving paracentesis (n=607)	Retrospective	Transplant free survival	Subanalysis - patients with SBP had increased risk of death if receiving beta blocker (HR 1.58, CI 1.098-2.274)

Sersté *et al. Hepatology*. 2010;52(3

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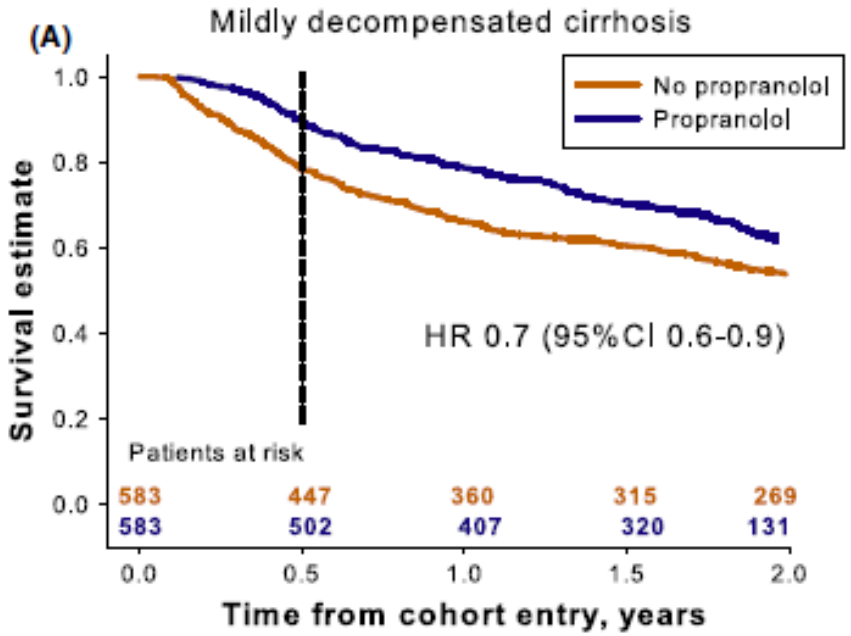
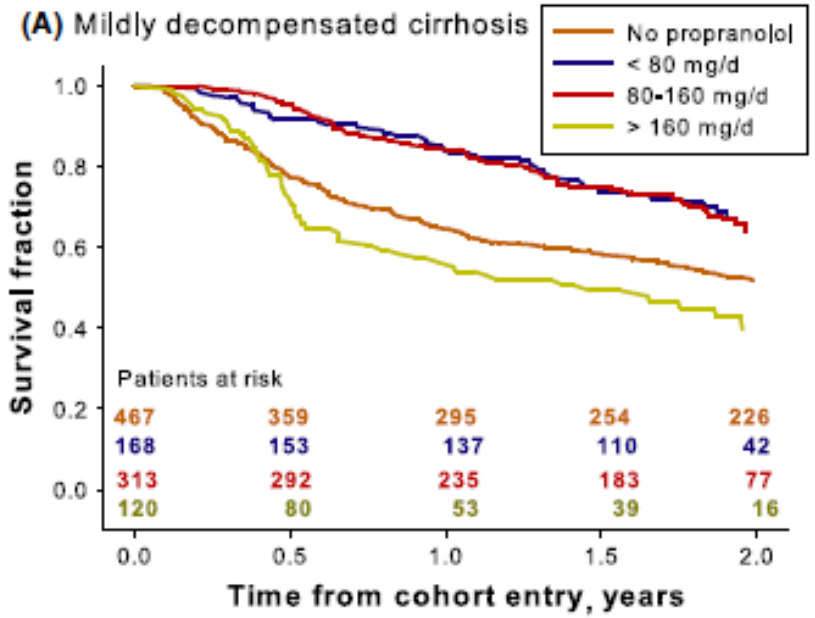
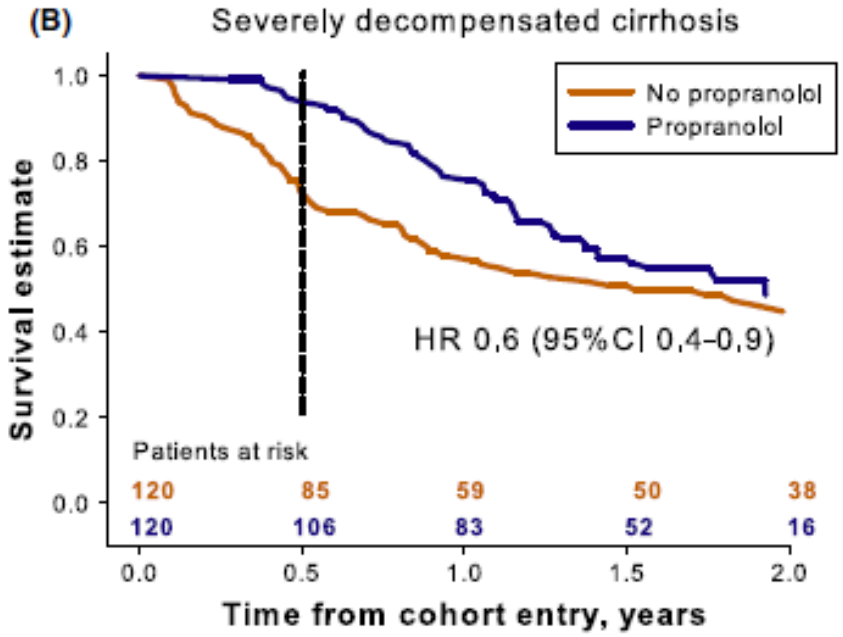
Benefit with Beta Blockers

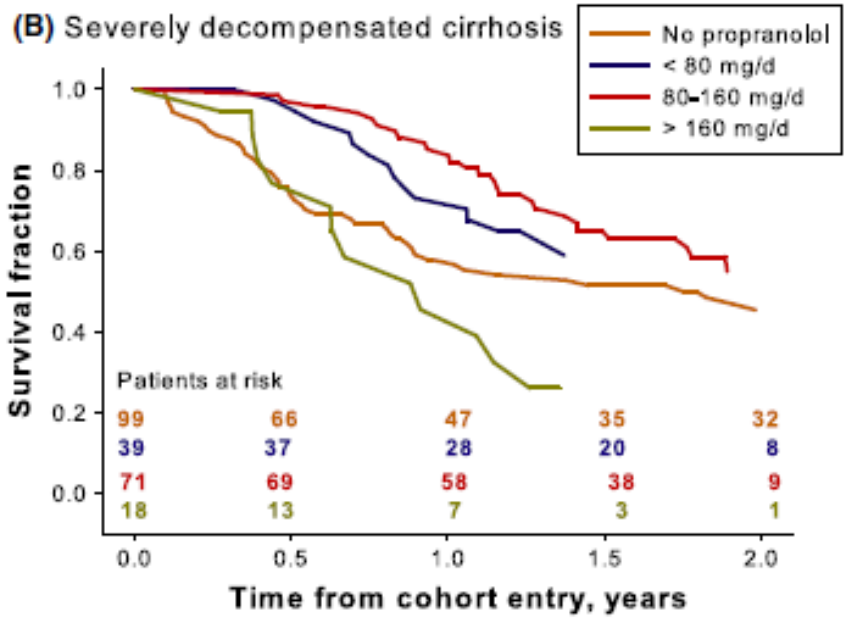
Author	Patients	Design	Outcome	Results
Leithead 2015	Cirrhosis (n=322)	Retrospective	Mortality	Beta blockers were associated with decreased mortality in overall analysis and in subgroup analysis of patients with refractory ascites (HR 0.35, CI 0.14 to 0.86)
Bossen 2016	Cirrhosis with ascites (n=1198)	Retrospective	Mortality	Beta blockers were associated with no difference in mortality in overall analysis and in subgroup analysis of patients with refractory ascites
Bang 2016	Decompensated cirrhosis (n=3719)	Retrospective	Mortality	Propranolol was associated with decreased mortality when used at doses less than 160 mg/day (HR 0.7, CI 0.6-0.9)

Leithead *et al*. *Gut*. 2015


(A)
Mildly decompensated cirrhosis
No propranolol
Propranolol
Survival estimate
HR 0.7 (95%CI 0.6-0.9)
Patients at risk
583 447 360 315 269
583 502 407 320 131
Time from cohort entry, years


(A) Mildly decompensated cirrhosis
No propranolol
< 80 mg/d
80-160 mg/d
> 160 mg/d
Survival fraction
Patients at risk
467 359 295 254 226
168 153 137 110 42
313 292 235 183 77
120 80 53 39 16
Time from cohort entry, years


(B)
Severely decompensated cirrhosis
No propranolol
Propranolol
Survival estimate
HR 0,6 (95%CI 0,4-0,9)
Patients at risk
120 85 59 50 38
120 106 83 52 16
Time from cohort entry, years


(B) Severely decompensated cirrhosis
No propranolol
< 80 mg/d
80-160 mg/d
> 160 mg/d
Survival fraction
Patients at risk
99 66 47 35 32
39 37 28 20 8
71 69 58 38 9
18 13 7 3 1
Time from cohort entry, years

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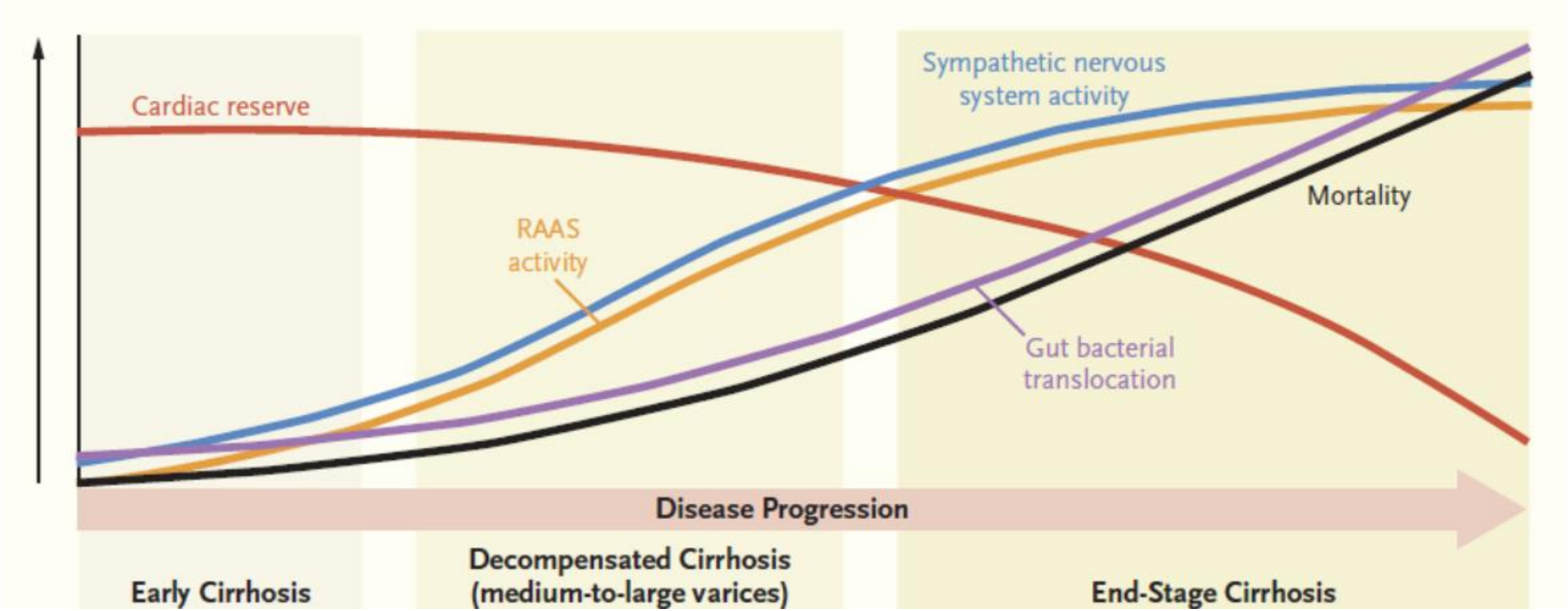
The Window Hypothesis



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The Window Hypothesis

- Early Cirrhosis
  - Beta blockers not indicated
  - Cardiac reserve, SNS activity, and RAAS activity at baseline
  - Low risk of SBP
- Decompensated Cirrhosis (Medium to Large Varices)
  - BB indicated for primary and secondary prophylaxis of VH
  - Decreased cardiac reserve, increased SNS and RAAS
  - Increased risk of SBP
- End-Stage Cirrhosis
  - BB decrease survival
  - Cardiac reserve critically impaired, SNS and RAAS maximally stimulated
  - Easy gut bacteria translocation

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Discontinuation of Beta Blockers

- Refractory ascites
- Systolic BP < 100 mmHg
- Mean arterial pressure ≤ 82 mmHg
- Serum sodium < 120 mEq
- Severe alcoholic hepatitis
- HRS
- SBP
- Sepsis
- Poor follow up or nonadherence
- AKI

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Hepatic Encephalopathy

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Hepatic Encephalopathy (HE)

- Spectrum of neuropsychiatric and psychometric abnormalities
- Often diagnosed by clinical observation after excluding other possible causes
- Significant contributor to morbidity, mortality, and healthcare costs

Suraweera D et al. Gut Liver 2016.

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Ammonia Hypothesis

Hyperammonemia

Glutamine accumulation in brain

Osmotic stress

Astrocytes in brain swell and malfunction

Suraweera D et al. Gut Liver. 2016.

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Hepatic Encephalopathy

Signs	Additional Considerations/Differentials
• Changes in sleep/wake cycles • Aggression • Confusion • Asterixis • Cognitive Defects	• Infection • Electrolyte disturbances • Sedatives • Dehydration • Medication non-adherence

Suraweera D, et al. Gut Liver. 2016.

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HE Treatment

Therapy	Mechanism	Dosing
	1ST LINE THERAPY	
Lactulose	Non-absorbable disaccharide	Initial: 25mL q1-2h until first bowel movement Maintenance: Titrate to maintain 2-3 bowel movements per day
	ADJUNCT	
Rifaximin	Antibiotic alters gut flora, reduces ammonia producing bacteria	Maintenance: 550 mg BID
	2ND LINE THERAPY	
	Transplant	

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Lactulose MOA

Broken into short chain fatty acid by colonic bacteria → pH ↓ in colon → $NH_3 \rightarrow NH_4^+$

- Releases hydrogen ions → bind to ammonia, creating ammonium
  - Positively charged and unable to cross the cell membrane to enter the bloodstream
- Produces an osmotic effect causing rapid laxation

Vistrup et al, Hepatology. 2014.

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Lactulose Adverse Effects

- Gastrointestinal:
  - Bloating
  - Abdominal cramping
  - Flatulence
  - Nausea/vomiting
  - Diarrhea
- Electrolyte imbalances:
  - ↑ Na+
  - ↓ K+

Vistrup et al, Hepatology. 2014.

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Hepatorenal Syndrome (HRS)

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Diagnosis

- Main etiologies for acute kidney injury (AKI) in cirrhosis
  - Prerenal
    - Hypovolemia
    - HRS-AKI (previously type 1 and 2)
  - Acute tubular necrosis (ATN)
    - Typically due to sepsis
    - Less commonly due to medications
- All other causes of AKI must be excluded before a diagnosis of HRS can be made
  - Differentiating between these is difficult and requires careful work up of all the above causes

Biggins, et al. 2021 Practice Guidance. Hepatol 2021.

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Treatment

Therapy	Dosing
First Line Recommendations	
Albumin	- 1g/kg day 1, followed by 40-50g daily
Vasopressors	- Terlipressin is preferred, but not available in the US (pending FDA approval) - In place of terlipressin, norepinephrine may be used
Alternatives	
Octreotide	- 100-200 mcg subcutaneously TID
Midodrine	- 5-15mg orally TID

Biggins, et al. 2021 Practice Guidance. Hepatol 2021.

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Summary

- Cirrhosis is a complex, progressive disease state that disproportionately effects underserved patients
- Complications of cirrhosis occur as a result of the development of portal hypertension
- Treatment for the complications of cirrhosis vary by complication, and are typically aimed and decreasing mortality and preventing complication recurrence

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Questions?

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Acute Complications of Cirrhosis

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