Acute Complications of Liver Disease

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Financial disclosure

- Nothing to disclose concerning possible financial or personal relationships with commercial entities (or their competitors) that may be referenced in this presentation

Objectives

- Define the various types of liver failure (including epidemiology, pathophysiology, and etiology) and the complications that may arise due to hepatic impairment
- Discuss the effects of ascites and portal hypertension and the management of related complications, including: spontaneous bacterial peritonitis, hemodynamic alterations, hepatorenal syndrome, and variceal hemorrhage
- Review the pathophysiology of coagulopathy and encephalopathy related to hepatic impairment and important treatment considerations for such

Cirrhosis

- Diffuse process characterized by replacement of normal liver tissue by fibrosis and regenerative nodule formation
  - Liver fibrosis leads to distortion of the hepatic vasculature
- Most common causes include: alcoholic liver disease, hepatitis B/C, nonalcoholic steatohepatitis
- Prevalence in the U.S. estimated at ~630,000

Lee S, et al. Wiley-Blackwell; 2015. p 3
Scaglione S, et al. *Journal of Clinical Gastroenterology*. 2015;49(8):690-696
Schuppan D, et al. *Lancet*. 2008;371(9615):838-851

Cirrhosis

- Classified as compensated or decompensated
- Decompensated cirrhosis is complicated by one or more of the following:
  - Jaundice
  - Ascites (+/- hepatorenal syndrome, hyponatremia, spontaneous bacterial peritonitis)
  - Hepatic encephalopathy
  - Variceal bleeding
- Median survival time:
  - >12 years (compensated)
  - ~2 years (decompensated)

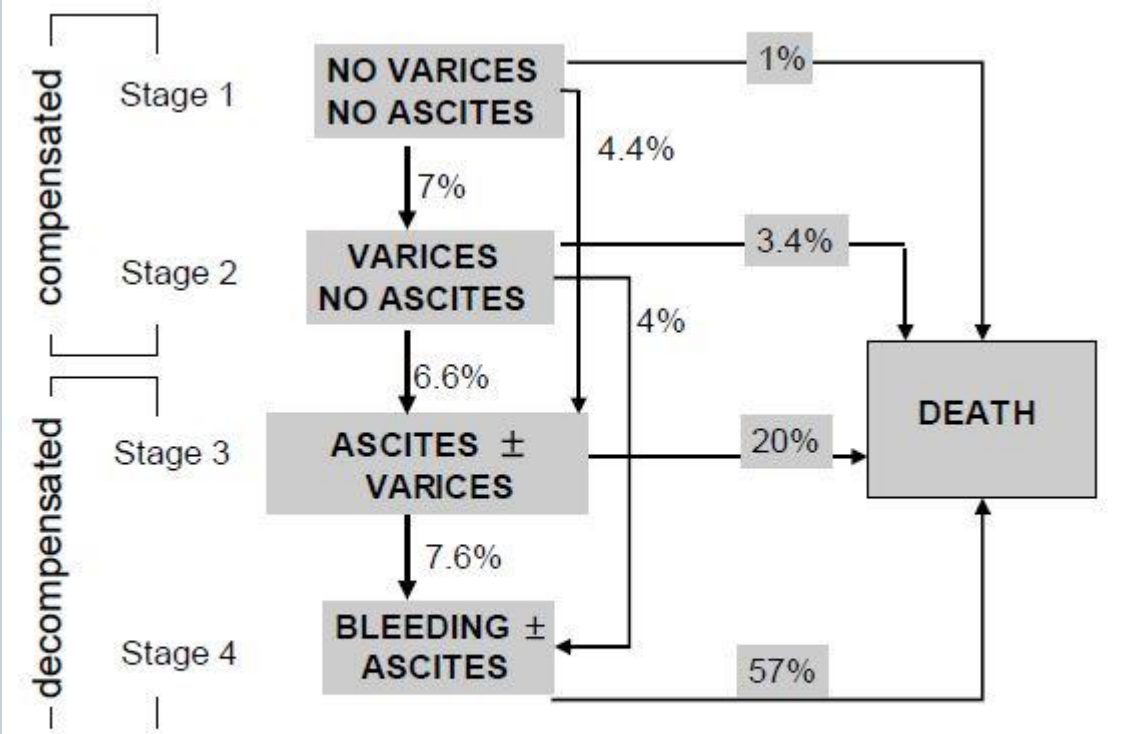


Fig. 4. Clinical course of cirrhosis: 1-year outcome probabilities according to clinical stages.

D'Amico G, et al. *Journal of Hepatology*. 2006;44(1):217-231.
Lee S, et al. Wiley-Blackwell; 2015. p

Acute liver failure (ALF)

Definition	Severe injury to liver cells which leads to altered coagulation and mentation in the absence of pre-existing liver disease
Incidence	2-3,000 cases per year in the U.S.
Timing	Hyperacute: clinically detectable within 6-36 hours Acute/subacute: 7 days to 24 weeks
Precipitating factor	Hyperacute: acetaminophen, ischemia Acute/subacute: idiosyncratic DILI, autoimmune hepatitis, viral hepatitis
Prognosis	~30% mortality; hyperacute liver injuries have better short-term survival than acute/subacute

Stravitz RT, Lee WM. Acute liver failure. *Lancet*. 2019;394(10201):869-881

Acute-on-chronic liver failure (ACLF)

APASL	EASL-CLIF	NACSELD
Acute hepatic insult manifesting as jaundice (bilirubin ≥5 mg/dL) and coagulopathy (INR ≥1.5) complicated within 4 weeks by clinical ascites and/or hepatic encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease/cirrhosis and is associated with a high 28-day mortality	Specific syndrome in patients with cirrhosis that is characterized by acute decompensation, organ failure, and high short-term mortality	Presence of at least 2 severe extrahepatic organ failures including shock, grade III/IV hepatic encephalopathy, renal replacement therapy, or mechanical ventilation

APASL, Asian Pacific Association for the study of the Liver; EASL-CLIF, European Association for the Study of the Liver-Chronic Liver Failure; NACSELD, North American Consortium for the Study of End-Stage Liver Disease

Bajaj JS, et al. *Am J Gastroenterol*. 2022;117(2):225-252.

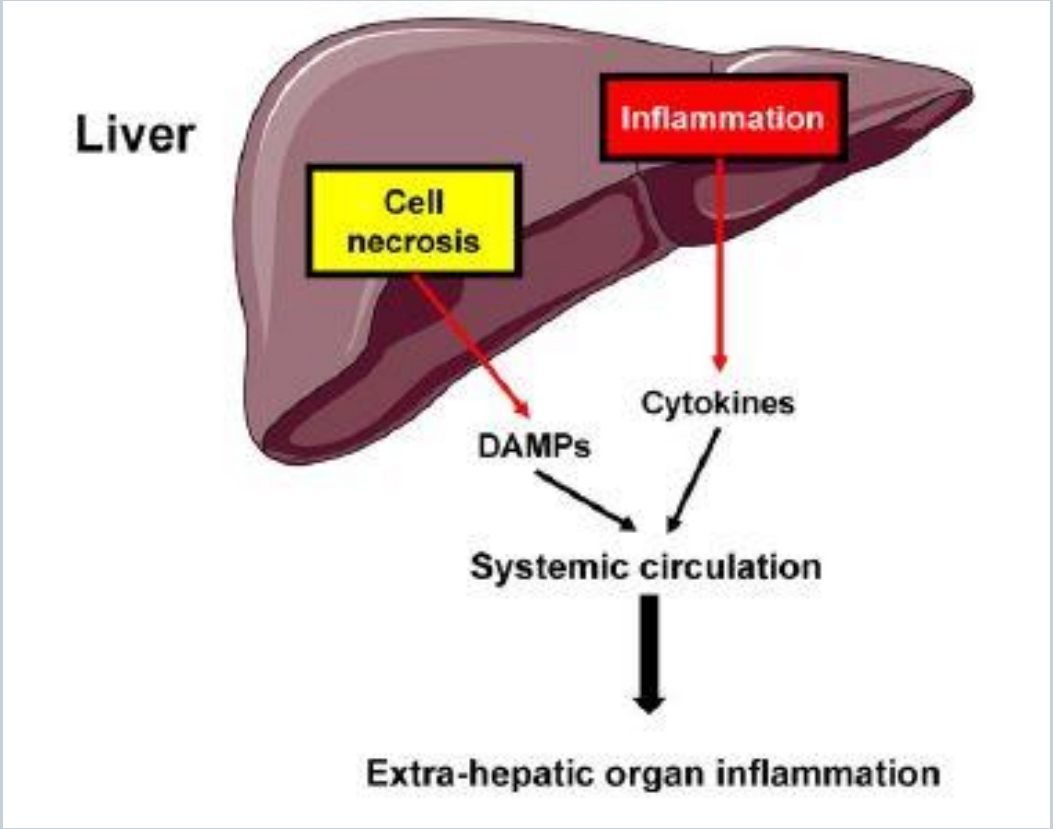
WGO definition of ACLF

- Syndrome in patients with chronic liver disease with or without previously diagnosed cirrhosis associated with increased mortality up to three months
- Characterized by acute hepatic decompensation resulting in liver failure
  - (jaundice and prolongation of the international normalized ratio or INR)
- One or more extrahepatic organ failures

Bajaj JS, et al. *Hepatology*. 2018;68(4):1621-1632

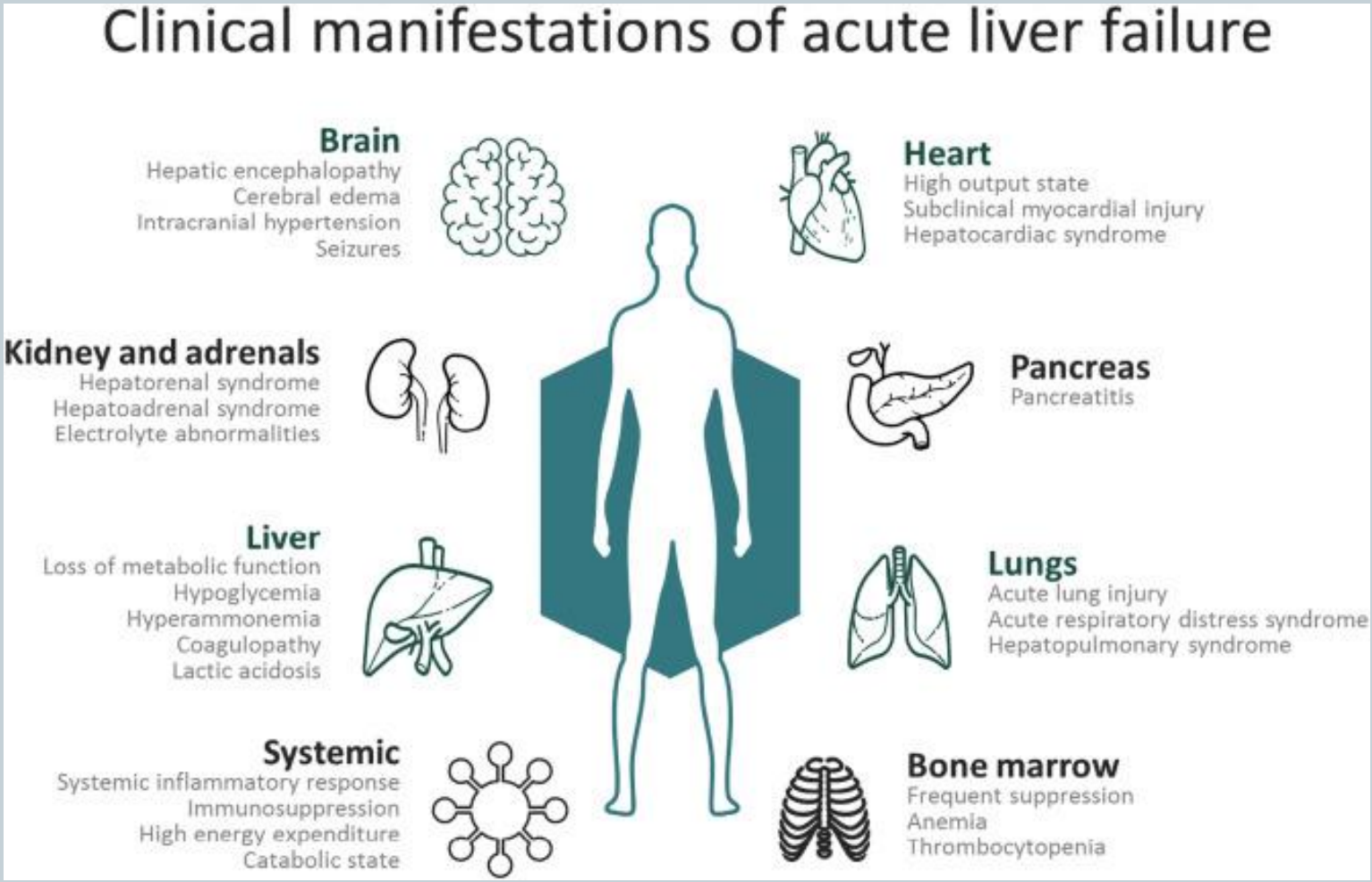
ACLF

Incidence	Occurs in 10-30% hospitalized patients with cirrhosis
Precipitating Factor	Infection, alcohol-associated hepatitis, DILI, viral hepatitis, surgery
Mechanism of injury	Thought to be heavily related to inflammation that originates in the liver and manifests systemically. Gut dysbiosis thought to contribute to inflammation of the liver
Prognosis	90-day mortality >50%



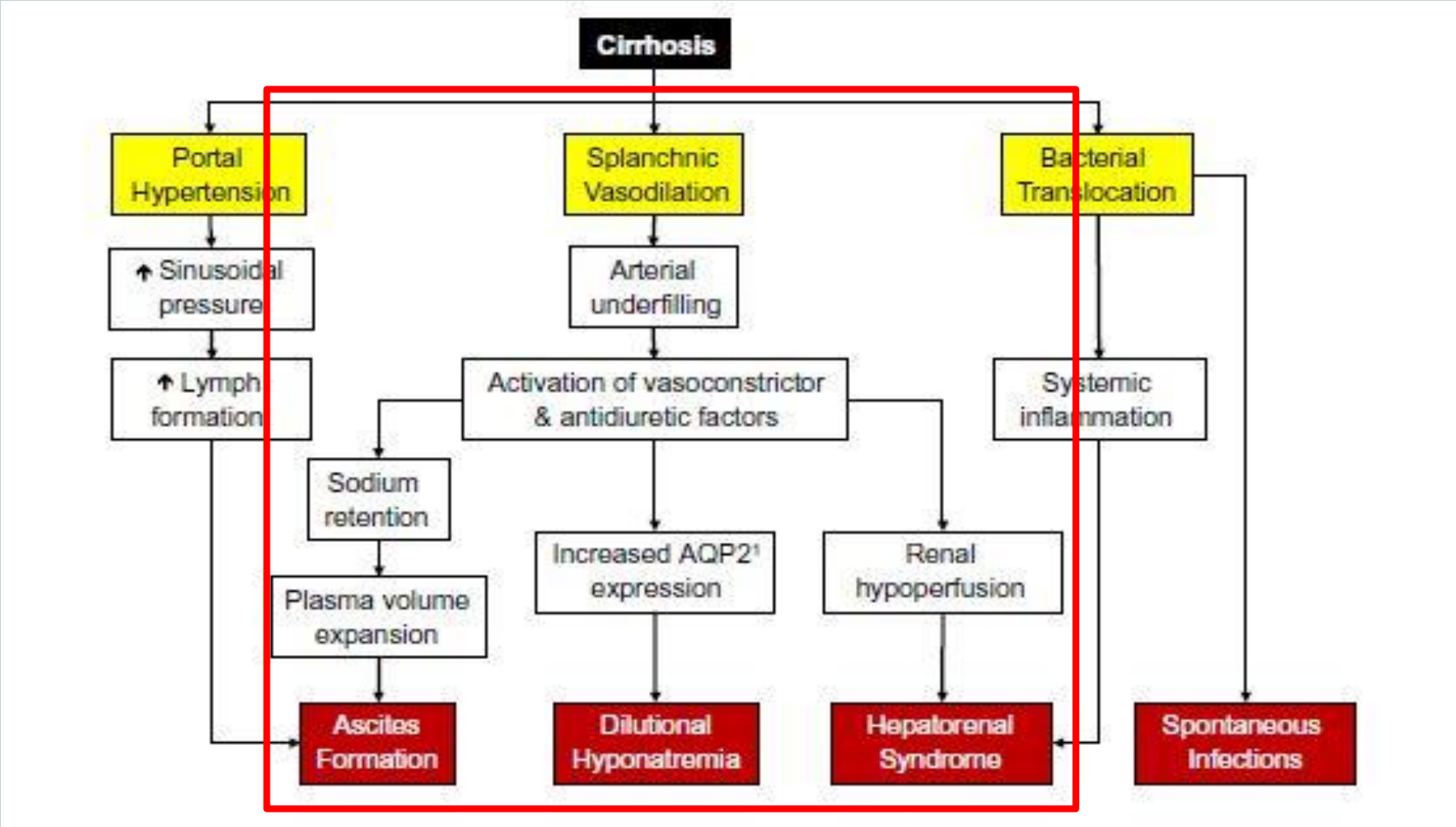
Bajaj JS, et al. *Am J Gastroenterol*. 2022;117(2):225-252.
Bajaj JS, et al. *Hepatology*. 2018;68(4):1621-1632
Mahmud N, et al. *Hepatology*. 2019;69(5):2150-2163

Consequences of Hepatic Failure



http://www.emdocs.net/acute-liver-failure-evidence-based-evaluation-and-management/

Pathophysiology of cirrhosis complications



Ascites

- Abnormal abdominal fluid collection
- Cirrhosis is most common cause
  - Could also be due to malignancy, heart failure, tuberculosis, and pancreatic disease
- Commonly the first decompensating event
- Development of ascites associated with a reduction in 5-year survival from 80% to 30%

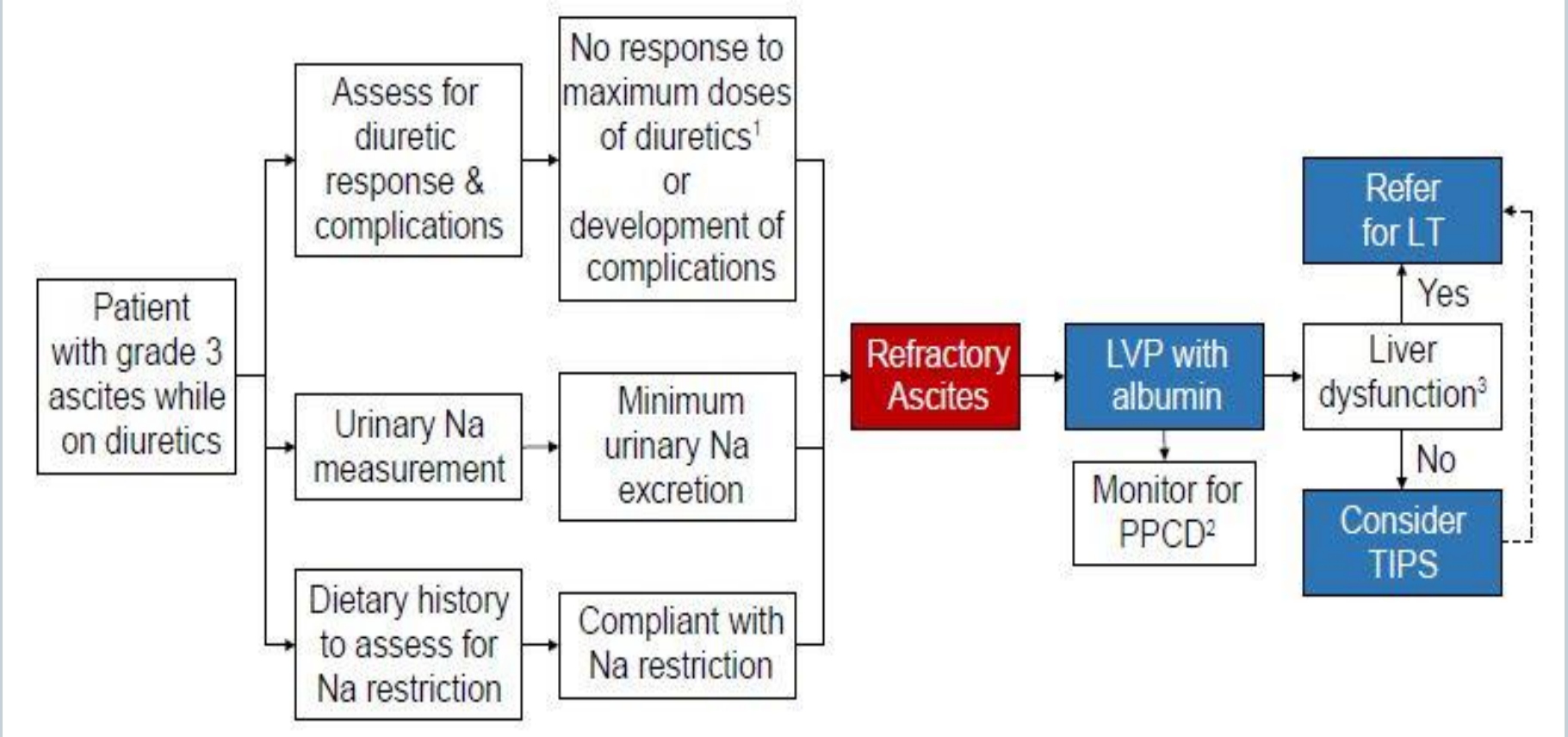
Biggins SW, et al. *Hepatology*. 2021;74(2):1014-1048

Classification of ascites

According to Amount of Fluid Accumulation		According to the Response to Treatment	
Grade 1. Mild ascites	Only detected by ultrasound	Responsive ascites	Ascites that can be fully mobilized or limited to grade 1 with diuretic therapy associated or not to moderate dietary sodium restriction
Grade 2. Moderate ascites	Moderate symmetric distension of abdomen	Recurrent ascites	Ascites that recurs on at least 3 occasions within a 12-month period despite dietary sodium restriction and adequate diuretic dosage
Grade 3. Large or gross ascites	Marked distension of the abdomen	Refractory Ascites	Ascites that cannot be mobilized or the early recurrence of which (i.e., after LVP) cannot be satisfactorily prevented by medical therapy

Biggins SW, et al. *Hepatology*. 2021;74(2):1014-1048

Treatment algorithm for Grade 3 ascites



Refractory ascites treatment

- Large-volume paracentesis (LVP) is initial treatment of choice
- Albumin crucial to prevent further reduction of effective arterial blood volume, which may precipitate postparacentesis circulatory dysfunction (PPCD)
  - Clinical manifestations of PPCD include: renal impairment (including hepatorenal syndrome), dilutional hyponatremia, hepatic encephalopathy, and death
- If more than 5 L of ascites fluid is removed, administer albumin dosed at 8 g for every liter of fluid removed
  - Ex. Administer 48 g of albumin if removing 6 L of ascitic fluid

Biggins SW, et al. *Hepatology*. 2021;74(2):1014-1048

Hyponatremia

- Classified as mild (126-135 mEq/L), moderate (120-125 mEq/L), or severe (<120 mEq/L)
- Most commonly hypervolemic hyponatremia
  - Hypovolemic hyponatremia can occur due to poor oral intake or from urinary/GI losses related to excess diuretic or laxative treatment
- Hyponatremia reflects worsening hemodynamic status as cirrhosis advances
  - Patients with Na <130 mEq/L are at increased risk for developing hepatic encephalopathy, hepatorenal syndrome, and spontaneous bacterial peritonitis

Biggins SW, et al. *Hepatology*. 2021;74(2):1014-1048

Treatment of hyponatremia

- Acute hyponatremia (onset within 48 hours): less common; correct rapidly to prevent cerebral edema without concern for osmotic demyelenation syndrome
- Chronic hyponatremia: goal rate of Na increase is 4-6 mEq/L per 24 hour period, not to exceed 8 mEq/L
- Hypovolemic hyponatremia: discontinue diuretic and/or laxative; provide fluid resuscitation with 5% albumin or balanced crystalloid

Biggins SW, et al. *Hepatology*. 2021;74(2):1014-1048

Treatment of hyponatremia

Hypervolemic hyponatremia	
Severity	**Treatment options**
Mild (126-135 mEq/L)	Monitoring and water restriction

Moderate (120-125 mEq/L)
Severe (<120 mEq/L)
	• Water restriction to 1 L/day and albumin
	• Vasopressin receptor antagonists (vaptans)
	  • Raise Na during treatment but transient effect
	  • Only used for short term (≤30 days) due to hepatotoxicity
	• Hypertonic saline
	  • Reserved for short-term treatment of patients with symptomatic or severe hyponatremia
	  • Can worsen hypervolemia and ascites

Biggins SW, et al. *Hepatology*. 2021;74(2):1014-1048

Infection

- Bacterial infections are present in approximately one-third of patients with cirrhosis who are hospitalized
  - Common yet unique type of infection is “spontaneous” infections (occur in the absence of an obvious source)
    - Includes peritonitis (SBP), spontaneous bacteremia, and empyema (SBE)
    - Bacterial translocation and decreased host defenses thought to be the pathogenesis behind these infections
    - Typically monobacterial. ~60% are Gram-negative bacteria vs <5% fungal
      - Most common: E. coli, K. pneumoniae, S. aureus, E. faecalis, and E. faecium
      - Infections by MDRO represent 35% of overall infections in patients with cirrhosis
- Common precipitant of acute deterioration leading to worsening hepatic decompensation and multiorgan failure, with the kidney being the most commonly affected organ

Biggins SW, et al. *Hepatology*. 2021;74(2):1014-1048

SBP

- Diagnosis established with ascitic fluid absolute neutrophil count >250/mm^3
- Diagnostic paracentesis should be performed in patients with:
  - Tense ascites and AKI
  - Cirrhosis and ascites hospitalized emergently for any reason

Biggins SW, et al. *Hepatology*. 2021;74(2):1014-1048

SBP treatment (antibiotic considerations)

- 3rd generation cephalosporin (ceftriaxone, cefotaxime)
- Growing number of MDROs
  - Broad Gram-negative coverage if nosocomial infections or critically ill
  - Daptomycin if known VRE or evidence of GI colonization
  - Carbapenem if known to harbor MDR Gram-negative organism
- Diagnostic paracentesis should be performed at 48 hours to assess response
  - Negative response defined by a decrease in polymorphonuclear (PMN) cell count <25% from baseline- broaden antibiotics
- Duration of abx therapy 5-7 days
- In patients with bacterascites but PMN <250/mm3 and no signs of infection:
  - Should not receive antibiotics (most cases it self-resolves or is a contaminant)
- Secondary prophylaxis: ciprofloxacin or TMP-SMX

Biggins SW, et al. *Hepatology*. 2021;74(2):1014-1048

SBP treatment (albumin)

- Albumin improves survival and renal impairment in patients with cirrhosis and SBP
  - Plays an important role in preventing the progression of AKI
- Patients who most benefited from albumin in studies:
  - Evidence of renal dysfunction (BUM >30 mg/dL or creatinine >1 mg/dL)
  - Severe hepatic decompensation (bilirubin >5 mg/dL)
- Albumin 25% dose: 1.5 g/kg at day 1 and 1 g/kg at day 3

Biggins SW, et al. *Hepatology*. 2021;74(2):1014-1048
Salerno F, et al. *Clin Gastroenterol Hepatol*. 2013;11(2):123-130.e1.

Sepsis and septic shock

- Effective broad-spectrum abx should be administered within 1 hour of ICU admission
  - Every hour delay in administration is associated with almost doubling in mortality
  - Guidelines recommend empiric therapy with vancomycin and meropenem
- General treatment of sepsis/septic shock should be in accordance with Surviving Sepsis Campaign recommendations

Bajaj JS, et al. *Am J Gastroenterol*. 2022;117(2):225-252

Hemodynamics

- Hyperdynamic state: increased cardiac output, decreased systemic vascular resistance, reduction in arterial blood pressure
- Assessment of volume status and volume resuscitation with crystalloids and/or albumin
  - Albumin may be beneficial in this population, especially if serum albumin <3 mg/dL
  - Albumin 5% for rapid volume resuscitation vs 25% for sustained volume expansion
- Norepinephrine 1st line vasopressor
  - Vasopressin as add-on therapy
- Steroids
  - Adrenal insufficiency common in critically ill cirrhotic patients
  - Adjunct to fluid resuscitation and vasopressors
  - Hydrocortisone 50 mg Q6H

Bernal W, et al. *J Hepatol*. 2021; 75 Suppl1:S136-S177
Nanchal R, et al. *Critical Care Medicine*. 2020;48(3):e173-e191
MacDonald AJ, et al. *Curr Opin Crit Care*. 2020;26(2):171-179.

Renal dysfunction

- AKI complicates ALF in 70% of patients and requires RRT in 30%
  - Early RRT in ALF patients associated with improved outcomes
- Hepatorenal syndrome (HRS) is usually observed as a specific type of "functional" AKI but may also be associated with parenchymal damage
  - Defined as renal dysfunction that occurs because of reduced renal perfusion (due to hemodynamic alterations in arterial circulation), as well as overactivity of endogenous vasoactive systems
- Classifications of HRS have updated:
  - Type 1 HRS → HRS-AKI
  - Type 2 HRS → HRS-CKD

Stravitz RT, et al. *Lancet*. 2019;394(10201):869-881
Angeli P, et al. *J Hepatol*. 2019;71(4):811-822

HRS-AKI

Baseline SCr	1. Stable SCr ≤3 months 2. If not available, a stable SCr closest to the current one 3. If no previous SCr, use admission SCr
Definition of AKI	Increase in SCr of ≥0.3 mg/dL ≤48 hours or 50% increase from baseline
Staging	Stage 1: Increase in SCr of ≥0.3 mg/dL ≤48 hours OR increase in SCr ≥1.5-2 times from baseline Stage 2: increase in SCr ≥2-3 times from baseline Stage 3: increase in SCr ≥3 times from baseline OR SCr ≥4 mg/dL with an acute increase of 0.3 mg/dL OR initiation of RRT
HRS-AKI diagnostic criteria	1. Cirrhosis and ascites 2. Stage 2 or 3 AKI 3. No improvement of SCr after at least 48 hr of diuretic withdrawal and volume expansion with albumin 4. Absence of hypovolemic shock or severe infection requiring vasoactive drugs to maintain arterial pressure 5. No current or recent treatment with nephrotoxic drugs 6. Proteinuria <500 mg/day and no microhematuria

Bajaj JS, et al. *Am J Gastroenterol.* 2022;117(2):225-252.

HRS treatment

Treatment	Drug(s)	Dose	Comments
Vasoconstrictors	Terlipressin	1 mg IV Q6H; may increase to 2 mg IV Q6H if desired response* not met by day 4	Not approved in the U.S.
	Norepinephrine	0.5 mg/hr; titrate by 0.5 mg/hr every 4 hours, up to max of 3 mg/hr, for desired response**	
+	Octreotide / midodrine	Octreotide: 100-200 mcg SQ TID or 50 mcg/hr continuous IV infusion Midodrine: 5-10 mg TID	Can be administered outside ICU
Albumin	25% albumin	Day 1: 1 g/kg (100 g max) Day 2 through end of therapy: 20-50 g/day	Albumin alone has not proven to be effective but is used as adjunctive therapy

*SCr decreased <30% from baseline

**Increase in MAP ≥10 mmHg or increase in UOP >200 mL/4 hour

Pitre T, et al. *Critical Care Medicine*. 2022;50(10):1419-1429
Bernal W, et al. *J Hepatol*. 2021; 75 Suppl1:S136-S177
Valerio C, et al. *WJH*. 2016;8(7):345

HRS treatment considerations

- Vasoconstrictors maintained until SCr returns to baseline values up to 14 days
  - If SCr is at or above baseline after 4 days of maximum therapy, may discontinue
- Recent meta-analysis compared vasoconstrictors in HRS
  - Terlipressin: high certainty of evidence for HRS reversal
  - Norepinephrine: may reverse HRS but lower efficacy than terlipressin
  - Octreotide/midodrine: very low certainty of evidence for HRS reversal
- Only evidence with vasopressin is a small retrospective study comparing to octreotide

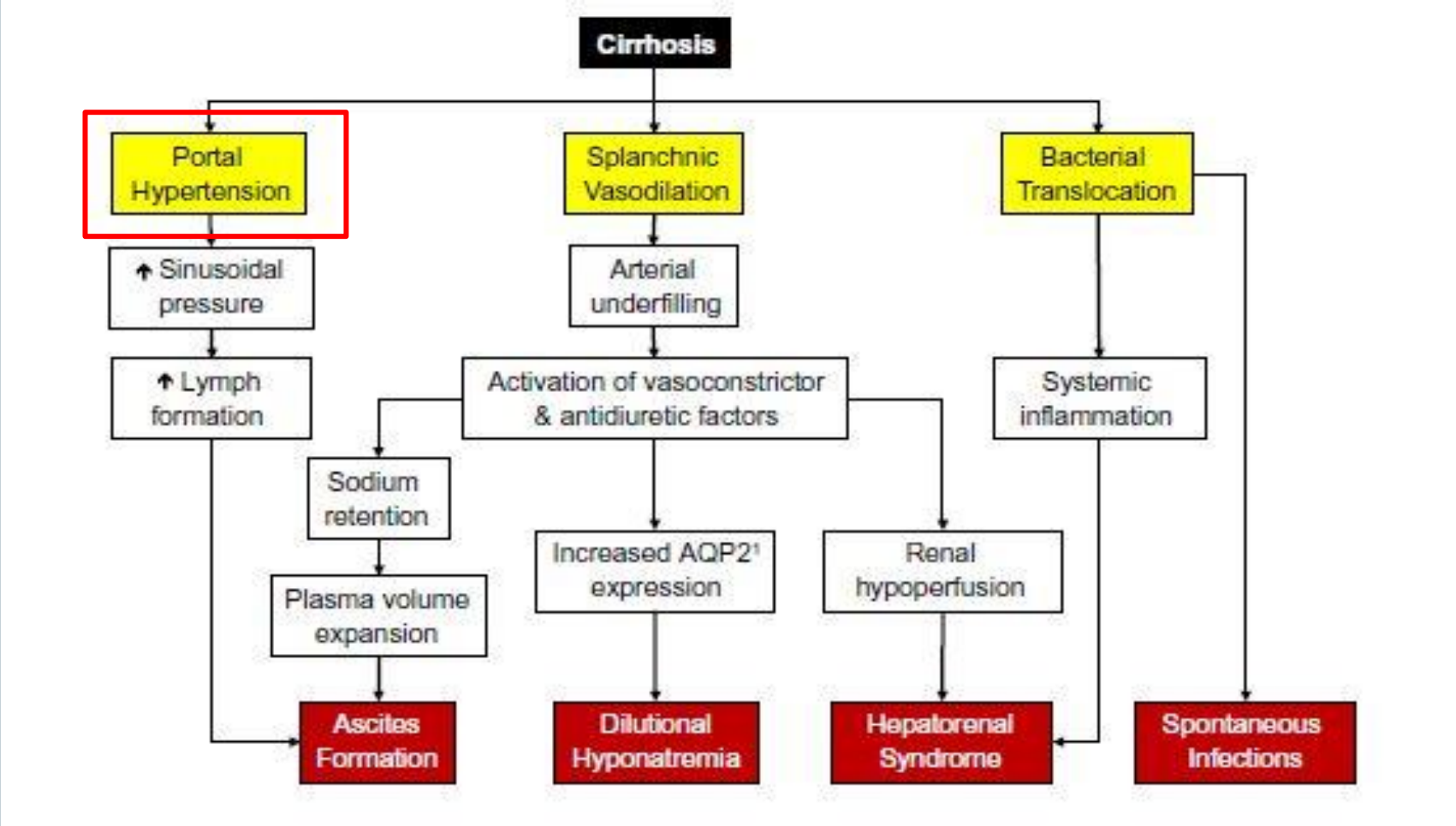
Pitre T, et al. *Critical Care Medicine*. 2022;50(10):1419-1429
Bernal W, et al. *J Hepatol*. 2021; 75 Suppl1:S136-S177
Kisher T, et al. *Nephrology Dialysis Transplantation*. 2005;20(9):1813-1820

Preventing AKI

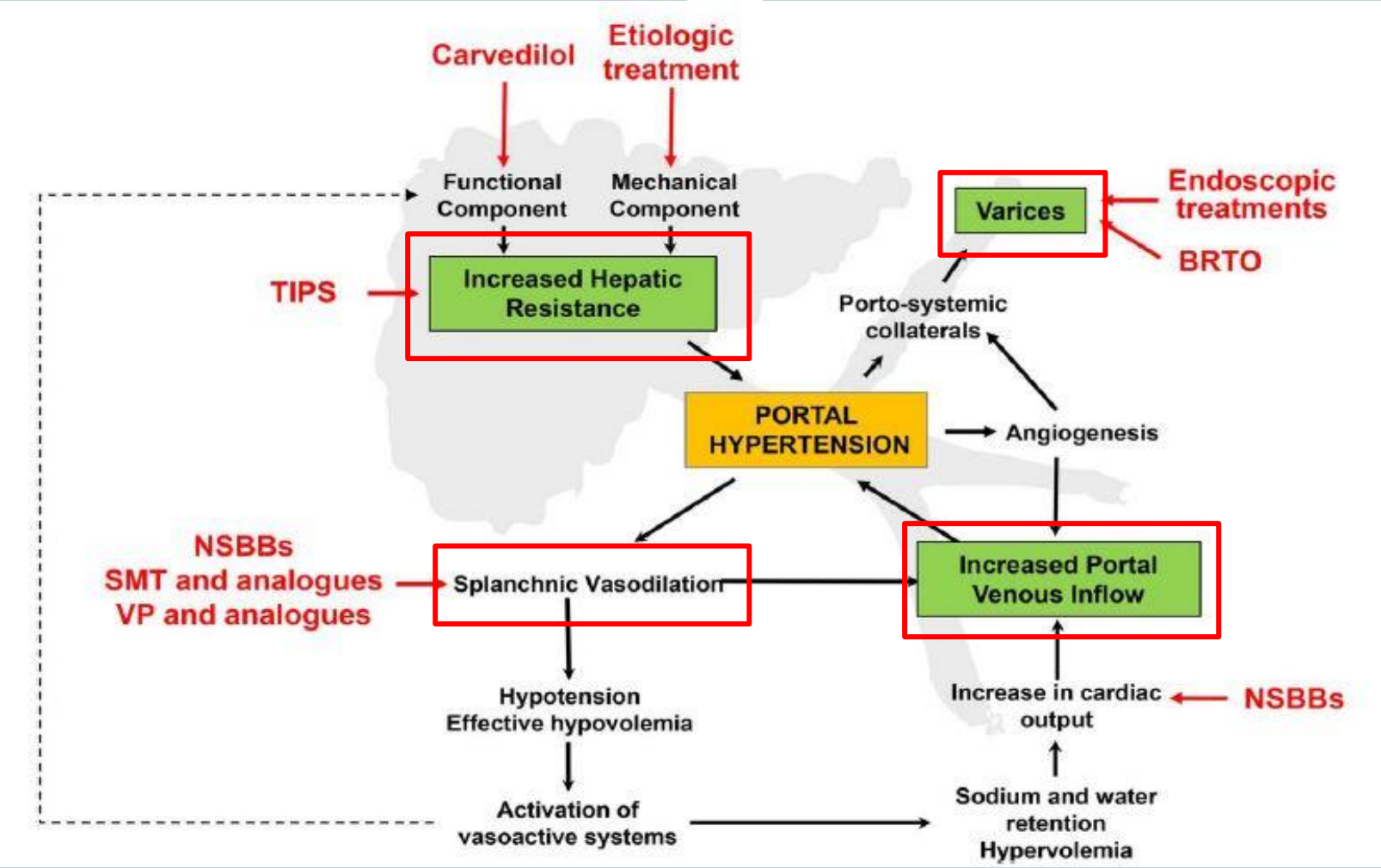
- Addition of albumin to antibiotics in patients with SBP
- Judicious use of laxatives and diuretics
- Albumin infusions with large-volume paracentesis
- Prompt treatment of GI bleeds and use of antibiotic prophylaxis
- Avoidance of nephrotoxic drugs or radiographic dye
- Primary prophylaxis against SBP in high-risk individuals and secondary prophylaxis for patients after initial episode

Bajaj JS, et al. *Am J Gastroenterol*. 2022;117(2):225-252.

Pathophysiology of cirrhosis complications

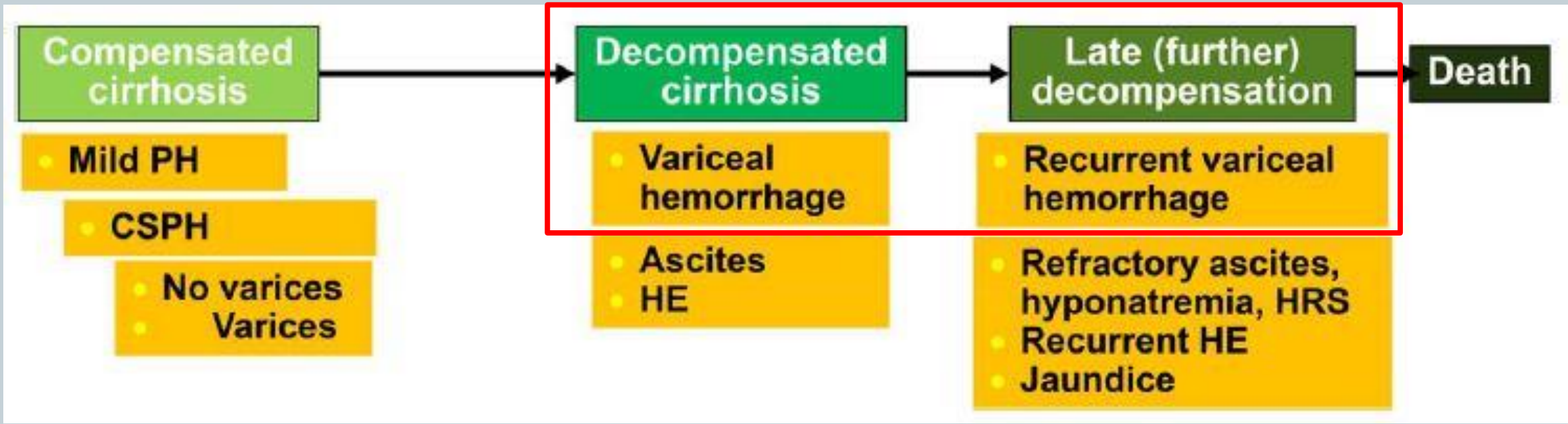


Pathophysiology of portal hypertension



Garcia-Tsao G, et al. *Hepatology*. 2017;65(1):310-335.

Variceal hemorrhage



Garcia-Tsao G, et al. *Hepatology*. 2017;65(1):310-335.

Variceal hemorrhage treatment

- Octreotide: 50 mcg IV bolus followed by continuous infusion of 50 mcg/hr for 2-5 days
- Vasopressin: 0.2-0.4 units/min with max dose of 0.8 units/min
  - Maximum duration is 24 hours at highest effective dose
  - Administer concurrently with IV nitroglycerin
- Ceftriaxone: 1 g Q24H max of 7 days
  - Consider stopping when bleeding stabilized and off vasoactive drugs

Garcia-Tsao G, et al. *Hepatology*. 2017;65(1):310-335.

Beta-blocker therapy

- Conflicting impact on outcomes in literature assessing non-selective beta-blockers (NSBBs)
  - Possible that NSBBs are useful during a "window period" in the natural history of cirrhosis
    - Use caution in patients with refractory ascites (especially if SBP <90 mmHg) serum Na <130 mmol/L, or SCr >1.5 mg/dL
    - Might be re-introduced if circulatory dysfunction improves
- Exposure to NSBB prior to sepsis may have a role in reducing mortality
  - Potentially explained by increased gut motility and reduced bacterial translocation resulting in decreased systemic inflammation
- Study showed carvedilol reduced 28-day mortality in ACLF patients compared with placebo
- However, patients with ACLF unlikely to tolerate clinically meaningful dose

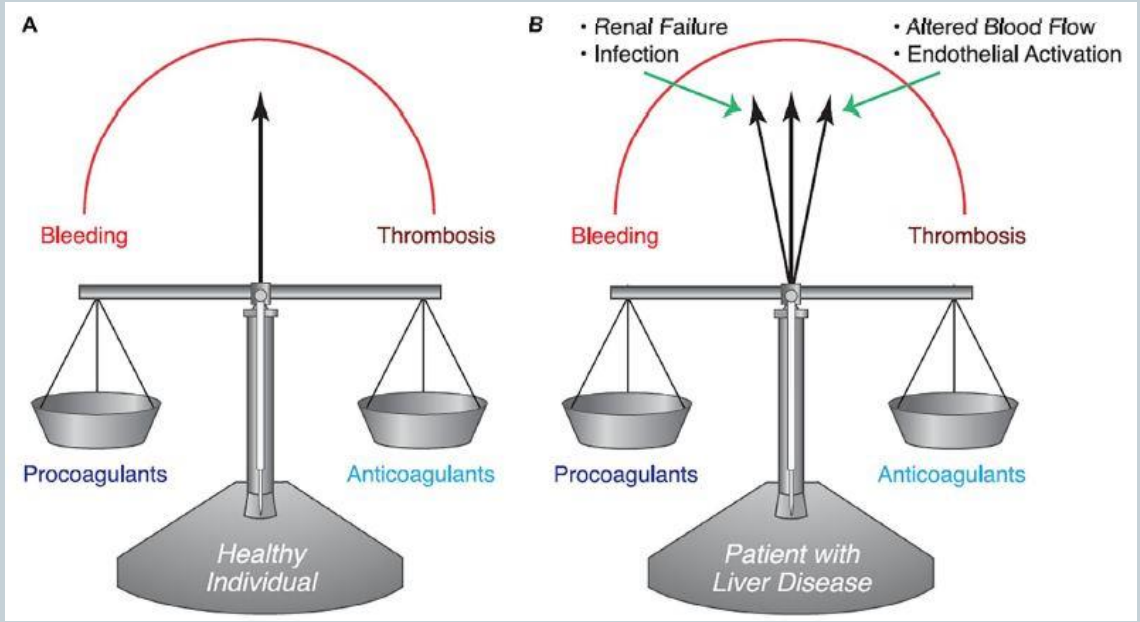
Biggins SW, et al. *Hepatology*. 2021;74(2):1014-1048
Bajaj JS, et al. *Am J Gastroenterol*. 2022;117(2):225-252.
Bernal W, et al. *J Hepatol*. 2021; 75 Suppl1:S136-S177

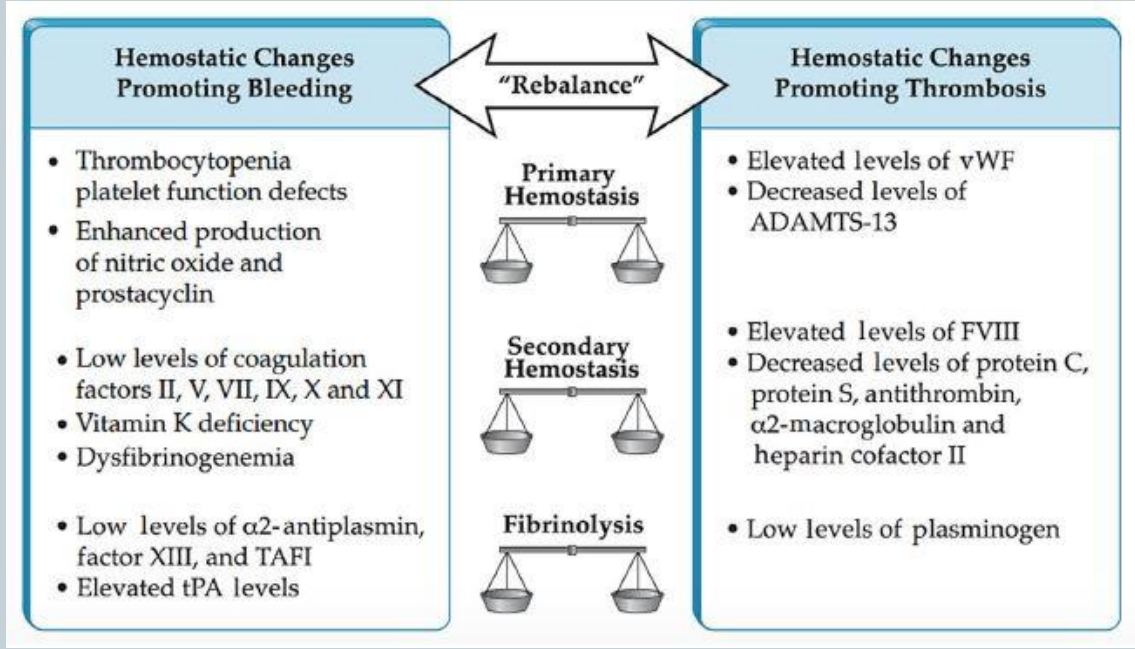
Coagulopathy

- Patients with ALF have elevated INR, prothrombin time, and variable degrees of thrombocytopenia
  - Despite these, bleeding complications are uncommon (~10%)
- In ACLF patients, disorders of coagulation (INR ≥2.5) are the most common extrahepatic organ failure apart from renal impairment
- Risk of bleeding remains a concern (especially during invasive procedures); however, cirrhotics are thought to be at greater risk of thrombotic complications
  - Portal vein thrombosis (PVT) risk ~8% annually in those awaiting liver transplant

Stravitz RT, Lee WM. Acute liver failure. *Lancet*. 2019;394(10201):869-881
MacDonald AJ, et al. *Curr Opin Crit Care*. 2020;26(2):171-179

Coagulopathy



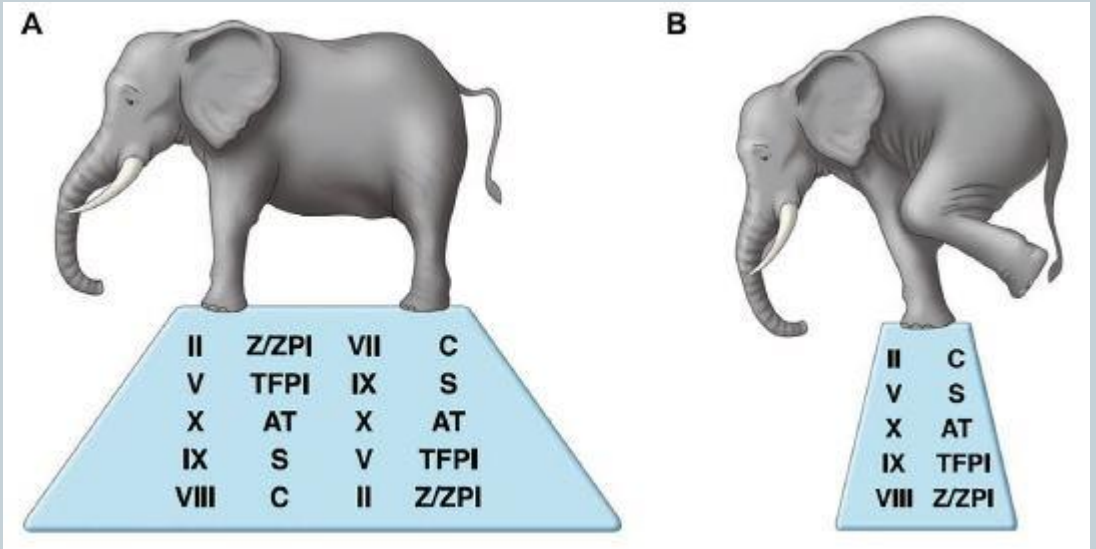


Northup P. *Clin Liver Dis*. 2020;16(S1):56-72.

Coagulopathy

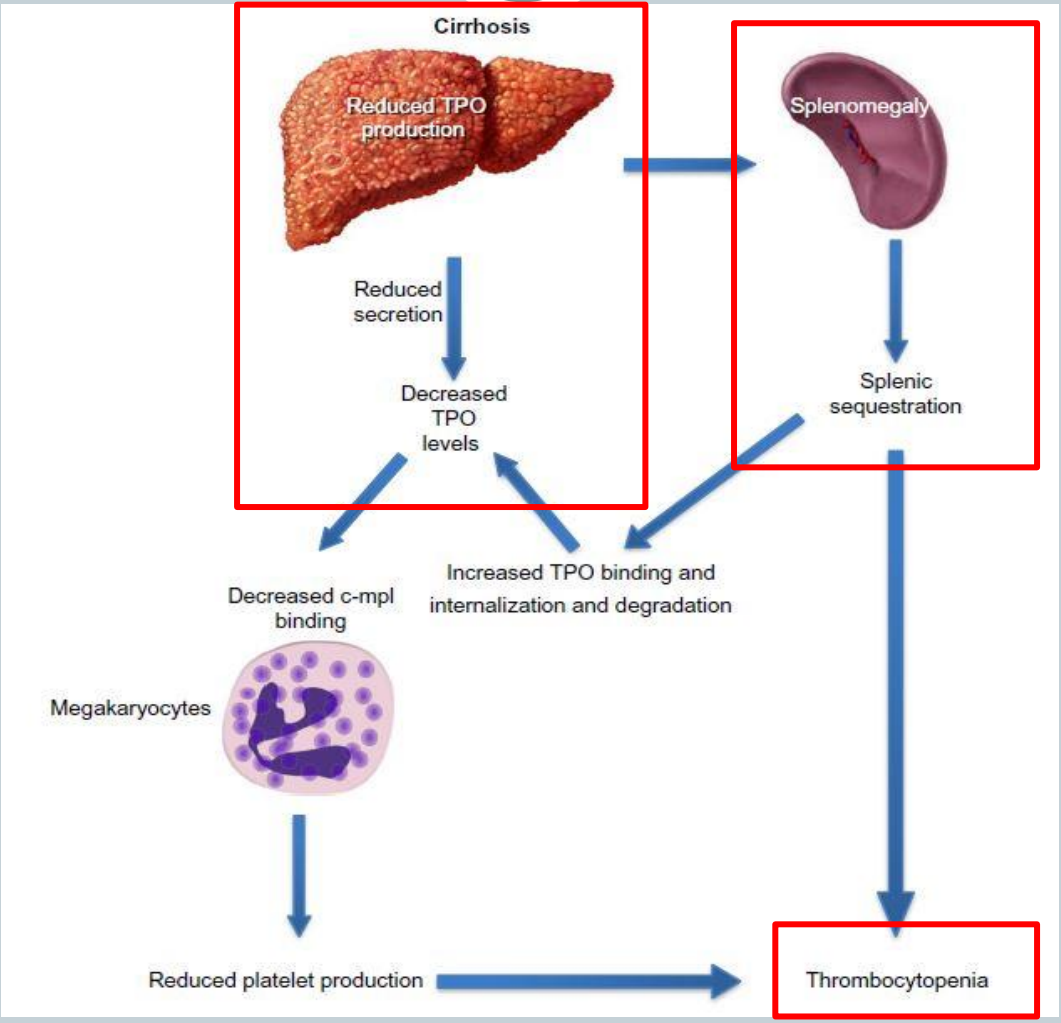
Table. Summary of factors associated with hemostasis (compiled[9,10,24,31]).

Procoagulants		Anticoagulants		Fibrinolytics	
Hepatic synthesis	Non-hepatic synthesis	Hepatic synthesis	Non-hepatic synthesis	Hepatic synthesis	Non-hepatic synthesis
Factors: I II(prothrombin) III IV V VI VII VIII* IX X XI XII Fibrinogen	Factors: VIII* von Willebrand (vWf) Platelets** Anti-phospholipid antibodies***	Proteins: C S Z Anti-thrombin III	Tissue factor pathway inhibitor	Plasminogen (zymogen) and plasmin	



Northup P. *Clin Liver Dis*. 2020;16(S1):56-72
Harrison M. *WestJEM*. 1996;19(5):863-871

Thrombocytopenia



Management

- Use viscoelastic testing over INR, platelet, or fibrinogen
- Use LMWH or VKA over no anticoagulation in patients with PVT or pulmonary embolism
- DVT prophylaxis with LMWH over pneumatic compression stockings in hospitalized patients with ACLF, insufficient data for ALF recommendation
  - Do not use if recent bleeding or significant thrombocytopenia (<50 x10^9/L)

Nanchal R, et al. *Critical Care Medicine*. 2020;48(3):e173-e191
Bajaj JS, et al. *Am J Gastroenterol*. 2022;117(2):225-252.

Anticoagulation PVT

- LMWH and VKA have been the standard of care for PVT treatment
- Handful of small studies assessing DOACs to standard of care in PVT
  - Thus far, appear as safe and possibly more effective than warfarin and LMWH
  - No endorsement by guidelines at this point given paucity of evidence
- Rivaroxaban may have a higher incidence of DILI compared to other DOACs and warfarin

Weinberg E, et al. *Semin Liver Dis*. 2019;39(02):195-208.

Encephalopathy

Type	Grade		Time Course	Spontaneous or Precipitated
A	MHE	Covert	Episodic	Spontaneous
	1			
B	2	Overt	Recurrent	Precipitated (specify)
	3			
C			Persistent	
	4			

A: Acute liver failure; B: bypass/shunts; C: cirrhosis
MHE: minimal hepatic encephalopathy, not clinically noticeable; Grade 1: mild cognitive changes with no Asterixis not easily noticed in clinics; Grade 2: confusion, disorientation to time, asterixis; Grade 3: disoriented to place and person, altered response to questions; Grade 4: comatose

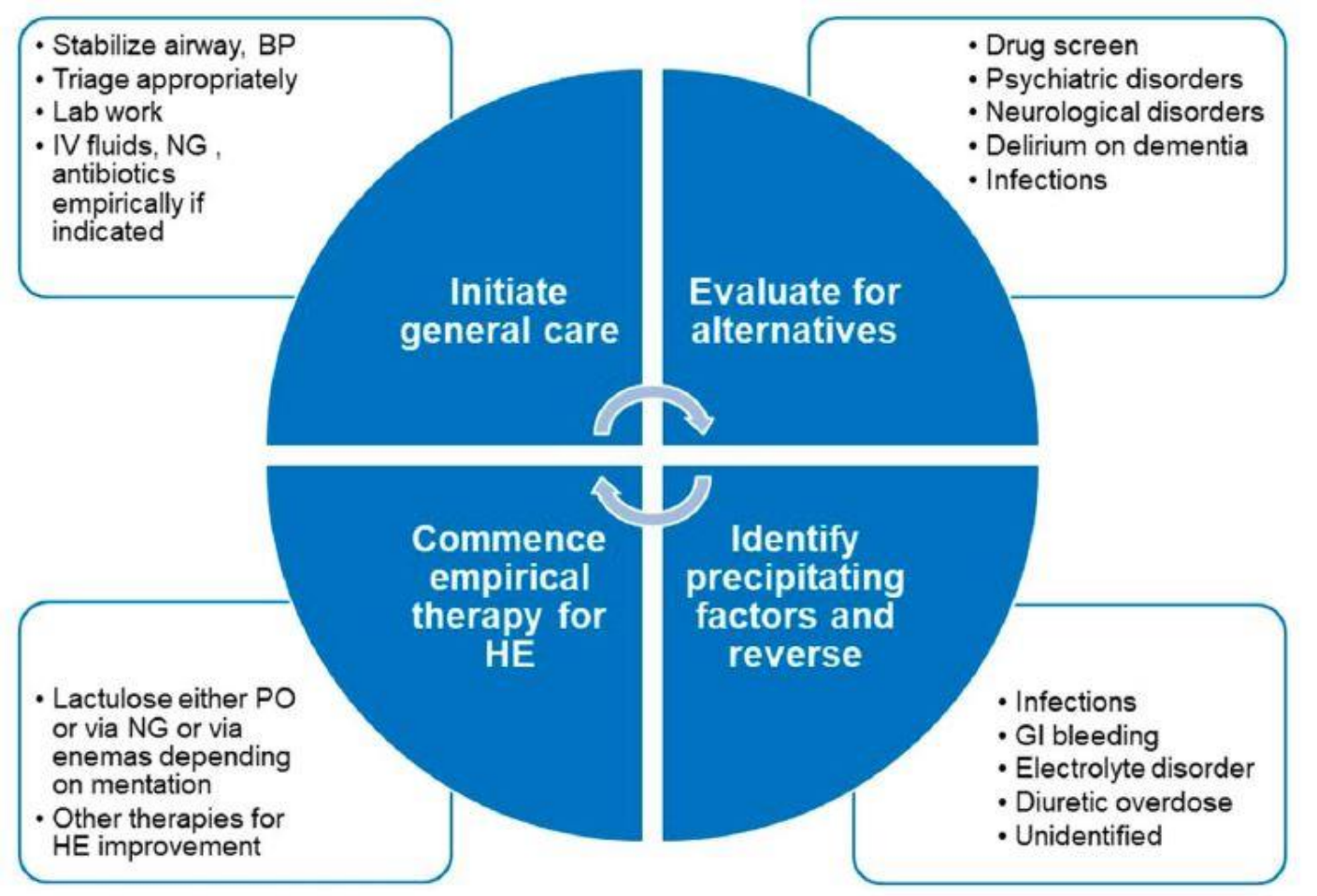
Vilstrup H, et al. *HEPATOLOGY*. 2014;60:715-735

Encephalopathy

- Hepatic encephalopathy (HE): neuropsychiatric impairment as a consequence of accumulating serum toxins (i.e., ammonia) in the setting of diffuse systemic inflammatory response
  - May be provoked by both impaired endogenous hepatic function as well as extrahepatic factors including: GI bleeding, renal impairment/failure, infection, and electrolyte disturbances (i.e., hyponatremia)
- Affects up to 20% of decompensated cirrhotic patients
  - First episode of overt HE associated with poor prognosis, independently associated with mortality

MacDonald AJ, et al. *Curr Opin Crit Care*. 2020;26(2):171-179
Acharya C, et al. *Am J Gastroenterol*. 2018;113(11):1600-1612

Initial care of patients with encephalopathy



Bajaj JS, et al. *Am J Gastroenterol*. 2022;117(2):225-252

Encephalopathy treatment considerations

- In patients with grade 3 or 4 HE treatment should consist of:
  - Care of the airway
  - Evaluation of other causes of AMS
  - Treatment of potential precipitating factors
  - Empiric HE should occur simultaneously

- Patients with cirrhosis are also prone to changes in mentation related to:
  - Medications (opioids, benzodiazepines, PPIs)
  - Infections
  - Altered electrolytes
  - Alcohol and illicit drugs, including withdrawal
  - Strokes

Bajaj JS, et al. *Am J Gastroenterol*. 2022;117(2):225-252.

Encephalopathy treatment

- Impaired hepatic metabolism in the setting of cirrhosis
- Short acting medications such as dexmedetomidine are preferred to benzodiazepines
- Propofol and fentanyl preferred to benzodiazepines

Bajaj JS, et al. *Am J Gastroenterol*. 2022;117(2):225-252.

Management

Drug	Mechanism	Dose	Comments
lactulose	Production of acetic and lactic acid → reduced pH → conversion of ammonia to ammonium rendering it less absorbable Osmotic laxative effect flushes the ammonium ion out	20 g (30 mL) orally/NGT every hour until passage of a BM (200 g/300 mL retention enema if enteral route not possible), then reduce to TID. Titrate to 2-3 soft stools/day	First-line agent. Caution with liberal dosing leading to hypovolemia and electrolyte disturbances
rifaximin	Non-absorbable antibiotic that reduces ammonia-producing gut microbiota. Also reduces production and absorption of gut-derived toxins	550 mg orally BID	Most effective adjunctive therapy. Add-on therapy if patient has previous HE episode

Alternative agents include: branch-chain amino acids, L-ornithine L-aspartate, neomycin, metronidazole

Acharya C, et al. *Am J Gastroenterol*. 2018;113(11):1600-1612
Bajaj JS. *Aliment Pharmacol Ther*. 2016;43:11-26
Vilstrup H, et al. *HEPATOLOGY*. 2014;60:715-735

Encephalopathy management in ALF

- In acute liver failure, standard ammonia-lowering drugs have not been systematically tested/have not shown beneficial outcomes
  - CVVHD used to lower ammonia levels
- Manage cerebral edema/elevated ICP with osmotic therapy
  - Mannitol or hypertonic saline boluses

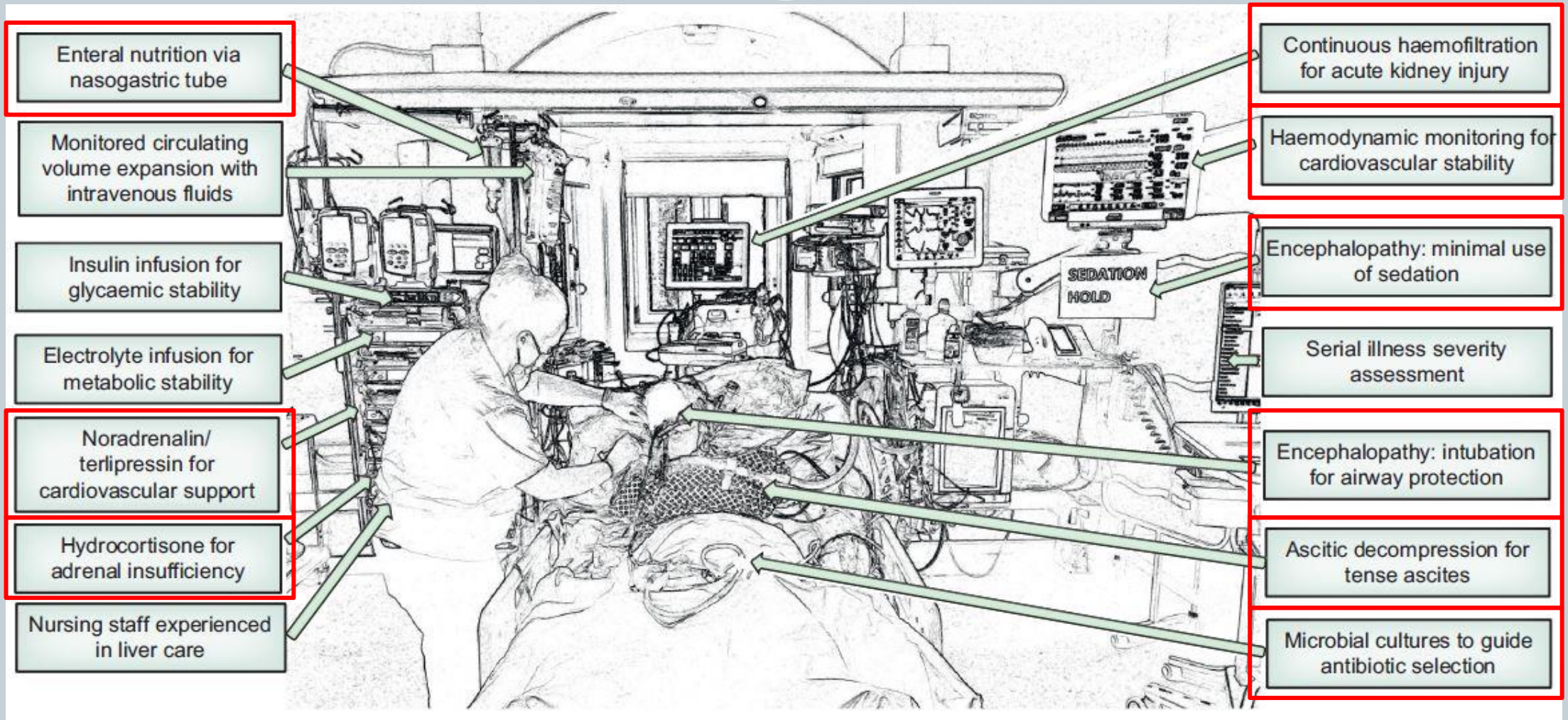
Stravitz RT, et al. *Lancet*. 2019;394(10201):869-881.

Nutrition

- Daily Tkcal goal of 35-40 kcal/kg IBW with 1.2-2 g/kg/day of protein
- Reductions in hepatic glycogen synthesis and storage → increased gluconeogenesis with rapid depletion of carbohydrate stores → increased utilization of amino acids and ammonia production
  - Protein restriction only worsens this response
- Metabolic derangements combined with poor oral intake (due to ascites, hepatic encephalopathy, etc.) lead to protein-calorie malnutrition, which negatively influences morbidity and mortality
- Enteral nutrition preferred over parenteral
  - However, be cautious of aspiration

Nanchal R, et al. *Critical Care Medicine*. 2020;48(3):e173-e191
Bajaj JS, et al. *Am J Gastroenterol*. 2022;117(2):225-252

Acute hepatic impairment considerations



Bernal W, et al. *J Hepatol*. 2021;75 Suppl 1:S163-S177

Question 1

- Which is the most appropriate antibiotic for a patient on hospital day 5 that is being transferred from the floor to the ICU due to worsening hemodynamics and suspected SBP?
  - A) piperacillin-tazobactam
  - B) ceftriaxone
  - C) ciprofloxacin
  - D) rifaximin

Question 2

- Which is the most appropriate empiric therapy for a patient with encephalopathy and no enteral access?
  - A) lactulose 300 mL + 700 mL NS enema retained for 30-60 minutes
  - B) cannot provide therapy until enteral access is obtained
  - C) IV metronidazole 500 mg TID
  - D) IV rifaximin 550 mg Q12H

Question 3

- Which is the most appropriate use of albumin?
  - A) 25 g of 25% albumin prior to large-volume paracentesis
  - B) 1 g/kg daily for hepatorenal syndrome
  - C) 1.5 g/kg on day 1 followed by 1 g/kg on day 3 for SBP
  - D) 12.5 to 25 g of albumin 25% scheduled Q6H for patient with a history of cirrhosis presenting with septic shock

Albumin summary

Indication	Conc.	Dose	Comments
LVP	25%	8 g albumin for every liter of ascitic fluid if removing ≥5 L	
SBP	25%	1.5 g/kg at day 1 and 1 g/kg at day 3	Improves survival and renal impairment
HRS	25%	Day 1: 1 g/kg (100 g max) Day 2 through end of therapy: 20-50 g/day	Albumin alone has not proven to be effective but is used as adjunctive therapy
Volume resuscitation	5% or 25%	25 g bolus dose based on assessment of volume status	Albumin 5% for rapid volume resuscitation vs 25% for sustained volume expansion
Hyponatremia	25%	Undetermined	Study found that albumin use was associated with improved resolution of hyponatremia, however was dosed for various other indications

Bajaj J, et al. *Am J Gastroenterol*. 2018;113(9):1339
Valerio C, et al. *WJH*. 2016;8(7):345

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