Chapter 14. Cirrhosis

14.1 Diagnosis & Prognosis

- **Diagnosis**
  - History = complications of bleeding, ascites, confusion
  - Physical Exam = hyperdynamic circulation (↓BP & ↑HR), stigmata of chronic liver disease *[see Chapter 2.4]*
  - Lab = AST >ALT, ↑ ALP, ↓ platelets, ↑ bilirubin, ↑ INR, ↓ albumin
  - Imaging = nodular liver or evidence of portal hypertension (big spleen)
  - Noninvasive = lab tests, transient or shear wave elastography *[see Chapter 3.8]*
  - Biopsy *[see Chapter 3.7]*
- **Prognosis**
  - Complications develop at a rate of approximately 5% per year
    - Variceal bleeding
    - Ascites
    - Encephalopathy
    - Hepatocellular carcinoma
  - Median survival
    - Compensated cirrhosis about 9 years
    - Decompensated cirrhosis < 2 years
  - Portal hypertension is responsible for the development of complications (decompensation)

- Portal pressure is estimated via the transjugular route by calculating the hepatic venous pressure gradient (HVPG) = wedged HV pressure – free HV pressure
- Patients with cirrhosis progress through four stages as portal hypertension worsens and HVPG increases

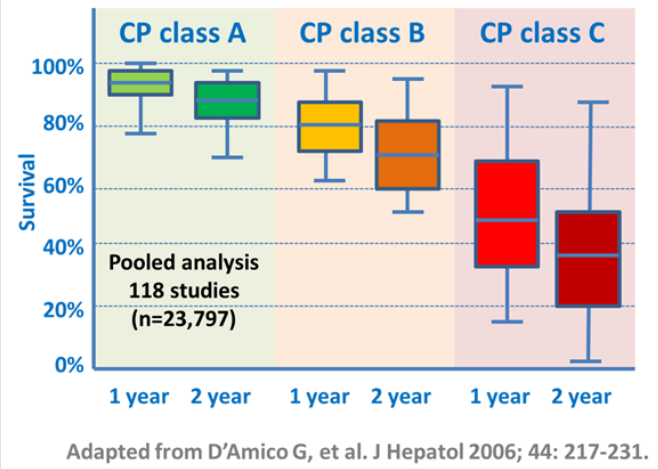
	Non-Cirrhotic	Compensated Cirrhosis		Decompensated Cirrhosis	
Histology	F1→ F3	F4	F4	F4	F4
HVPG (mmHg)	<6	6-10	10-12	>12	>16
Symptoms	None	No varices No ascites	Varices No Ascites	Variceal Bleeding Ascites HE	Recurrent Bleeding Refractory Ascites Infections HRS Refractory HE
Mortality @ 1 year		1%	3%	10-30%	>60%

Adapted from Abillos A, Garcia Tsao G. Dis Markers 2011; 31(3):121-8.

- **Predicting Prognosis**
  - **Child Pugh (CP) Score**
    - Developed for prediction of death after portosystemic shunt surgery in cirrhotics
    - Initially had nutrition variable, but later updated to include blood clotting time
    - Two clinical variables (encephalopathy and ascites) and three laboratory variables (bilirubin, albumin and INR) are used to predict survival according to class
      - CP A (5-6 points)
      - CP B (7-9 points)
      - CP C (10-15 points)

Criteria	1	2	3
Encephalopathy	None	Mild	Severe
Ascites	None	Controlled	Uncontrolled
Bilirubin	≤ 33	34-50	≥ 51
Albumin	≥ 36	28-35	≤ 27
INR	≤ 1.6	1.7-2.2	≥ 2.3

Class	A = 5-6 pts	B = 7-9 pts	C = 10-15 pts

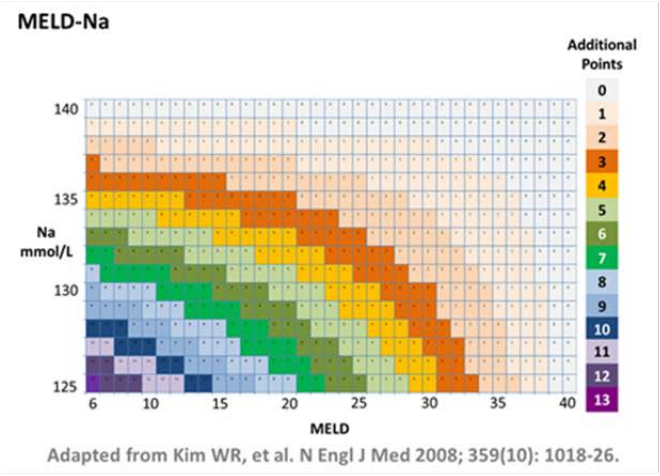


Adapted from D'Amico G, et al. J Hepatol 2006; 44: 217-231.

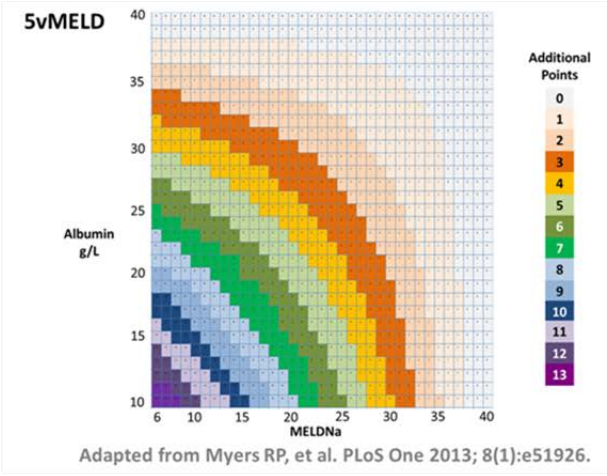
- **Model for End-stage Liver Disease (MELD) Score**
  - Developed to predict survival after transjugular portosystemic shunt (TIPS) insertion
  - Model includes bilirubin, INR, creatinine (logarithmic transformations)
  - Used for liver transplant (LT) allocation in USA since 2002 and in Canada since 2004 by a "sickest first policy"
  - MELD score ranges from 6 to 40 (higher score = ↑mortality)
  - Modifications have improved the accuracy of the model for predicting who is next most likely to die awaiting LT
- **MELD-sodium (MELD-Na)**
  - Hyponatremia is an independent predictor of survival in patient with cirrhosis
  - Develops from dilution (retention of free water) in patients with ascites
  - Na interacts with MELD and its inclusion in the model has the biggest impact in patients with low MELD scores
  - Canada and USA recently adopted MELD-Na for organ allocation for LT

- **5vMELD**
  - Hypoalbumenia is an independent predictor of survival in patient with cirrhosis, as is evident by its inclusion in the Child Pugh score
  - Calgary Liver Unit revised MELD-Na to include albumin (5 variable MELD)

Albumin interacts with MELD-Na and its inclusion in the model has the biggest impact in patients with low MELD-Na scores



Adapted from Kim WR, et al. N Engl J Med 2008; 359(10): 1018-26.



Adapted from Myers RP, et al. PLoS One 2013; 8(1):e51926.

14.2 Varices, PHG and GAVE

Pathophysiology & Natural History

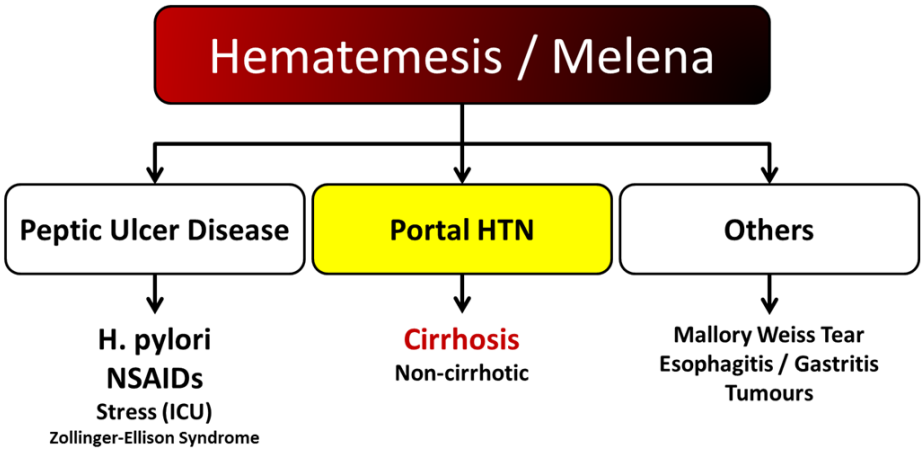
- **Pathophysiology**
  - Varices form in response to portal hypertension and represent the reopening of connections between the portal and systemic circulation
  - They are most commonly seen in the distal esophagus, stomach and rectum
- **Natural History**
  - **Prevalence** of varices depends on Child Pugh (CP) score
    - CP A = 40%
    - CP B = 65%

- CP C = 85%

- Varices classification
  - None → small (<5mm) → large (>5mm)
  - Risk of progression between these groups is 7-8% per year
- Risks for bleeding
  - **Size** = Large varices (15% per year) higher than small varices (3-5% per year)
  - **Red markings** = thin walls on varices
  - **Decompensation** = CP B/C higher than CP A

- **Clinical Presentations (scheme below)**
  - Patients may present with hematemesis (vomiting blood), passage of melena (black stools), hematochezia (passage of red / maroon blood per rectum due to brisk upper GI bleed) or occult bleeding with iron deficiency anemia

    NOTE: in cirrhotics, one-third of upper GI bleeds will be from causes other than portal hypertension (e.g. peptic ulcer disease, Mallory Weiss tear)



Adapted from U of C Black Book

Screening & Management

Esophageal Varices

- **Surveillance**
  - Recommended that cirrhotics undergo surveillance endoscopy to look for varices
  - However, if FibroScan™ (FS) <20 kPa AND platelets >150, endoscopy can be avoided as these patients are unlikely to have varices
  - Recall depends on size of varices and if patients are compensated or decompensated

    NOTE: Non-selective beta-blockers (NSBB) do NOT prevent varices from forming
- **Primary prophylaxis**
  - There are two options for prevention of first bleeding
    - NSBB **OR** banding
  - **Non-selective beta-blockers (NSBB)** (e.g. nadolol, propranolol, carvedilol) work on both β1 & β2 receptors and the blockade of β2 receptors in splanchnic circulation leads to unopposed alpha mediated vasoconstriction, reducing blood flow into the portal circulation

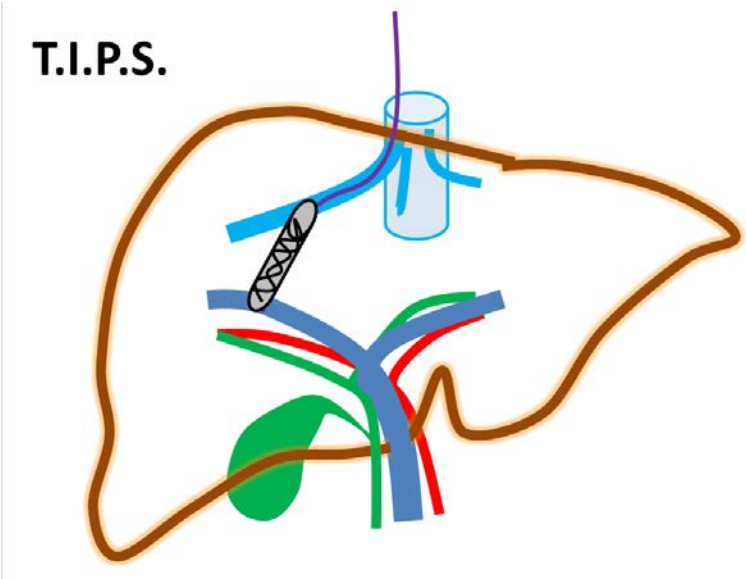
    NOTE: if tolerating NSBB there is no need for further endoscopies but if intolerant (fatigue, low BP, etc.) then prophylactic banding should be done
  - **Banding** uses an attachment at the end of the gastroscope to apply rubber bands to esophageal varices, which fall off after a few days leaving behind an ulcer that heals as a scar (drives the blood deeper into the tissues and thereby reducing bleeding risk)

    NOTE: banding is superior to sclerotherapy
- **Variceal Bleeding**
  - Acute GI bleeding is an emergency

- Give IV volume expansion (normal saline) and transfuse packed RBCs, but keep hemoglobin between 70-90 g/L as this improves survival

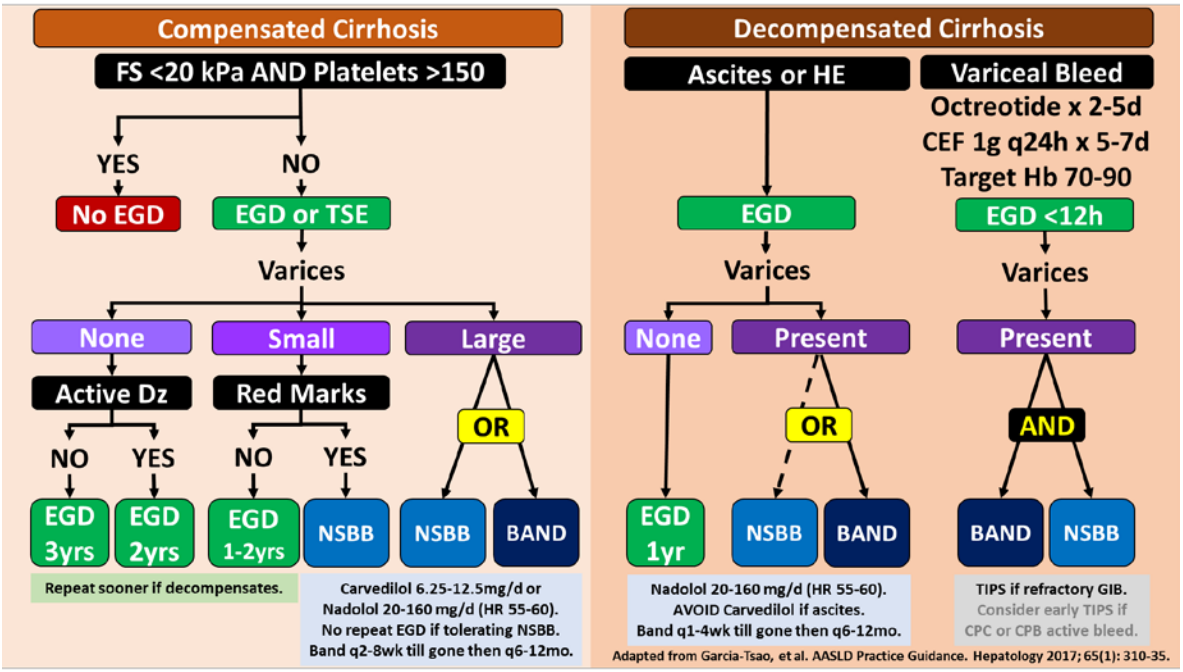
  NOTE: DO NOT OVER TRANSFUSE as this worsens portal hypertension

- Give up to 7 days of antibiotics to any cirrhotic with GI bleeding, as this will:
  - Prevent infections (e.g. spontaneous bacterial peritonitis or urinary tract infections)
  - ↓ rebleeding and ↓ mortality (meta-analysis of RCTs)
- Octreotide 50μg IV bolus followed by 50μg/hr infusion x 3-5 days reduces rebleeding by decreasing blood flow into splanchnic circulation
- EGD should be done within 12 hrs for banding
- If banding doesn't control bleeding, balloon tamponade can temporize (max 24 hrs)
- **Transjugular intrahepatic portosystemic shunt (TIPS)** should be done for uncontrolled or recurrent bleeding
  - Early TIPS should be considered as RCTs have demonstrated ↓rebleeding, ↓ time in the ICU and ↓ mortality with TIPS



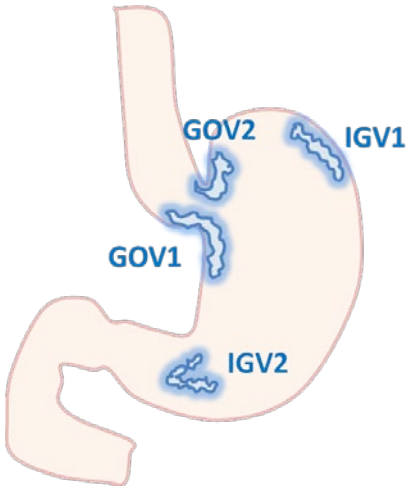
- **Secondary prophylaxis**
  - Combination of NSBB **AND** banding is used to prevent rebleeding
  - Endoscopy and banding should be done every 2-4 weeks until varices are obliterated

Summary – Management of Esophageal Varices



Gastric Varices

- **Classification**
  - Gastroesophageal varices at GE junction
    - **GOV1** along lesser curvature
    - **GOV2** along greater curvature
  - Isolated gastric varices
    - **IGV1** in the fundus
    - **IGV2** elsewhere in the stomach



- **Primary Prophylaxis**
  - Injection of glue (cyanoacrylate) superior to NSBB in preventing the first bleed
- **Variceal Bleeding**
  - Gluing is preferred, as banding in the stomach is difficult (scope is in retroflexion)
  - TIPS is used for uncontrolled bleeding
- **Secondary Prophylaxis**
  - NSBB and gluing or consider TIPS for recurrent bleeding

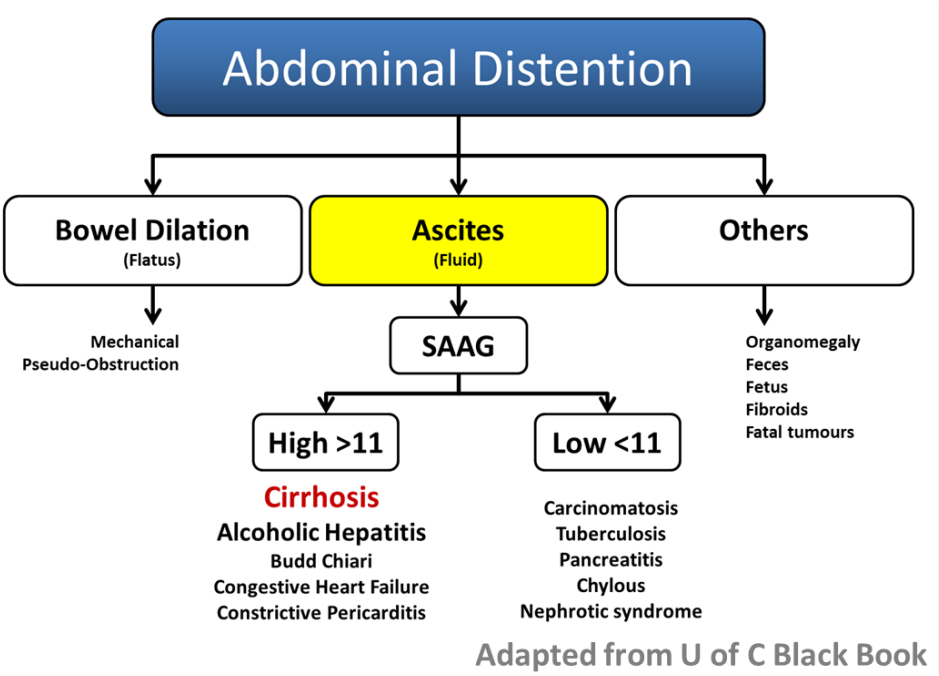
Portal Hypertensive Gastropathy (PHG) & Gastric Antral Vascular Ectasia (GAVE)

- **PHG** is a mosaic pattern in the stomach due to congestion ("snake-skin boot" appearance) and may have erythema or red spots
- **GAVE** presents with linear red streaks in the antrum ("watermelon stomach"), or a more diffuse pattern similar to PHG, and is seen with cirrhosis and connective tissue diseases
- Both can lead to bleeding, which may be overt (melena) or occult (iron deficiency anemia)
- **Management**
  - **PHG =** NSBB, octreotide for acute bleeding, TIPS or liver transplant for refractory bleeding
  - **GAVE =** argon plasma coagulation (APC) or Nd:YAG laser, estrogen therapy, banding may be helpful in antrum, surgery (if not cirrhotic)

14.3 Ascites, SBP and HRS

Pathophysiology & Natural History

- **Clinical Presentation** (scheme below)
  - Patients present with a distended abdomen, often accompanied by ankle edema and weight gain from fluid retention
  - Ascites can be demonstrated by shifting dullness if moderate volume or the fluid wave if tense *[see Chapter 2.4]*
    - Small amounts of ascites may only be seen on imaging with US, CT or MRI

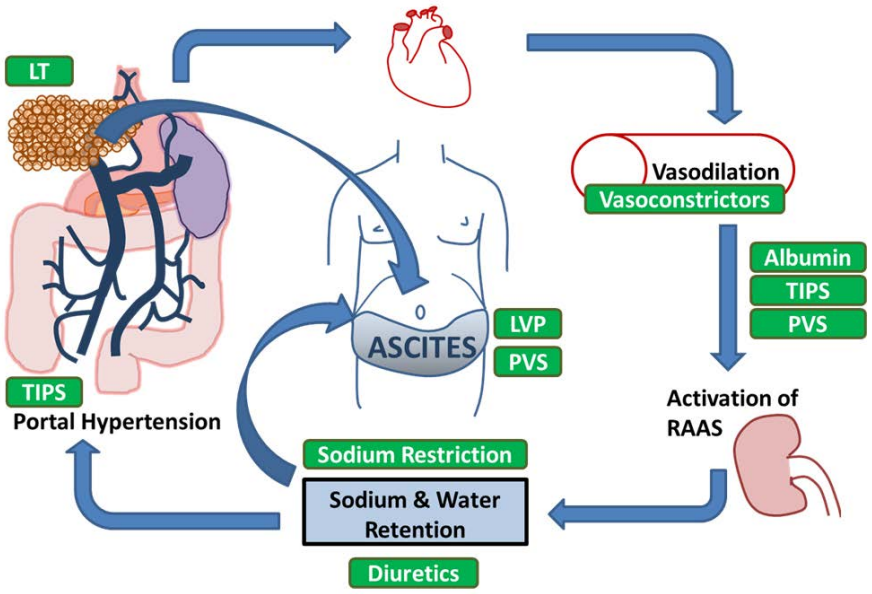


- **Causes**

HIGH GRADIENT (SAAG>11)	LOW GRADIENT (SAAG<11)
o Cirrhosis = 85% of all ascites	o Cancer
o Alcoholic Hepatitis	o Pancreatitis
o Heart failure	o Nephrotic syndrome
o Acute Liver Failure	o Tuberculosis
o Budd Chiari Syndrome	o Post-op lymphatic Leak
o Sinusoidal Obstruction Syndrome	o Myxedema
	o Mixed Ascites

- **Pathophysiology of Ascites in Cirrhosis**
  - Cirrhosis leads to portal hypertension → vasodilators (nitric oxide, carbon monoxide) are produced in response to high pressure in liver and portal circulation → vasodilators get into systemic circulation via collaterals → leads to vasodilation in the systemic circulation (hyperdynamic circulation with ↓ BP and ↑ HR) → kidneys respond to this with activation of renin-angiotensin-aldosterone system (RAAS) → sodium and water retention → worsen portal hypertension → ascites eventually is forced through the liver capsule and peritoneal lining into abdominal cavity

    NOTE: patients often have cirrhotic cardiomyopathy and low albumin, which contribute to ascites formation
  - Therapies work on different aspects of this pathogenesis (in green below)
    - Abbreviations: LT = liver transplantation, LVP = large volume paracentesis, PVS = peritoneovenous shunt, TIPS = transjugular intrahepatic portosystemic shunt



Adapted from Garcia-Taso G. Gastroenterology 2001; 120: 726-748.

- **Natural History**
  - Ascites formation in a cirrhotic has mortality of 40% at 1 year and 50% at 2 years
  - Refractory ascites has median survival of 6 months
  - Spontaneous Bacterial Peritonitis (SBP) has mortality 20% and often leads to hepatorenal syndrome (HRS)
  - Type 1 HRS has a median survival of 2 weeks
  - Ascites, and its complications, are therefore indications for liver transplantation (LT)

Management

- **Investigations**
  - Any patient with new ascites require a diagnostic paracentesis
  - Tests to order include:
    - **Albumin** → calculate serum ascites albumin gradient (SAAG)
    - **Protein** → high in Budd Chiari Syndrome; low is a risk for SBP

- **Cell count + differential** → neutrophils (PMN) >250 /mm^3 or >250 x 10^6/L = **SBP**
- **Culture + Sensitivity** → directly spike into blood culture bottles to increase yield

- Other tests sometimes ordered include cytology (malignant ascites), triglycerides (chylous ascites), and amylase (pancreatic ascites)

- **Differential Diagnosis**

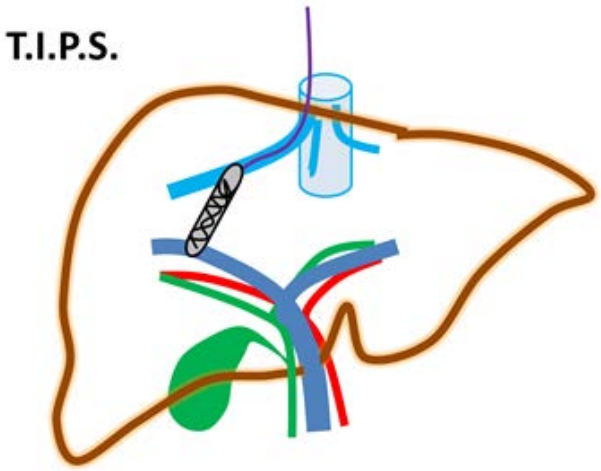
Transudate (SAAG >11)	**Exudate (SAAG <11)**
Portal Hypertension	Malignancy
Cirrhosis	Ovarian, GI
Non-cirrhotic	Pancreatic
Budd-Chiari	Infection → TB
Cardiac	Chylous ascites
CHF	Perforated viscous
Constrictive pericarditis	Nephrotic syndrome

- **Management**
  - **First line**
    - **2000mg sodium restricted diet** (must read processed food labels)
    - Diuretics (must monitor electrolytes and creatinine carefully)
      - **Spironolactone** (50mg -> 100mg -> 200mg -> 300mg -> 400mg) is direct aldosterone antagonist (potassium sparing diuretic) and is therefore very potent in cirrhotics with RAAS activation but can cause painful gynecomastia (switch to amiloride if this occurs)

- **Furosemide** (20mg -> 40mg -> 80mg -> 120mg -> 160mg) is loop diuretic (potassium losing) and can therefore help maintain potassium in normal range when given with spironolactone

- Stop alcohol (worsens portal HT) and use of NSAIDS (↓ renal blood flow)
- Consider the patient for liver transplant

- **Second line (refractory ascites)**
  - **Large volume paracentesis (LVP)**
    - LVP is safe even in patients with high INR and low platelets (intraperitoneal bleeding or perforation of bowel are rare complications)
    - Fresh frozen plasma (FFP) or platelets are not required before LVP (*Choosing Wisely Canada™ Recommendation*)
    - Give 8 grams of 25% IV albumin per litre of fluid removed (100mL bottle of 25% IV albumin / 3L tap) to prevent post paracentesis circulatory dysfunction, further activation of RAAS and renal dysfunction
  - Consider stopping non-selective beta-blockers (NSBB), angiotensin converting enzyme inhibitors (ACE-I) and angiotensinogen receptor blockers (ARB) as these can lower BP and worsen fluid retention
  - Consider adding midodrine (an oral alpha agonist) which can increase BP and therefore renal perfusion
  - **Transjugular intrahepatic portosystemic shunt** or TIPS (works by lowering portal pressure, improving renal perfusion and resetting RAAS system) but can be complicated by hepatic encephalopathy (HE) in 10-50% and should be avoided if bilirubin > 85, INR > 2, chronic HE, significant cardiopulmonary disease on echocardiogram, and if Child Pugh score > 11 or MELD score > 18



- **Third line**
  - Peritoneovenous shunt (PVS) takes fluid from abdomen directly to the jugular vein, but is not often done as it is frequently complicated by infection

Summary – Ascites Management

- Cessation of alcohol use
- Sodium restricted diet & diet education [2000mg/d]
- Dual diuretics (spironolactone & furosemide)
- Discontinue NSAIDs
- Evaluation for LT

- Consider stopping NSBB, ACE-I and ARBs
- Consider adding midodrine
- Serial LVP → give 25% iv albumin (8g/L removed)
- TIPS

- Peritoneovenous shunt (PVS)

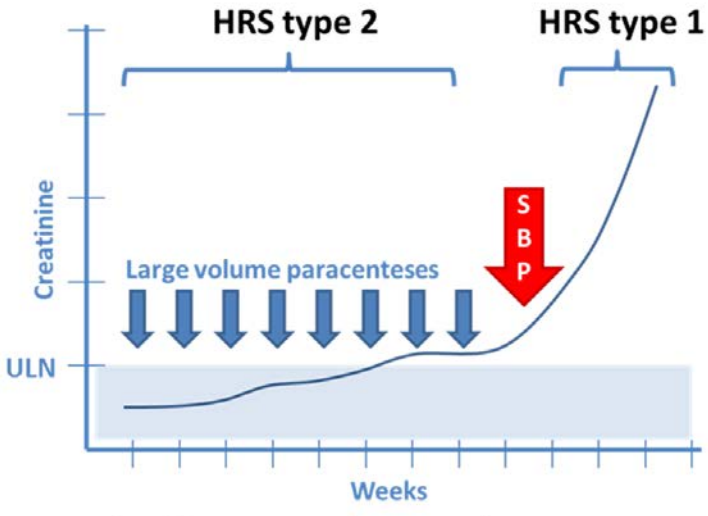
Adapted from https://www.aasld.org/practiceguidelines/ascitesupdate2013.pdf

Spontaneous Bacterial Peritonitis (SBP)

- Paracentesis to rule out SPB should be done in any:
  - Hospitalized patient with ascites
  - Outpatient where infection is suspected due to:
    - abdominal pain (usually don't have "peritonitis")
    - fever
    - new or worsening hepatic encephalopathy
    - renal dysfunction (↑ creatinine)
    - unexplained ↑ WBC
- **Diagnosis**
  - Fluid neutrophils (total WBC x % neutrophils) > 250 $x10^6$/L
  - Do NOT wait for positive cultures to treat (cultures only positive in 50% of cases)
- **Treatment**
  - **Antibiotics x 5 days** to cover gram negative bacteria **AND** intravenous **albumin**
  - Cefotaxime 2gm IV q8h or ceftriaxone 1gm IV q24h, but ciprofloxacin orally may be acceptable for outpatients with normal renal function
  - IV albumin (1.5g/kg on Day 1 and 1.0g/kg on Day 3) prevents HRS and ↓ mortality
- **Prophylaxis**
  - Primary prophylaxis is given for 7 days in cirrhotics with GI bleeding
  - Primary prophylaxis can be considered if fluid protein is low (<15g/L)
  - Secondary prophylaxis, after first episode of SBP, is given with norfloxacin or TMP/SMX daily, until death or liver transplant, to prevent further SBP

Hepatorenal Syndrome (HRS)

- **Definition (EASL guidelines)**
  - Cirrhosis with ascites
  - Serum creatinine 133 μmol/L
  - Absence of shock
  - Absence of hypovolemia = 2 days without diuretics, albumin IV 1 g/kg/d (100 g/d)
  - No nephrotoxic drugs
  - No parenchymal renal disease = proteinuria <0.5 g/day, no hematuria (<50 RBC/hpf), normal renal ultrasonography
- **Types of HRS**
  - **Type II** = slow increase in creatinine in patients with refractory ascites undergoing frequent LVP, which often responds to lowering diuretics
  - **Type I** = rapid deterioration in renal function, often precipitated by infection or NSAIDs



Adapted from Arroyo V, et al. Gastroenterology 2002; 122:1658-76.

- **Treatment**
  - **MOA** = **midodrine** orally (to increase BP), **octreotide** subcutaneously (to lower portal pressure) and **albumin** intravenously (to improve circulation)
    - If responding consider TIPS
  - Terlipressin (to increase BP and renal perfusion) is given with albumin

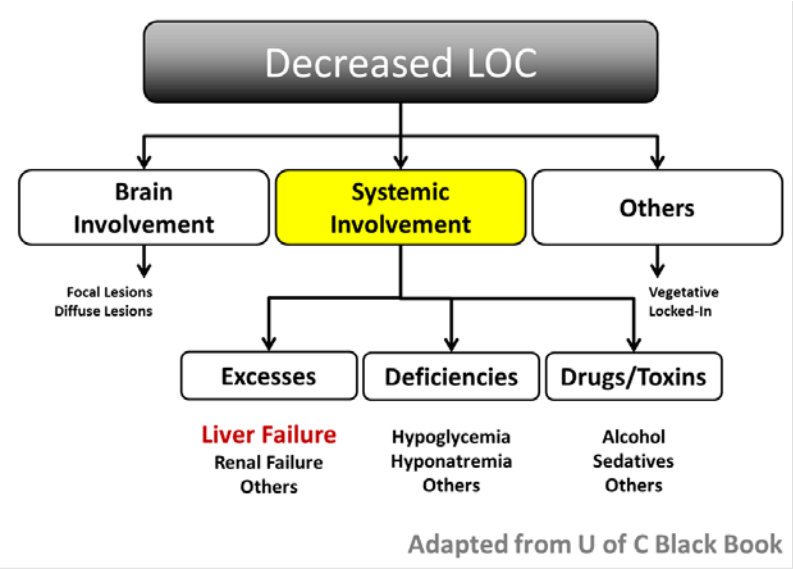
    NOTE: not available in Canada
  - As prognosis is very poor, HRS is an indication for **liver transplant** (LT)
    - Renal function usually improves after LT if on dialysis for <8-12 weeks (otherwise consider liver-kidney transplant)

14.4 Hepatic Encephalopathy

Definition & Classification

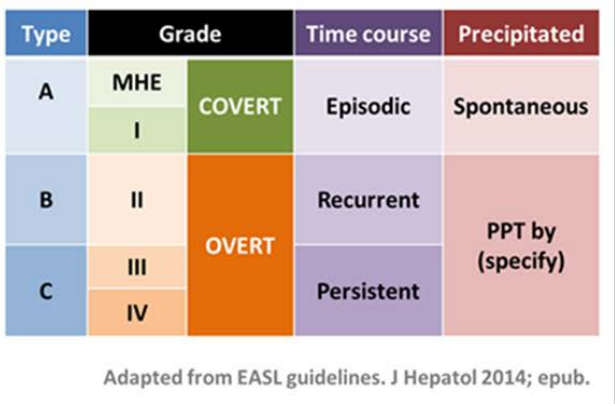
- **Definition**
  - Hepatic encephalopathy (HE) is a brain dysfunction caused by liver insufficiency and/or portosystemic shunting which manifests as a wide spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma
- **Differential Diagnosis** (scheme below)
  - Diabetic → hypoglycemia, ketoacidosis, hyperosmolar, lactic acidosis
  - Alcoholic → intoxication, withdrawal, Wernicke's encephalopathy
  - Drugs → benzodiazepines, opioids
  - Neuroinfection
  - Epilepsy

- Psychiatric
- Intracranial bleed or stroke
- Severe medical stress → organ failure



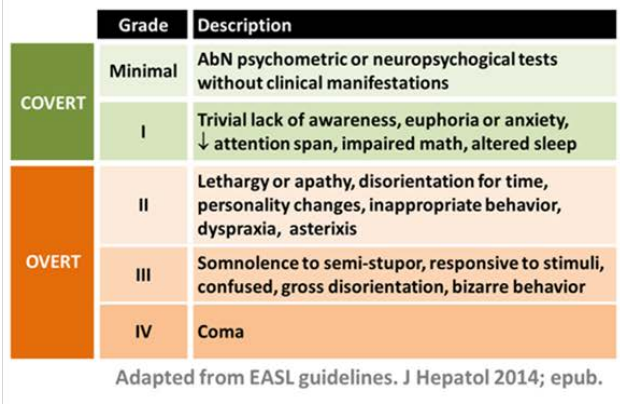
- **Classification**
  - Type (underlying disease)
    - A = Acute Liver Failure
    - B = Portosystemic shunt
    - C = Cirrhosis
  - Spontaneous or Precipitated (PPT)
  - Grade = West Haven classification
    - Covert or Overt
    - Grade I → IV
  - Time Course
    - Episodic, Recurrent, Persistent

REMEMBER: Always ask, "What precipitated this HE event?"



Type	Grade		Time course	Precipitated
A	MHE	COVERT	Episodic	Spontaneous
	I			
B	II	OVERT	Recurrent	PPT by (specify)
C	III		Persistent	
	IV			

Adapted from EASL guidelines. J Hepatol 2014; epub.



	Grade	Description
COVERT	Minimal	AbN psychometric or neuropsychogical tests without clinical manifestations
	I	Trivial lack of awareness, euphoria or anxiety, ↓ attention span, impaired math, altered sleep
OVERT	II	Lethargy or apathy, disorientation for time, personality changes, inappropriate behavior, dyspraxia, asterixis
	III	Somnolence to semi-stupor, responsive to stimuli, confused, gross disorientation, bizarre behavior
	IV	Coma

Adapted from EASL guidelines. J Hepatol 2014; epub.

Pathophysiology & Natural History

- **HE is a clinical diagnosis**
  - **Asterixis** = asymmetrical flap of outstretched hands indicates grade II HE
    - Ammonia (NH_3), from our diet and produced by bacteria in the colon, is implicated in the pathogenesis

      NOTE: NH_3 testing does NOT add any diagnostic, staging or prognostic value in CLD and should not be ordered *(Choosing Wisely Canada™ Recommendation)*
- **Natural History**
  - 10% of cirrhotics have HE at time of diagnosis (20% if decompensated)
  - HE occurs in 10-50% after TIPS
  - 30-40% with cirrhosis will develop HE at some time
  - Once HE develops, 40% will have another episode with a year
  - Leads to ↓ quality of life, care-giver burden and frequent hospitalizations

Management

- You should identify AND treat any precipitating factors (in order of importance)[5]

Episodic	**Recurrent**
▪ Infections	▪ Electrolyte disorders
▪ GI bleeding	▪ Infections
▪ Diuretics	▪ Unidentified
▪ Electrolyte disorder	▪ Constipation
▪ Constipation	▪ Diuretics
▪ Unidentified	▪ GI bleeding

- **Lactulose** is mainstay of therapy
  - Should titrate to 3-4 bowel movements per day
  - Works in more ways than just a laxative
    - As a prebiotic it promotes growth of beneficial organisms in colon
    - It is converted to lactic acid in colon creating acidic environment which slows NH3 absorption
- **Antibiotics**
  - **Rifaximin** (550mg twice daily) is an oral non-absorbable antibiotic which leads to a 50% reduction in need for hospitalization in those already on lactulose
  - Metronidazole and neomycin have been used but have toxicity issues with long-term use
- **Other therapies**
  - Branch chain amino acids (BCAA) given orally

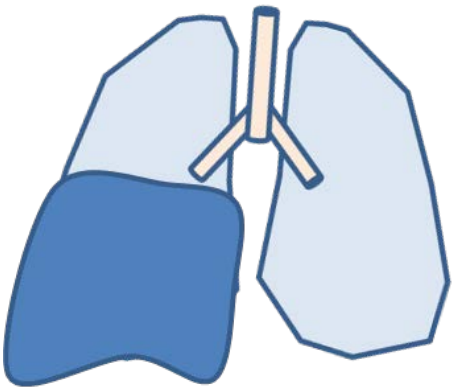
- L-ornithine L-aspartate (LOLA) given intravenously
- Liver transplantation if refractory

NOTE: NEVER PROTEIN RESTRICT CIRRHOTIC PATIENTS

14.5 Other Complications of Cirrhosis

Hepatic Hydrothorax

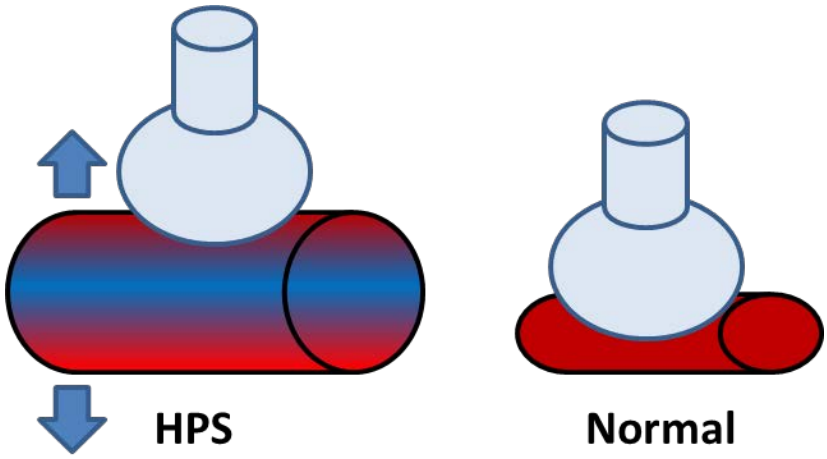
- Collection of transudate fluid in pleural space (right is more common than left)
- May be due to ascites travelling through diaphragm
- Managed just like ascites *[see Chapter 14.3]*
- Can be complicated by infection or spontaneous bacterial empyema (SBE) which is managed like SBP
- **AVOID** the use of a chest tube



Hepato-Pulmonary Syndrome

- Vasodilators from cirrhotic liver affect the pulmonary circulation leading to dilatation of pulmonary capillaries next to alveoli and impaired gas exchange

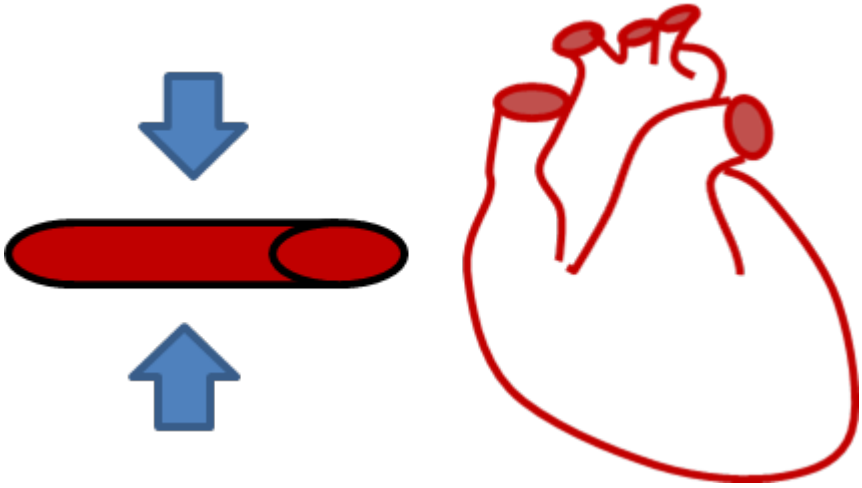
- Symptoms include shortness of breath (platypnea) and hypoxia (orthodeoxia) which is relieved by lying flat but is worsened with sitting or standing
- Screening = low oxygen saturations
- Arterial blood gas shows low PaO2
- Echocardiogram shows agitated bubble pass from right heart to left heart quickly (through the dilated capillaries in the lungs)
- Technetium99 labelled macro-aggregated albumin (Tc99 MAA) study shows shunting through lungs (uptake in brain)
- There are no effective therapies other than liver transplantation (LT)



Porto-Pulmonary Hypertension

- Unexplained vasoconstriction of pulmonary circulation (opposite of HPS)
- Present with shortness of breath and right heart failure
- Screening = echocardiogram (RVSP >35mmHg)
- Confirmed by performing right heart catheterization
  - MPAP >25, PVR >240 dyn.sec.cm^{-5}, PCWP <15

- Treatment is with vasodilators = phosphodiesterase inhibitors, endothelin-receptor antagonists, prostacyclin
- If responding to these therapies the patient can be considered for LT



Metabolic Bone Disease

- Osteoporosis is very common in cirrhotics
  - Especially in cholestatic liver diseases and can worsen after liver transplant
- Diagnosis = bone densitometry by DEXA (T score < 2.5)
- Treat with calcium, vitamin D, bisphosphonates or parathyroid hormone

Sexual Dysfunction

- Loss of libido and erectile dysfunction (ED) in men are very common
- Consider testosterone supplementation for men
- Therapies for ED can lower blood pressure (use with caution if ascites)

Pain

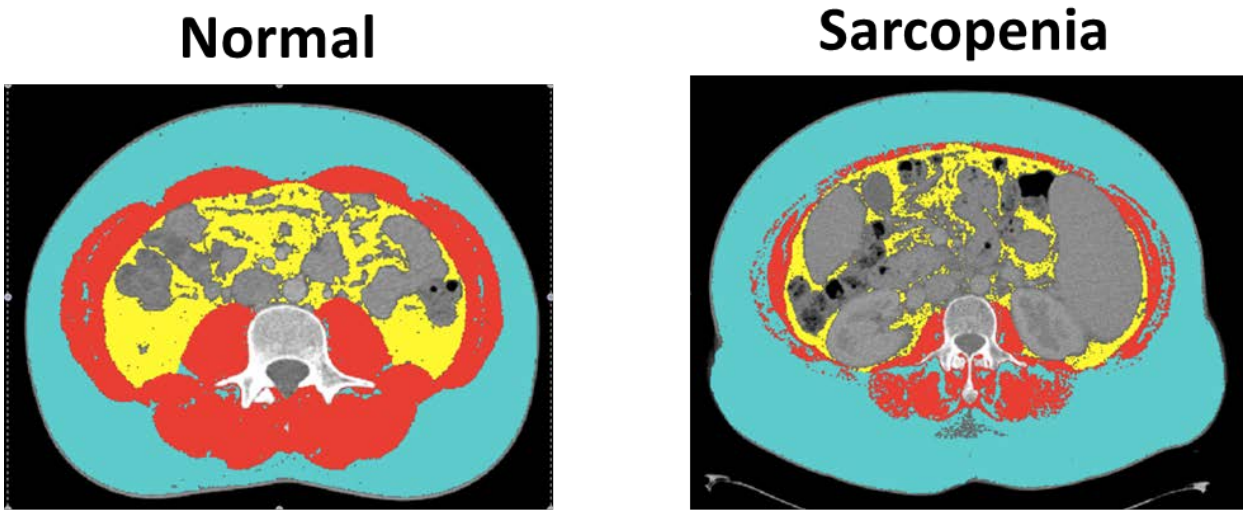
- Pain is a common symptom and is often under treated because medications may have side effects in cirrhotics

- Acetaminophen must be avoided if actively abusing alcohol
- NSAIDS can precipitate GI bleeding and hepatorenal syndrome
- Opioids can accumulate and precipitate hepatic encephalopathy

- Palliative care should be involved in the care of patients with cirrhosis
  - Especially important when they have decompensated due to their poor prognosis

Malnutrition & Sarcopenia

- Sarcopenia is loss of muscle mass
- Multifactorial = ↑ energy requirements, poor oral intake (massive ascites), malabsorption
- Associated with poorer outcomes after LT
- Cirrhotics need high caloric intake (35-40 kcal/kg/day) and high protein (1.2-1.5 g/kg/day) intake
- Exercise is helpful for maintaining muscle mass and sense of well being



Images courtesy of Dr. Puneeta Tandon (UofA)

Abbreviations:

5vMELD – 5 variable Model for End-Stage Liver Disease

ACE-I – angiotensin converting enzyme inhibitors

APC – argon plasma coagulation

ARB – angiotensinogen receptor blockers

BCAA – branch chain amino acids

BP – blood pressure

CHF – congestive heart failure

DEXA – dual energy Xray absorptiometry

EASL – European Association for the Study of the Liver

ED – erectile dysfunction

EDG – endoscopy

GAVE – gastric antral vascular ectasia

GE junction – gastroesophageal junction

hpf – high power field

HPS – hepato-pulmonary syndrome

HRS – hepatorenal syndrome

ICU – intensive care unit

LOC – level of consciousness

LOLA – L-ornithine L-aspartate

LVP – large volume paracentesis

LT – liver transplant

MHE – minimal hepatic encephalopathy

MOA – midodrine, octreotide, albumin

MPAP – mean pulmonary artery pressure

Nd:YAG laser – neodymium-doped yttrium aluminium garnet laser

NSAIDs – non-steroidal anti-inflammatory drugs

NSBB – non-selective beta-blockers

PaO2 – arterial partial pressure of oxygen

PCWP – pulmonary capillary wedge pressure

PHG – portal hypertensive gastropathy

PMN – polymorphonuclear neutrophil

PPT – precipitated

PVR – pulmonary vascular resistance

PVS – peritoneovenous shunt

RAAS – renin-angiotensin-aldosterone system

RBC – red blood cells

RCTs – randomized clinical trials

RVSP – right ventricular systolic pressure

SAAG – serum ascites albumin gradient

SBE – spontaneous bacterial empyema

SBP – spontaneous bacterial peritonitis

Tc^{99}MAA – technetium^{99}-labelled macro-aggregated albumin

TIPS – transjugular intrahepatic porto-systemic shunt

TMP/SMX – trimethoprim/sulfamethoxazole (Bactrim®)

TSE – thin scope endoscopy

Figure Citations

Cirrhosis Stages. Adapted from Abillos A, Garcia-Tsao G. Classification of cirrhosis: the clinical use of HVPG measurements. *Dis Mark* 2011; 31(3):121-8.

Child Pugh Class and Survival. Adapted from D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. *J Hepatol* 2006; 44:217-231.

MELD-Na. Adapted from Kim WR, Biggins SW, Kremers WK, et al. Hyponatremia and mortality among patients on the liver-transplant waiting list. *N Engl J Med* 2008; 359(10): 1018-26.

5vMELD. Adapted from Myers RP, Shaheen AA, Faris P, Aspinall A, **Burak KW**. Revision of MELD to include serum albumin improves prediction of mortality on the liver transplant waiting list. *PLoS One* 2013; 8(1):e51926.

Ascites Pathogenesis and Management. Adapted from Garcia-Tsao G. Current management of the complications of cirrhosis and portal hypertension: variceal hemorrhage, ascites, and spontaneous bacterial peritonitis. *Gastroenterology* 2001; 120:726-748.

Ascites Management. Adapted from Runyon BA, American Association for the Study of Liver Diseases. Introduction to the revised American Association for the Study of Liver Diseases Practice Guidelines management of adult patients with ascites due to cirrhosis 2012. *Hepatology* 2013; 57(4):1651-1653.

HRS Types. Adapted from Arroyo V, Guevara M, Ginès P. Hepatorenal syndrome in cirrhosis: pathogenesis and treatment. *Gastroenterology* 2002; 122:1658-76.

Esophageal Varices Management. Adapted from Garcia-Tsao G, Abraldes JG, Berzigotti A, and Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the Study of Liver Diseases. *Hepatology* 2016; 65(1):310-335.

HE Classification and Grading. Adapted from Vistrup H, Amodio P, Bajaj J, et al. Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. *J Hepatol* 2014; 60(2):715-735.

Sacrcopenia. Images courtesy of Dr. Puneeta Tandon.

SCHEMES: Hematemesis, Ascites, Decreased LOC. Adapted from University of Calgary Black Book. Available at http://blackbook.ucalgary.ca/

References

1. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey WD, Practice Guidelines Committee of American Association for Study of Liver Diseases, Practice Parameters Committee of American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Am J Gastroenterol* 2007; 102(9):2086-102.
2. Garcia-Tsao G, Abraldes JG, Berzigotti A, and Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the Study of Liver Diseases. *Hepatology* 2016; 65(1):310-335.
3. European Association for the Study of the Liver. EASL Clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. *J Hepatol* 2010; 53(3):397-417.
4. Runyon BA, American Association for the Study of Liver Diseases. Introduction to the revised American Association for the Study of Liver Diseases Practice Guidelines management of adult patients with ascites due to cirrhosis. *Hepatology* 2013; 57(4):1651-1653.
5. Vistrup H, Amodio P, Bajaj J, et al. Hepatic encephalopathy in chronic liver disease: 2014 practice guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. *J Hepatol* 2014; 60(2):715-735.