Cirrhosis and It’s Management

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Disclosures

Speaker for Gilead Health Sciences; Viral Hepatitis C Division

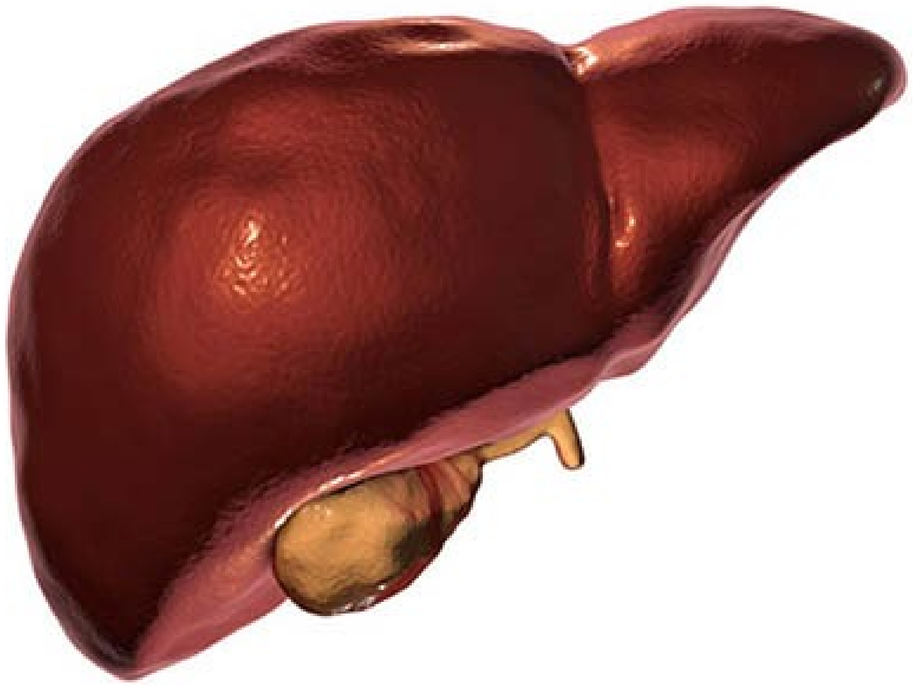
Cirrhosis

Objectives

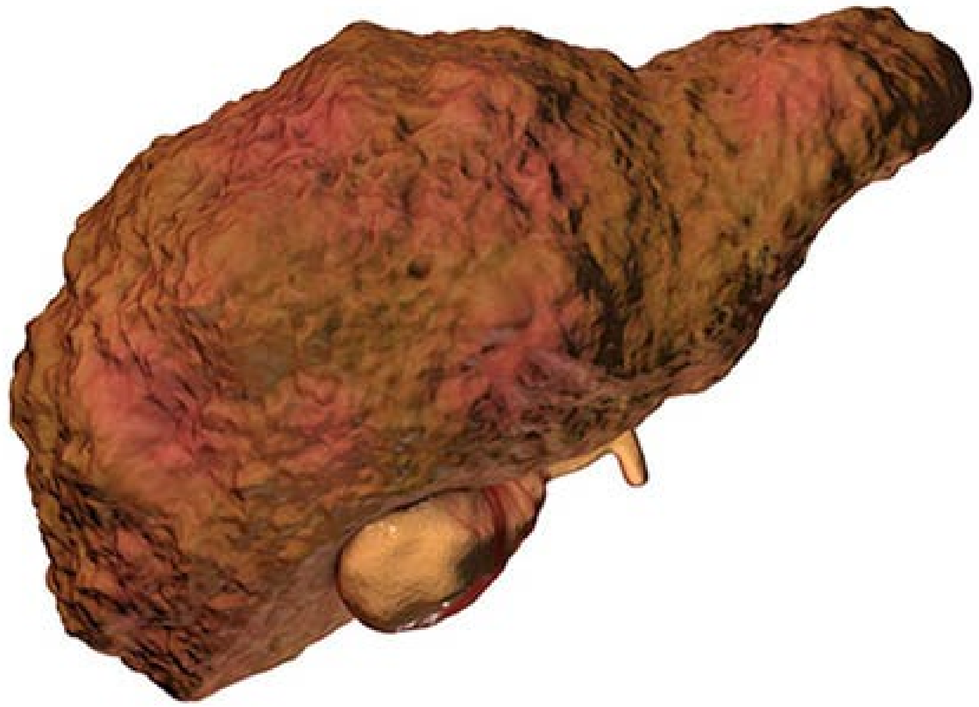
- What is it?
- What causes it?
- How do we diagnose it?
- How do we manage it?
  - Inpatient
  - Outpatient

Cirrhosis

What is it? What are the stages?



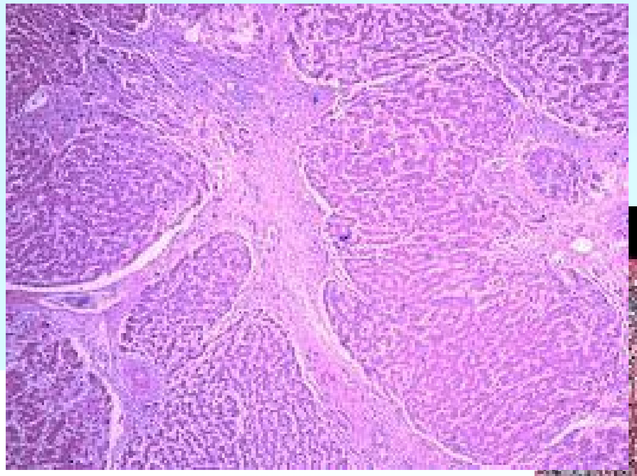
Healthy liver

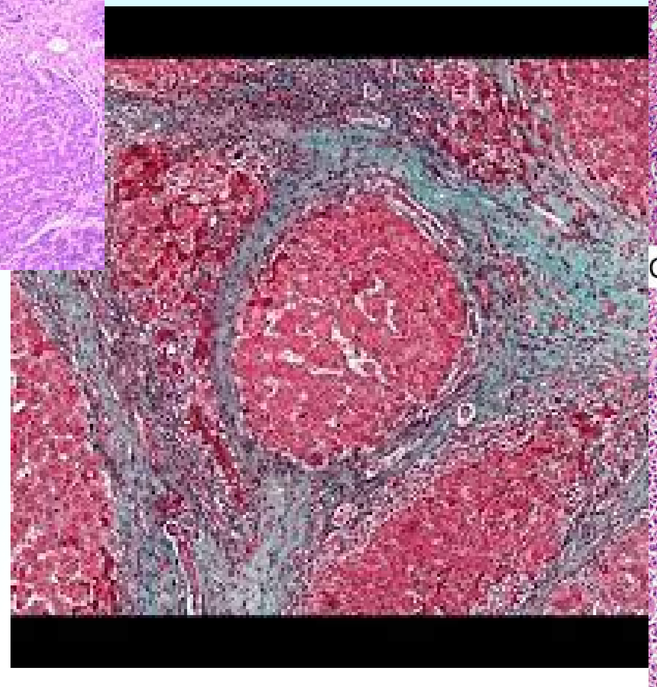


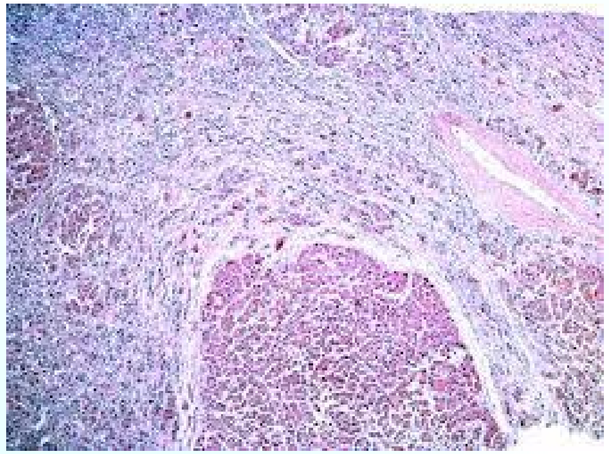
Cirrhotic liver

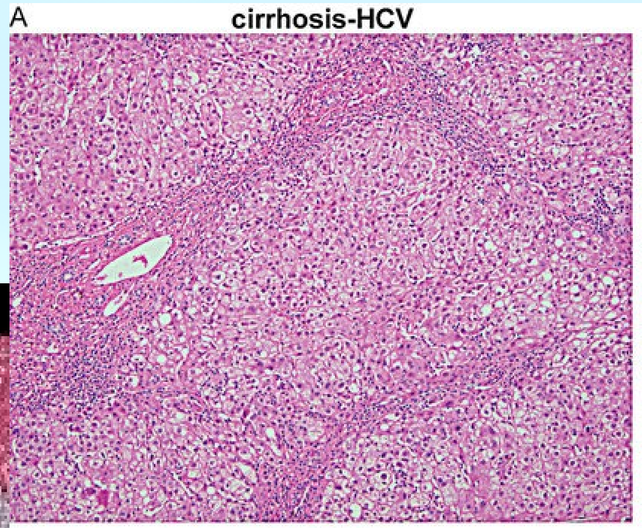
Cirrhosis

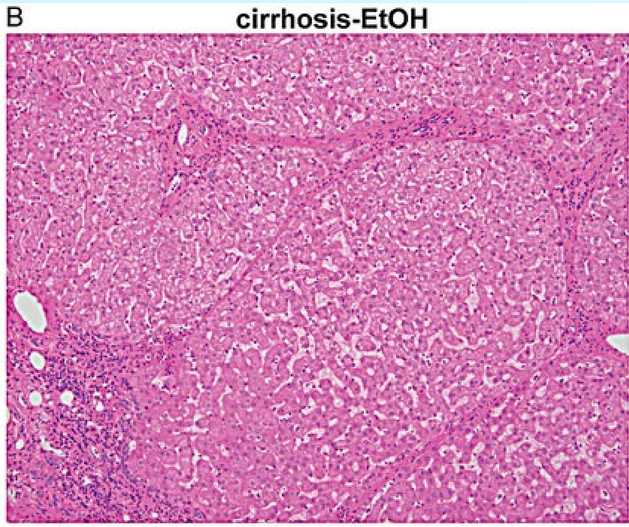
Histology appearance

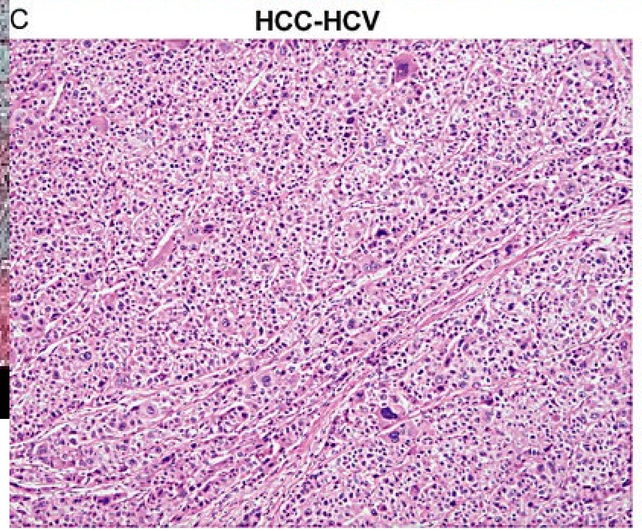


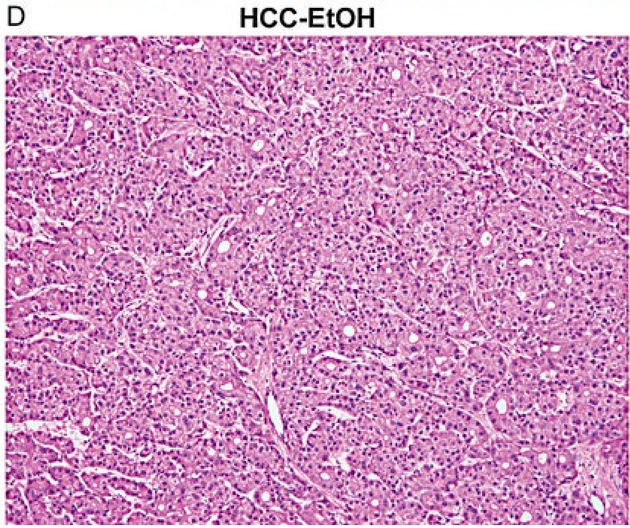












Stages of Cirrhosis/Fibrosis

- Stages 0 (normal) through stage 4 (cirrhosis)
  - Can use terms “advanced fibrosis” for stages 1-3
  - Most test results can vary 1 stage above/below the given stage result
  - Fibrosure blood test
  - Liver Elastography (ultrasound)
  - APRI
  - FIB-4
  - Liver biopsy is still gold standard (bruising, bleeding, infection, death)

QUESTION

WHAT IS THE BEST SINGLE LAB TO LOOK AT FOR PREDICTING CIRRHOSIS?

- ANSWER?

THE BEST SINGLE LAB FOR PREDICTING CIRRHOSIS

ANSWER

- PLATELETS, PLATELETS, PLATELETS, PLATELETS, THROMBOCYTES

  - IF LESS THAN 70,000 rules in cirrhosis
  - IF GREATER THAN 200,000 rules out cirrhosis
  - <150,000 is concerning for cirrhosis
  - My cutoff if anything <100,000 is high risk of having cirrhosis

J Gen Intern Med. 2015 Aug; 30(8): 1112–1117.

WHAT CAUSES CIRRHOSIS?

Multiple Etiologies

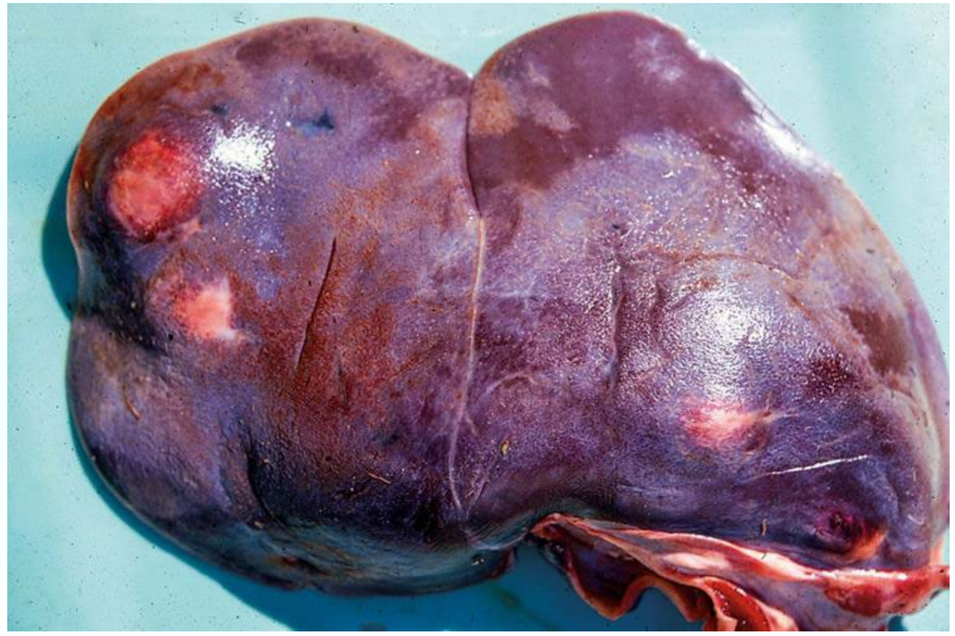
- Viral Hepatitis, A, B, C, D, E (also remember EBV, CMV, Herpes for other viral causes of acute hepatitis, Covid)
  - 6 genotypes worldwide (1-6 with subtypes)
- Alcohol
- MASH, metabolic dysfunction associated steatohepatitis (formerly NASH)
- Medications (amiodarone), supplements, herbals, acetaminophen
- Autoimmune hepatitis, PBC, PSC (ANA, AMA, ASMA. Have other autoimmune diseases, “run in packs”)
- Wilson’s disease (young females, psychiatric disorders, Kaiser Fleischer rings)
- Hemochromatosis
- Parasitic infections
- High blood galactose levels, glycogen storage disorders
- Alpha 1 antitrypsin deficiency (liver and lung disease)
- Biliary atresia (congenital, Kasai procedure)

Kaiser Fleischer Ring

Parasitic Infections That Cause Cirrhosis

Liver Flukes

- *Schistosoma haemotobium/mansoni*
- *Clonorchis sinensis*
- *Fasciola hepaticum/magna*



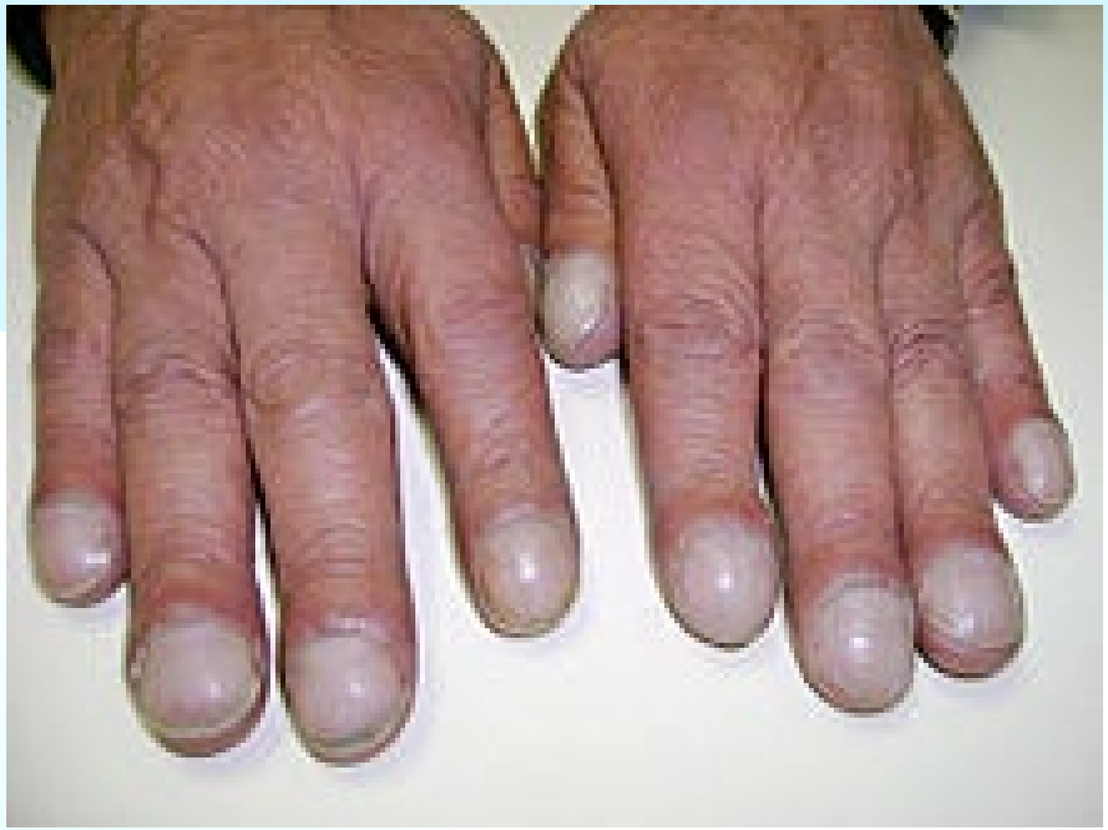
Live Parasite
~Liverfluke ~

Live Parasite in
Intestine

Live Liver fluke (parasite) encountered during the ERCP

Physical Exam Findings of Cirrhosis

Clubbing

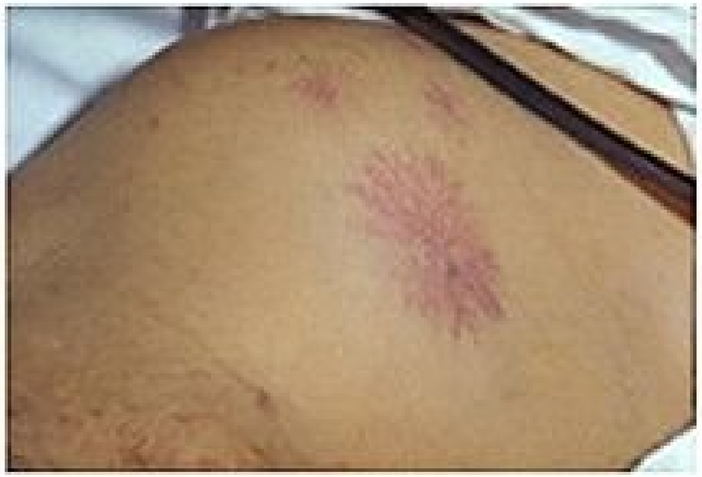


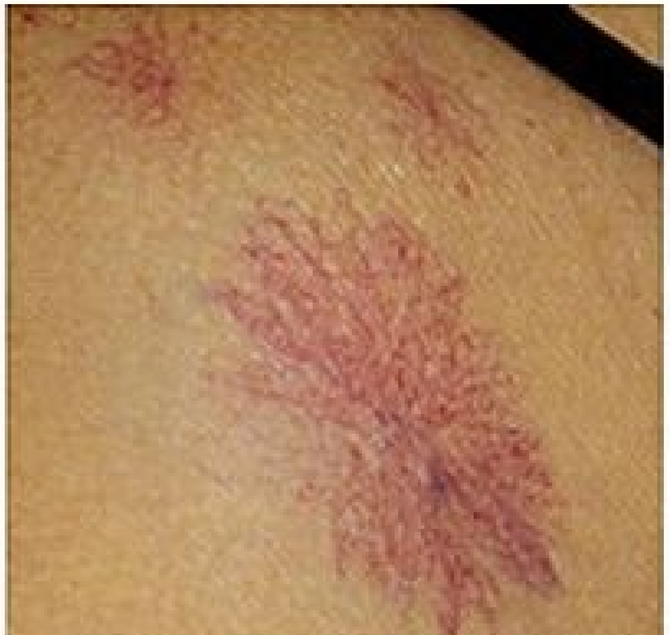
- Heart, Lung and Endocrine disease
- GI diseases
  - Crohn’s and UC
  - Malabsorption
  - Cirrhosis (especially PBC)
  - Hepatopulmonary syndrome
  - Caused from overproduction of hepatocyte growth factor/platelet derived growth factor and/or dysfunctional prostaglandin metabolism

Physical Exam Findings of Cirrhosis

Spider Angiomas

- 33% of cirrhotics have these
- Due to high levels of estrogen
- Seen in distribution of superior vena cava
- Fill from the center outwardly
- Due to failure of the sphincteric muscle surrounding the cutaneous arteriole
- Can also see these during normal pregnancy



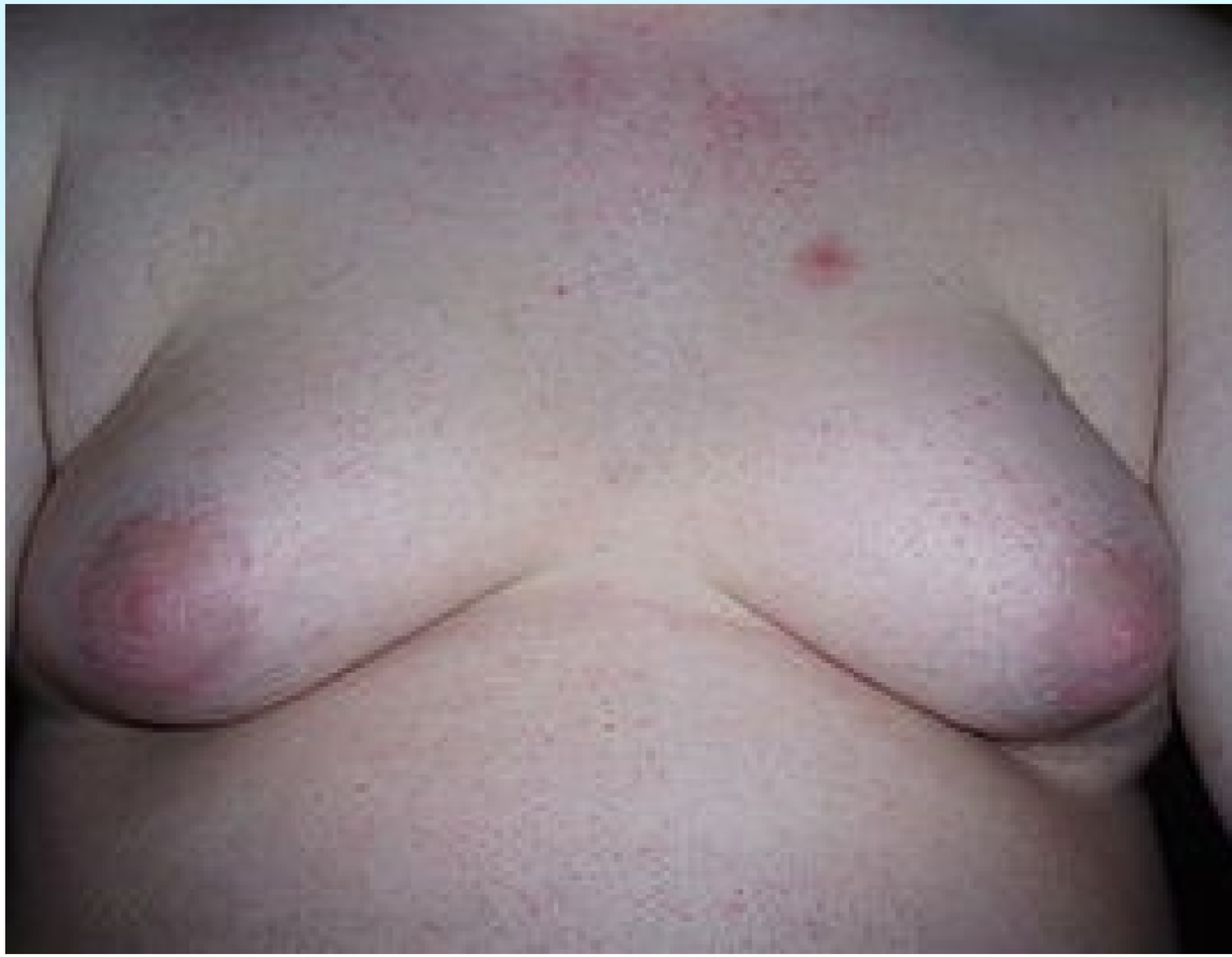


Physical Exam Findings of Cirrhosis

Gynecomastia

- Due to decreased metabolism of estrogen
- Alcohol also decreases the production of testosterone

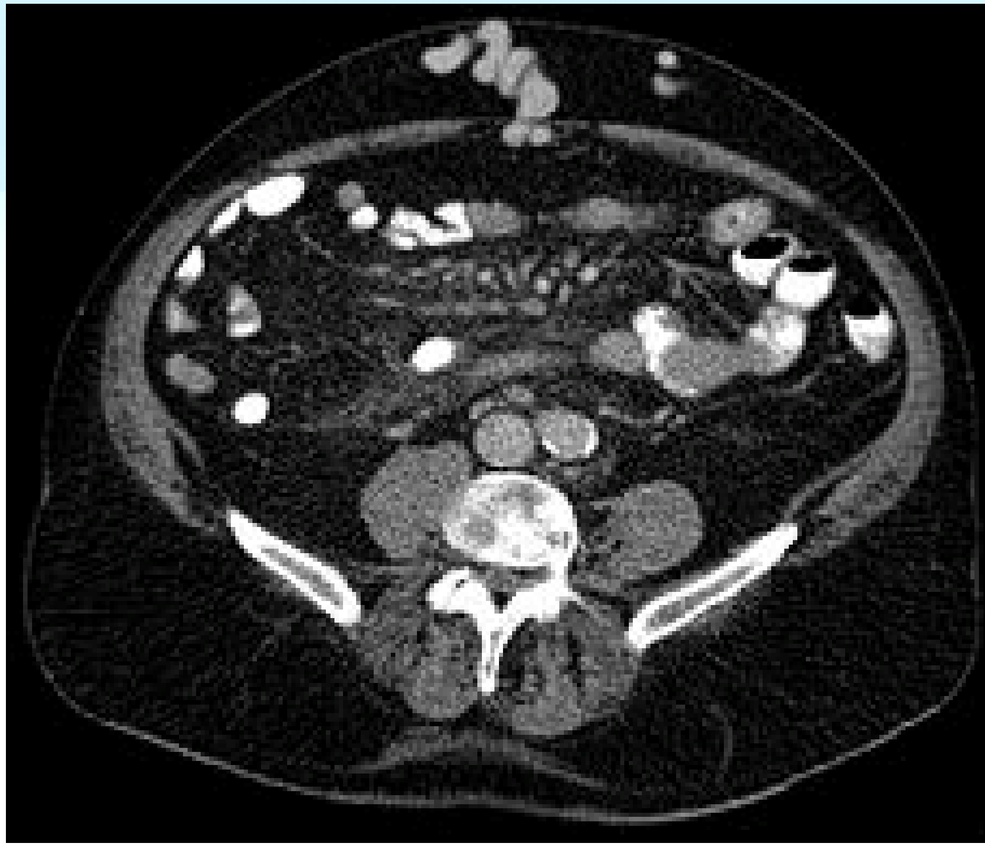
- What medication can cause gynecomastia?



Physical Exam Findings of Cirrhosis

Caput medusae

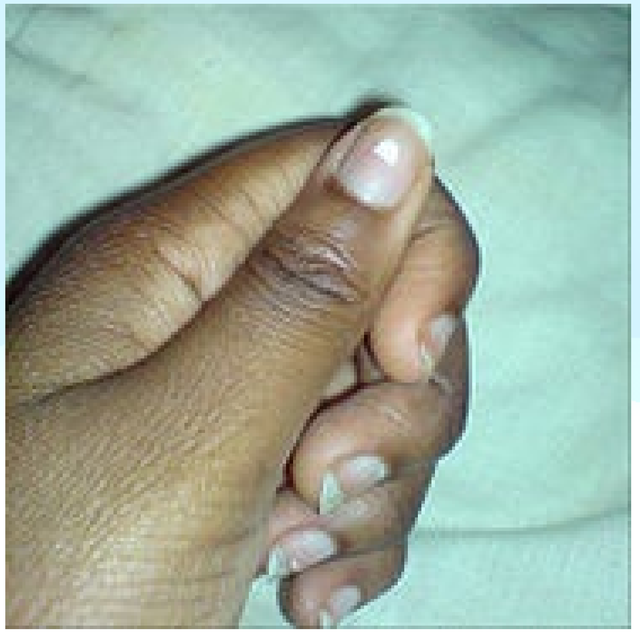
- Cardinal sign of portal hypertension
- “Palm tree” sign
- Due to porto-systemic collateral circulation at the umbilical vein
- No surgical intervention (unless absolutely emergent), treat with medications, TIPS



Physical Exam Findings of Cirrhosis

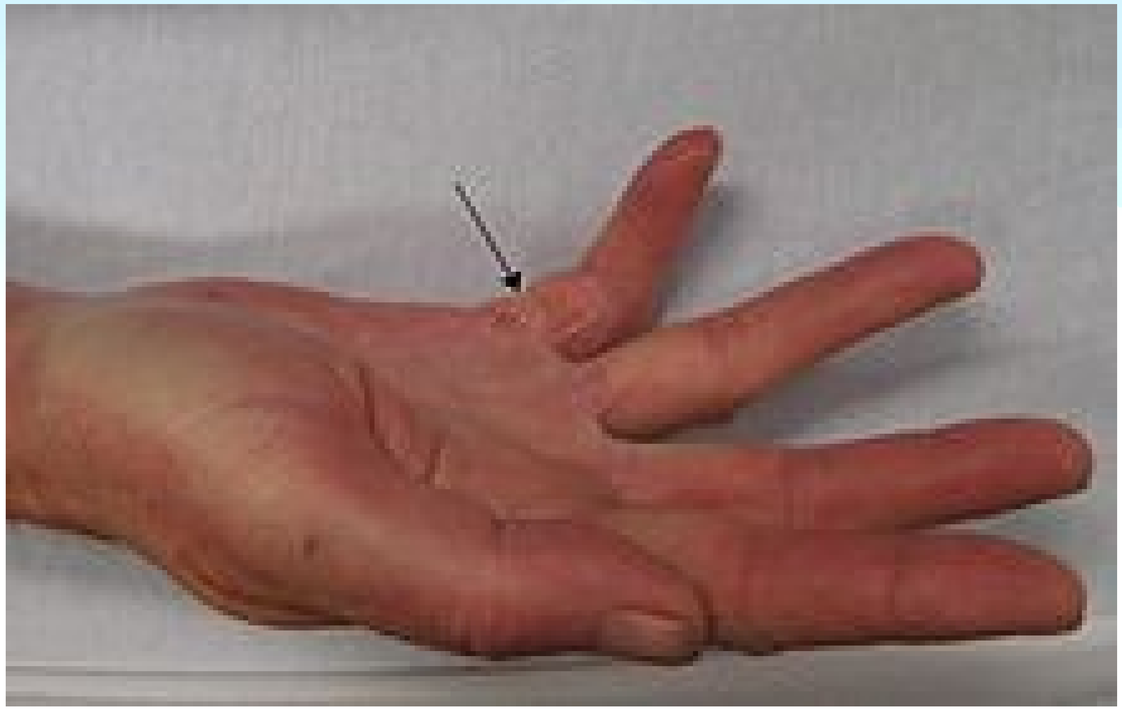
Leukonychia

- totalis”
  - Liver failure, kidney failure, malabsorption syndromes, sulfonamides
- “partialis”
- “striata”
  - Mees’ lines
    - Trauma, heavy metal poisoning (arsenic, lead), chemotherapy, severe illness with high fevers such as measles, malaria, herpes and leprosy
    - Cirrhosis



Dupeytren’s Contracture

Caused by tobacco, ETOH, diabetes, anti-seizure medications



Other Physical Exam Findings of Cirrhosis

And Labs Pointing to Cirrhosis

- Palmar erythema
- Feminising hair distribution
- Testicular atrophy
- Anemia
- Thrombocytopenia, elevated PT/INR,
- Bruising/bleeding dysfunction
- Jaundice
- Hypoalbuminemia
- Hyponatremia
- Elevated ALT/AST ***
- Elevated GGT (seen mostly in EtOH liver disease)
- Hematemesis/Melena

PE Findings, Signs/Symptoms Affiliated with Decompensation

(Can be indicative of “Decompensated Liver Disease”)

- Drowsiness, Day/Night reversals (HE)
- Hyperventilation (HE)
- Metabolic Flap/Asterixis (HE)
- Jaundice (Excretory dysfunction), Scleral icterus
- Leukonychia (Hypoalbuminemia)
- Peripheral Edema (Hypoalbuminemia)
- Easy Bruising (Coagulopathy)
- Ascites (Hypoalbuminemia, Portal HTN)

How Do We Manage Cirrhosis?

Inpatient and Outpatient Management

PRACTICE GUIDELINES

AASLD Practice guidance on Acute-on-chronic liver failure and the management of critically Ill patients with cirrhosis

Karvellas, Constantine J.[1]; Bajaj, Jasmohan S.[2]; Kamath, Patrick S.[3]; Napolitano, Lena[4]; O'Leary, Jacqueline G.[5]; Solà, Elsa[6]; Subramanian, Ram[7]; Wong, Florence[8]; Asrani, Sumeet K.[9]

Author Information

Hepatology ():10.1097/HEP.0000000000000671, November 9, 2023.

Management of Complications of Cirrhosis

Variceal Hemorrhage, Portal Hypertensive Gastropathy

- Mortality:15-20% in 30 days with acute variceal bleeding
- Portal Hypertensive Gastropathy (Congestive Gastropathy)
  - Rare source of bleeding
  - Caution with PPI usage decompensated cirrhosis. Why?
- EGD is warranted with ALL new diagnoses of cirrhosis
  - If varices seen or banded, then repeat banding q 2-4 weeks
  - Repeat yearly if no varies noted (or sooner if hematemesis noted)

Management of Complications of Cirrhosis

Ascites, edema, anasarca

- Diuretics
  - Lasix
  - Spironolactone
  - What is the appropriate ratio?
  - What max dosages of both medications is considered diuretic failure?
  - What medication can be give if patient becomes hypotensive on diuresis?
- Fluid restriction (used if Na level <125 mmol/L), challenging for patients

Management of Complications of Cirrhosis

Spontaneous Bacterial Peritonitis

- Fever >100 F, abdominal pain/tenderness, MS change, or asymptomatic
- Have low threshold for paracentesis
  - Positive bacterial culture on ascitic fluid AND/OR PMN count >250 cells/mm3
- Start ABX after paracentesis
- 3rd gen Cephalosporin, Cefotaxime 2 gm q 8, Ceftriaxone 2 gm q day
- Carbapenem (per hospital formulary), may have benefit in critically ill patients
- Fluoroquinolone, Cipro 400 IV BID (DO NOT USE IN PATIENTS USING FQ FOR SBP PROPHYLAXIS)
- Resistance to these drugs is a concern

Management of Complications of Cirrhosis

SBP

- Renal dysfunction in SBP
  - Seen in 30-40% patients with SBP and is a major cause of death
  - 25% albumin infusion, 1.5 g/kg within 6 hours and 1 g/kg on day 3 if Cr>1, Bili>4 or BUN>30
  - May need octreotide and midrodrine
- Antibiotic prophylaxis for SBP if…
  - Ascites fluid protein <1g/dl, variceal bleeding, prior SBP diagnosis, impaired renal function (Cr>1.2 or BUN>25) or in liver failure (CTP score >9 and bilirubin >3)
  - Bactrim DS 1 qd or Cipro 500 mg qd (CTP A) or BID dosing if CTP B or C

Management of Complications of Cirrhosis

Hepatocellular carcinoma

- Imaging of the liver (HCC screening) q 6 months
- AFP q 6 months
- Watch for any signs of decompensation and suspect HCC if previously compensated and now decompensating *
- Change imaging modalities if AFP elevating or signs of decompensation
  - MRI with gadolinium (liver protocol)
  - Triple Phase CT scan (liver protocol)

Hepatocellular Carcinoma

3rd to 4th MCCOD due to cancer in the world

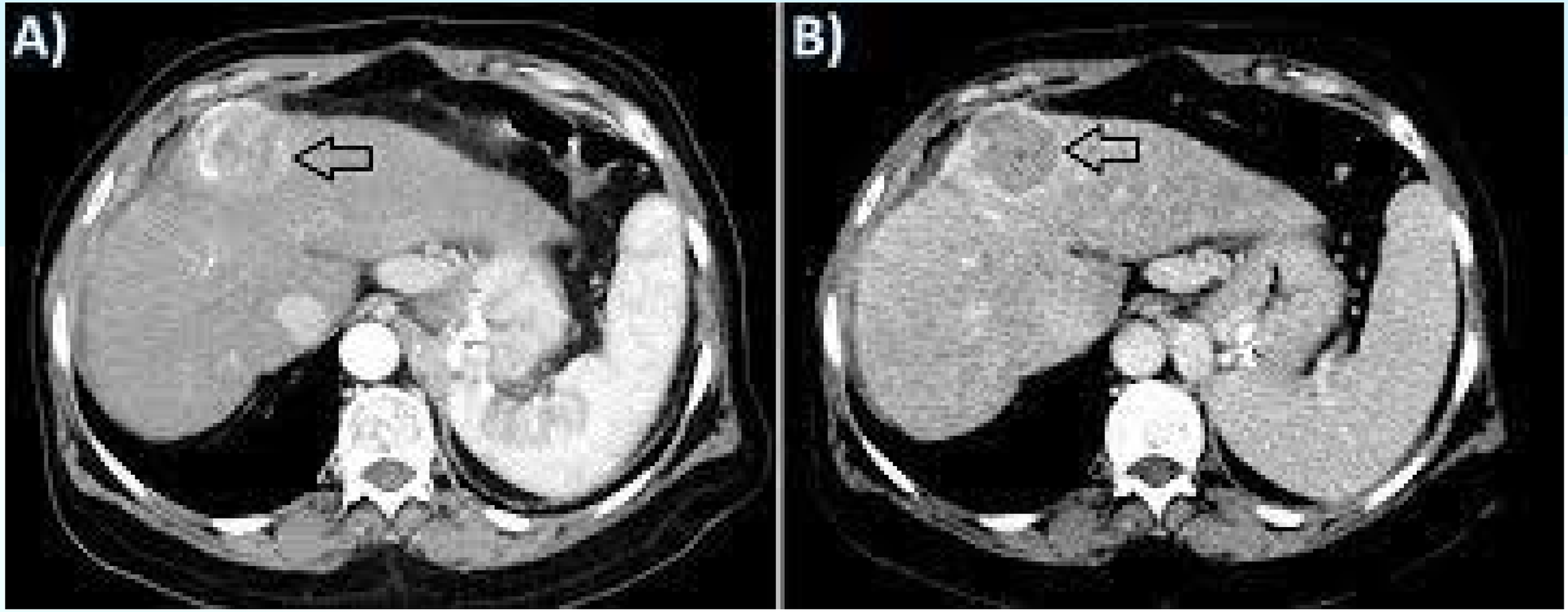
- Typically seen in cirrhotics

- HCC rates have tripled in the past 3 decades Why?

- Name two chronic liver disease states where HCC can arise WITHOUT CIRRHOSIS?
  - ???
  - ???

Hepatocellular Carcinoma

“Washout phase” on Triple Phase CT Imaging



Hepatocellular Carcinoma

Milan Criteria vs. UCSF Criteria

- Milan: Single lesion >/=2cm but not >/=5 cm or 3 or less lesions all >/=1cm or </=3 cm, no mets, no vascular involvement

- UCSF: Solitary lesion </=6.5 cm, </=3 nodules with the largest lesion of 4.5 cm and a total tumor diameter of </=8 cm

- Must have good staging imaging for this.

Number of Liver Transplants

Worldwide

- 34,944 livers transplanted in 2023 world wide
- 23% were living donor transplants
- Highest number of transplants per million people population
  - Korea
  - United States

Liver Transplantation 2023: Status Report, Current and Future Challenges. Norah A. Terrault,. Clinical Gastroenterology and Hepatology 2023;21:2150–2166

Number of Liver Transplants

In the United States

- For the first year ever, more than 10,000 liver transplants were performed in 2023.
- There were 10,660 liver transplants performed (an 11.9 percent increase over 2022 and continues an 11-year trend of annual records)

- Lung transplants exceeded 3,000 for the first time (3,026 total)
- All-time volume records were also set for kidney transplants (27,329)
- All-time volume records were set for heart transplants (4,545)

UNOS News Bureau. Continued increase in organ donation drives new records in 2023; New milestones exceeded. January 10, 2024

Hepatorenal Syndrome

Indicates Liver Decompensation

- Development of renal failure in cirrhosis, acute hepatitis or with large liver tumor burden
- What hides this renal change initially?
  - Decreasing muscle mass and hepatic urea production so plasma BUN and Cr can remain stable
  - Diagnosis of exclusion
    - R/O volume depletion
  - Poor prognosis

Hepatopulmonary Syndrome

Defined by a Triad

- Liver Disease
- Increased AA gradient while on room air
- Evidence for intrapulmonary vascular abnormalities on imaging
- No real effective therapy other than transplant

Hepatic Hydrothorax

Be aware of this one!

- Pleural effusion (usually R sided) with patient with cirrhosis with normal heart and lungs
- Treatment
  - Diuretics and fluid restriction
  - Frequent thoracentesis
  - TIPS
  - DO NOT PLACE A LARGE BORE CHEST TUBE!!!

Management of Complications in Cirrhosis

More Cardiac and Lung Issues

- Portopulmonary Hypertension
  - Pulm HTN in patients with portal HTN
  - ~2%
  - Dx with Echo or R heart Cath
  - Perioperative mortality with liver transplant is high
- Cirrhotic Cardiomyopathy
  - Normal to increased cardiac output but have blunted response to pathologic, pharmacologic, physiologic stressors
  - Can have EKG abnormalities

Complications of Cirrhosis

Hepatic Encephalopathy

- A “spectrum of potentially reversible neuropsychiatric abnormalities.”
- Symptoms of HE are similar to those driving intoxicated.
- Patients with HE have 4-5 times higher risk of accidents while driving.
- I recommend to my patients they DO NOT drive if have documented HE.
- West Haven Criteria, Psychometric testing, critical flicker frequency, lymphocyte to monocyte ratio, Albumin level of 2.8 g/dl or less

Hepatic Encephalopathy

Treatments

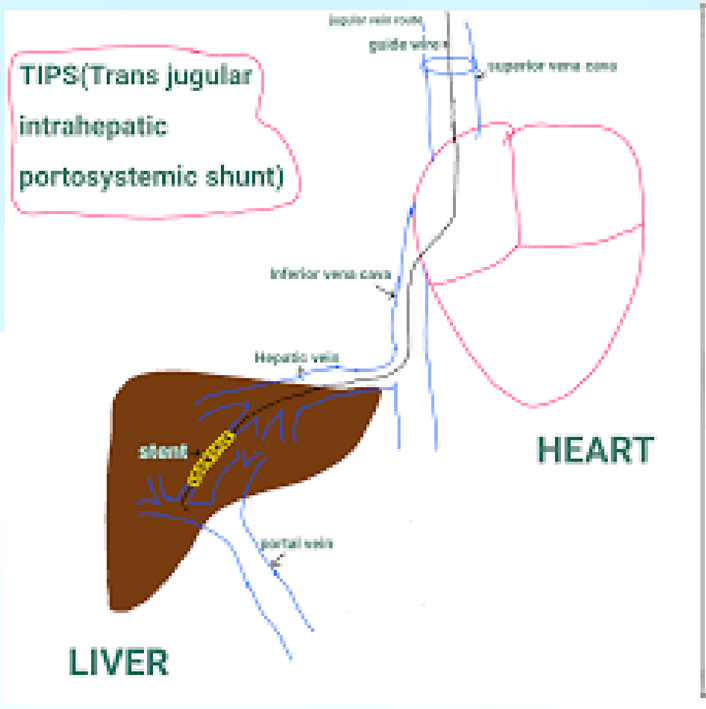
- Lactulose, titrate to goal of 2-3 soft BMs daily, can give rectally
- Xifaxin 550 mg BID
- Avoid dehydration (with lactulose and diuretics)
- Ammonia levels can be very confusing. Most hepatologists do NOT order them. Dame Sheila Sherlock

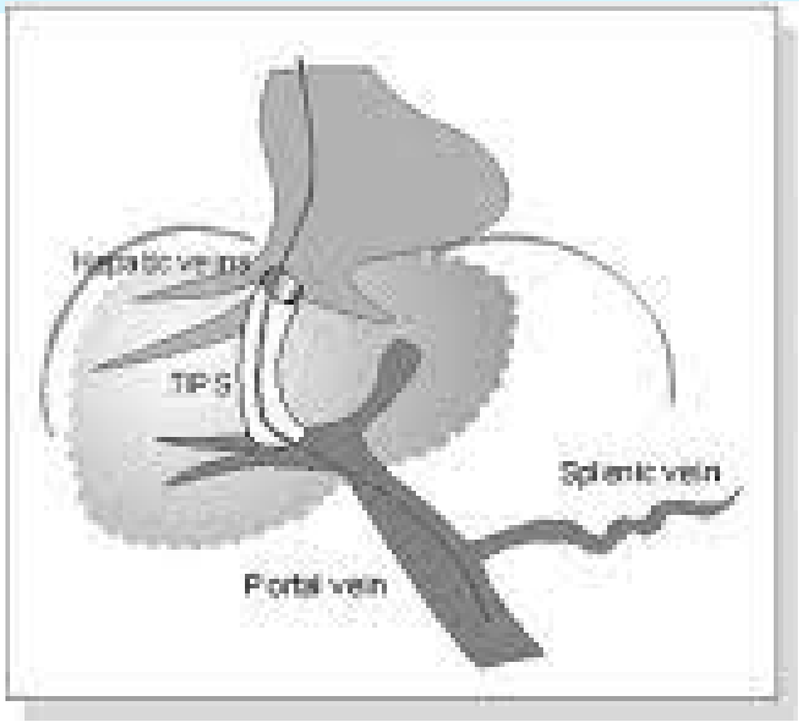
Indications for TIPS (transjugular intrahepatic portosystemic shunt)
Bleeding/Fluid accumulations

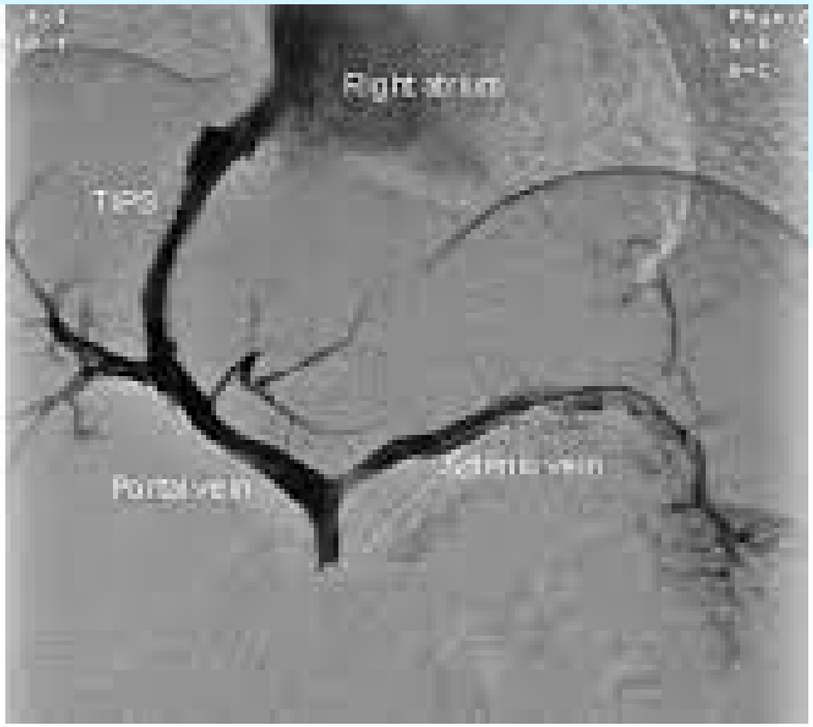
- Active esophageal/gastric variceal bleeding
- Preventing recurrent bleeding
- Portal hypertensive gastropathy
- Refractory ascites
- Hepatic hydrothorax
- Budd Chiari Syndrome
- Complication/Morbidity rates for TIPS up to 20%

What is a “TIPS”?

An endovascular procedure by Interventional Radiology







Contraindications for TIPS

(Not everyone is a candidate)

- CHF
- Severe TR
- Severe pulmonary HTN; intervention should be reconsidered or pursued with caution when right atrial pressure exceeds 20 mm Hg, and a pulmonary arterial pressure greater than 45 mm Hg should contraindicate TIPS
- Polycystic liver disease
- Active infection/sepsis
- Unrelieved biliary obstruction

Valji K. Hepatic, splenic, and portal vascular systems. In: Valji K, ed. Vascular and interventional radiology, 2nd ed. Philadelphia, PA: Elselvier, 2006:269-319

Relative Contraindications for TIPS

- Hepatic tumors (centrally located)
- HE
- PV thrombosis
- Thrombocytopenia <20,000
- Moderate pulmonary HTN
- MELD >18 have higher 3 month mortality that MELD <18

Inpatient Management of Cirrhosis

Not much different than outpatient management.

- I would recommend calling a transplant institution for discussion of the patient and seeing if transfer of the patient is ever warranted and DOCUMENT SUCH DISCUSSION.
- Can be more aggressive with diuretics
- Can ask IR if TIPS is warranted

Review

Key points to remember about cirrhosis

- What is it?
- What causes it?
- How do we diagnose it?
- How do we manage it?

REMEMBER!

KEY POINTS to patients with cirrhosis

- TREND YOUR PATIENTS PLATELET COUNTS. If they are dropping then think about portal hypertension/advancing fibrosis/cirrhosis
- Follow their MELD score (use APP/medical calculator)
- Do not forget to screen for varices in all cirrhotics
- Screen for HCC every 6 months with AFP and use APPROPRIATE imaging
- Appropriate referral to transplant center at MELD >10 (sooner rather than later)
- Caution against/NO driving with HE (can hurt themselves or others)
- Can always refer to GI to help follow these challenging patients
- Refer to AASLD for cirrhosis management guidelines

Thank You!

(Now lets have a beer!)

- Questions?