Caring for the Hospice Patient with Liver Disease

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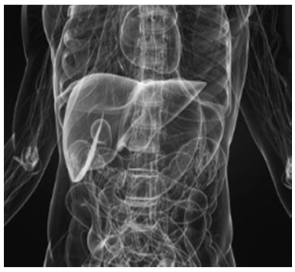
Objectives

- Common Causes of Liver Disease
- Hospice Criteria for Terminal Diagnosis of Liver Disease
- Treatment of Symptoms of Liver Disease



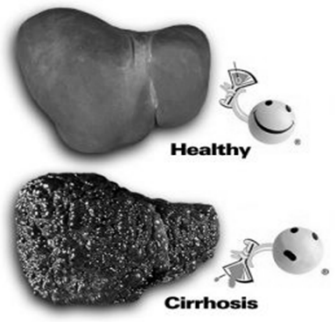
Common Causes of Liver Disease

- Cirrhosis of Liver without Alcohol 571.5
- Alcoholic Cirrhosis 571.2
- Chronic Hepatitis (HBV, HCV) 571.4
- Hepatocellular Carcinoma 155.0
- Primary Biliary Cirrhosis 571.6
- Autoimmune hepatitis 571.42
- Hepatic Encephalopathy 572.2

Common Causes of Liver Disease

- Hepatorenal Syndrome 572.4
- Hepatopulmonary Syndrome 573.5
- Hemochromatosis 275.03
- Primary Sclerosing Cholangitis 576.1
- Alpha-1-antitrypsin Deficiency 273.4
- Nonalcoholic Fatty Liver Disease 571.8

Cirrhosis



Cirrhosis

- 4.5-9.5% of global population
- Histological development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury that leads to portal hypertension and end stage liver disease
- Usually indolent, asymptomatic and unsuspected until complications of liver disease
- Biopsy is gold standard for diagnosis

Classification of Cirrhosis

- Child-Pugh-Turcotte (CPT): based on encephalopathy, ascites, bilirubin, albumin, and PT/INR
- One year survival for class A (100%), B (80%), C (45%); also predicts complications

Classification of Cirrhosis

- Model for End Stage Liver Disease (MELD): predicts 3 month survival based on creatinine, bilirubin, and INR and gives transplant priority to those more likely to die without
- Further refinement by giving extra points for hyponatremia and HCC

Clinical and Lab Criteria	Points*		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3

Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)
Class A = 5 to 6 points (least severe liver disease)
Class B = 7 to 9 points (moderately severe liver disease)
Class C = 10 to 15 points (most severe liver disease)

Model for End Stage Liver Disease (MELD)

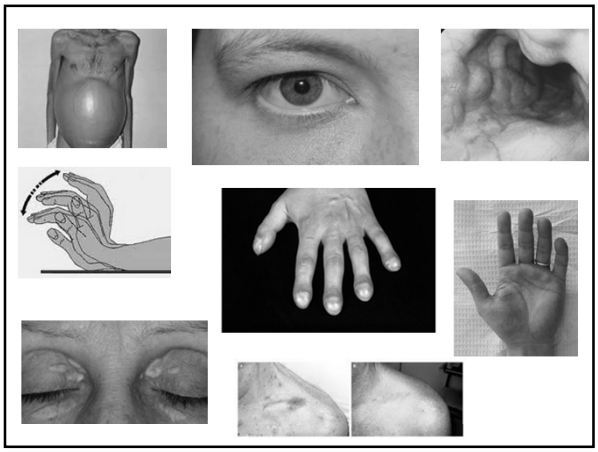
MELD score= 10x[0.957x log e (creatinine) + log e (bilirubin) + 1.12 x log e (INR)] + 6.43

3 month mortality according to MELD score

MELD score	<=9	10-19	20-29	30-39	>=40
Hospitalized pt.	4%	27%	76%	83%	100%
Outpatient cirrhotic	2%	6%	50%		

Cirrhosis

- Signs/Symptoms:
  - jaundice
  - nodular liver
  - ascites
  - palmar erythema
  - Dupuytren's contracture
  - gynecomastia
  - hypogonadism
  - foetor hepaticus
  - fatigue
  - muscle atrophy
  - variceal bleeding
  - bacterial infections
  - spider angiomata
  - splenomegaly
  - caput medusae
  - white nails
  - clubbing
  - loss of male hair pattern
  - asterixis
  - anorexia
  - weight loss
  - diabetes
  - encephalopathy
  - muscle cramps
  - hypertrophic osteoarthropathy
  - spontaneous bacterial peritonitis

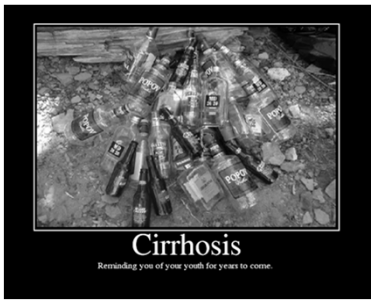


Cirrhosis

- Increased: AST/ALT, ALP, GGT, bilirubin, immunoglobulins
- Decreased: albumin, prothrombin time, sodium, hemoglobin, platelets, WBCs.
- Consequences: impaired hepatocyte function, increased intrahepatic resistance, and hepatocellular carcinoma
- Prognosis and Treatment depend on etiology

Transplant

- Indications: CPT>7 or appropriate MELD score, unresectable liver malignancy, inherited metabolic disorder, no alternative therapy, medical compliance and funding
- Contraindications: HIV, methadone dependence, stage 3 HCC, extrahepatic malignancy, AIDS, cholangiocarcinoma, severe systemic infection, multiorgan failure, advanced cardiopulmonary disease, active substance abuse



Alcoholic Liver Disease

- Signs/Symptoms:

fever	hepatosplenomegaly
jaundice	anorexia
liver bruit	encephalopathy
bleeding	palmar erythema
gynecomastia	caput medusa
clubbing	Dupuytren's contractures
neuropathy	testicular atrophy
ascites	spider angiomata

Alcoholic Liver Disease

- Disproportionate elevation of AST:ALT usually >2:1, AST and ALT usually <300 IU/L
- Macrocytosis
- Folate and B12 deficiency
- Thrombocytopenia
- Leukocytosis
- Elevated alcohol
- Elevated GGT
- Elevated bilirubin

Alcoholic Liver Disease

- Biopsy indicated if enzyme elevations persist for >6 months, other lab evidence of liver failure, uncertain diagnosis, in patients with more than 1 liver disease, prognostication
- Patients with alcoholic cirrhosis without alcohol consumption without transplant have 5 year survival of 60% versus 30% for those who continue to drink alcohol

Hepatitis B Infection

- Signs/Symptoms:
  - fatigue
  - jaundice
  - ascites
  - encephalopathy
  - edema
  - splenomegaly
- Extrahepatic manifestations:
  - polyarteritis nodosa
  - glomerular nephropathy and nephritis
  - aplastic anemia

Hepatitis B Infection

- Treatments: antivirals such as entecavir, tenofovir, and, lamivudine, interferon alpha
- 5 year survival:
  - decompensated liver disease is 14-35%
  - compensated liver disease is 85-90%
- 5 year rate of progression to cirrhosis 12-20%
- HBV may lead to hepatocellular carcinoma without evidence of cirrhosis

Hepatitis C Infection

- Acquired through IV drug use (68%) and STD (15-20%) and needle sticks (4%)
- Cases acquired through blood transfusion in 1960-1980 now increasing morbidity and mortality and cost of HCV
- 60-80% develop long term HCV infection and 20-30% of those develop cirrhosis
- HCV accounts for 1/3 of HCC

Hepatitis C Infection

Factors that increase risk of cirrhosis:

- age
- male
- Caucasian
- HIV
- HBV
- schistosomal
- infection
- alcohol
- NASH
- iron overload

Hepatitis C Infection

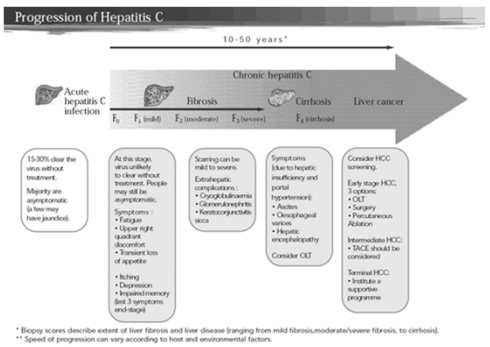
- Signs/Symptoms:
  - fatigue
  - RUQ pain
  - nausea
  - anorexia
  - weakness
  - musculoskeletal pain
  - weight loss
  - abdominal swelling
  - dark urine
  - fluid retention
  - itching

Hepatitis C Infection

- Extra-hepatic manifestations of chronic HCV:
  - mixed cryoglobulinemia
  - B-cell non-Hodgkin's lymphoma
  - glomerulonephritis
  - seronegative arthritis
  - keratoconjunctivitis sicca
  - lichen planus
  - neuropathy
  - cognitive disorders
  - porphyria cutanea tarda
  - thyroiditis
  - autoantibodies
  - diabetes mellitus

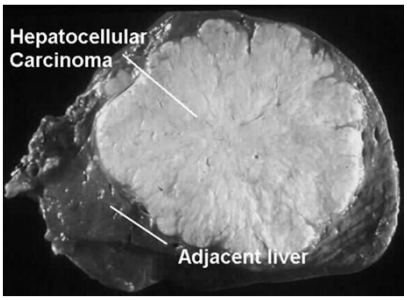
Hepatitis C Infection

- Most common cause of chronic liver disease and indication for transplant in U.S.
- 6 genotypes: type 1 most common in U.S. (70-75%) and most resistant to interferon therapy
- Treatment: Interferon alpha
- Decompensated cirrhosis 5 year survival is 50%
- CDC estimates 8000-13000 deaths per year from chronic HCV



Hepatocellular Carcinoma

- 5th most common neoplasm in the world and 2nd most common cause of cancer-related death
- Affects mainly patients with cirrhosis mostly from HCV, HBV, and/or alcohol abuse
- Signs/Symptoms: pain, early satiety, jaundice, palpable mass



Hepatocellular Carcinoma

- Risk factors:

cirrhosis	decompensated cirrhosis
HBV	HCV
NASH	hemochromatosis
aflatoxin	co-infection with HCV/HBV/HIV
male	increasing age
alcohol	positive family history
diabetes	contaminated drinking water
Betel nuts	abnormal epidermal growth factor
tobacco	alpha1antitrysin deficiency
red meat	saturated fat
coffee	statins

Hepatocellular Carcinoma

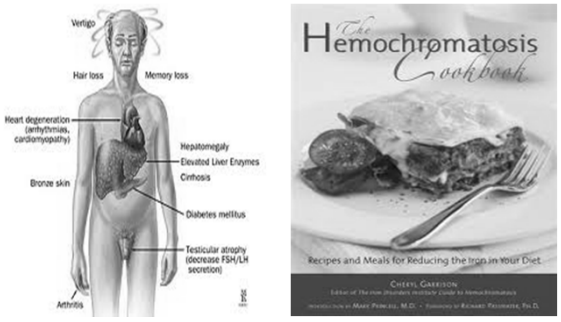
- Paraneoplastic manifestations: erythrocytosis, hypercalcemia, hypoglycemia, diarrhea
- Treatments:
  - surgical resection
  - liver transplant
  - percutaneous ablation with ethanol
  - radiofrequency ablation
  - arterial embolization
  - chemotherapy
  - palliation

Hepatocellular Carcinoma

- Yearly screening of cirrhosis patients with imaging in recommended
- Patient with HCV/HCC has 1% 2 year survival
- Mortality is expected to double or triple over next decade.
- Even though new HCV infection is declining, cirrhosis and HCC is increasing.
- With transplant, 1 year survival is 83% and 5 year survival is 70% (UNOS)

Hemochromatosis

- Autosomal recessive iron overload disease
- Inappropriate increase in iron absorption in the duodenum and upper small intestine
- Deposition of iron in liver, pancreas, heart, joints, skin, pituitary gland

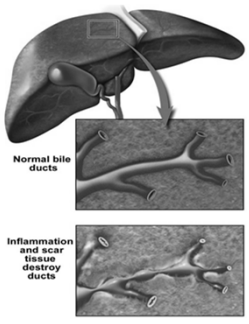


Hemochromatosis

- Leads to cirrhosis, restrictive cardiomyopathy, diabetes, arthropathy, hyperpigmentation, gonadal failure
- Increased risk of cirrhosis and hepatocellular carcinoma
- Treatment: phlebotomy (goal: ferritin <50ng/ml), chelation therapy, transplant

Primary Biliary Cirrhosis

- Autoimmune, chronic, cholestatic, granulomatous, progressive destruction of small intrahepatic bile ducts with portal inflammation and fibrosis
- Predominantly affects middle-aged women
- Leads to impaired bile secretion
- Diagnosis 2 out 3: elevated ALP, AMA, and histology showing destruction



Primary Biliary Cirrhosis

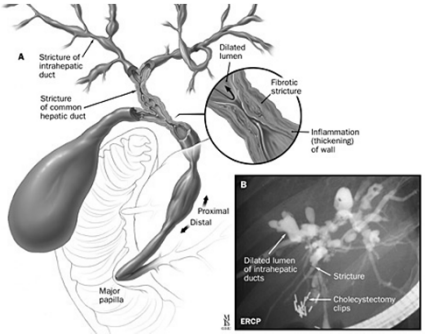
- Signs/Symptoms/Extramanifestations:
  - hepatosplenomegaly
  - hyperpigmentation
  - osteoporosis
  - cirrhosis stigmata
  - cutaneous scleroderma
  - vitamin D deficiency
  - hyperbilirubinemia
  - Sjogren's syndrome
  - cognitive impairment
  - xanthelasmas
  - itching
  - osteomalacia
  - hemorrhage
  - CREST syndrome
  - steatorrhea, cytopenias
  - arthritis
  - RUQ pain

Primary Biliary Cirrhosis

- Labs: Elevated alkaline phosphatase, GGT, anti-mitochondrial antibodies and IgM, ANA, lipids, later elevated bilirubin
- Treatment:
  - Ursodeoxycholic acid (bile acid replacement) turns off cycle, 30% respond
  - Budesonide
  - plasmapheresis with FFP
  - ion-exchange resins (questran)
  - S-adenosyl-L-methionine
  - transplant

Primary Sclerosing Cholangitis

- Chronic cholestatic liver disease with inflammation, fibrosis, and strictures of bile ducts leading to end stage liver disease
- Primarily affects young-middle aged men
- Elevated ALP and nonspecific antibodies
- Cholangiography is gold standard for diagnosis



Primary Sclerosing Cholangitis

- Signs/Symptoms:
  - pruritus
  - abdominal pain
  - weight loss
  - fever/chills
  - fatigue
  - jaundice
  - gallstones
  - polyps
  - IBD
  - vitamin deficiencies
  - hyperpigmentation
  - steatorrhea
  - night sweats
  - metabolic bone disease
  - peristomal varices
  - bacterial cholangitis
  - biliary strictures
  - cholangiocarcinoma

Primary Sclerosing Cholangitis

- Treatment: ursodeoxycholic acid (most studied, but not proven), endoscopic dilatation, sphincterotomy, stent, surgical resection, and transplant
- Survival rate without transplant 10-18 years
- Cholangiocarcinoma occurs in 7-15%

Alpha-1-Antitrypsin Deficiency

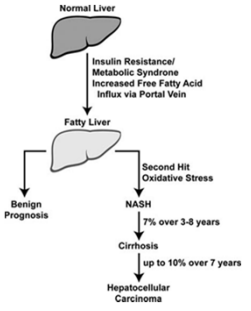
- Protein made in liver and transported in blood to lungs where it protects fragile aveoli
- Common genetic disorder with pulmonary emphysema and liver cirrhosis and panniculitis
- 1 in 5000 in U.S. newborns, Scandinavian
- Accelerated by smoking and dust exposure and increased prevalence of HCC

Alpha-1-Antitrypsin Deficiency

- Signs: Prolonged jaundice after birth, bleeding, and abnormal liver enzymes
- Cirrhosis/liver failure around age 50
- Emphysema in 30-40s with smoking and 50-60s if no smoking
- Panniculitis manifests as spontaneous necrosis
- Treatment: IV alpha-1-antitrypsin augmentation therapy, vaccines, bronchodilators, inhaled corticosteroids, transplant

Nonalcoholic Fatty Liver Disease

- Most common form of chronic liver disease in Western world (20-35% adults and 5-17% children)
- Dysregulation of lipid metabolism and immune system, genes, environment
- Independent risk factor for CV disease
- Nonalcoholic steatohepatitis 3-5% and cirrhosis 3-5%
- Risk factors: metabolic syndrome, obesity, diabetes II, dyslipidemia



Nonalcoholic Fatty Liver Disease

- NASH also associated with TPN, rapid weight loss, hypothyroidism, abdominal surgery, drugs
- Signs/Symptoms: fatigue, malaise, RUQ pain, elevated enzymes
- Biopsy is gold standard for diagnosis
- Treatment: no proven effective therapy, lifestyle modification including diet and exercise, bariatric surgery, insulin sensitizing drugs

Autoimmune Hepatitis

- Chronic, with circulating autoantibodies and high serum globulin
- Type 1: ANA and/or ASMA and/or AAA
- Type 2: ALKM-1 and or ALC-1
- Diagnosis: serologic and histologic findings and exclusion of other liver disease and scoring system

Autoimmune Hepatitis

- Signs/Symptoms:
  - hepatosplenomegaly
  - stigmata of liver disease
  - elevated transaminases
  - anorexia
  - abdominal pain
  - arthralgias
  - jaundice
  - fatigue
  - malaise
  - nausea
  - itching

Autoimmune Hepatitis

- Glucocorticoids, Azathioprine, Cyclosporine, Tacrolimus, Methotrexate, Mycophenolate mofetil, Transplant
- Immunosuppressive treatment should be instituted in patients with serum aminotransferases greater than 10-fold the upper limit of normal, at least five-fold the upper limit of normal in conjunction with serum gamma-globulin levels at least two-fold the upper limit of normal, and/or histologic features of bridging necrosis or multilobular necrosis.

Hospice Criteria for Terminal Diagnosis of Liver Disease

Local Coverage Determination (LCD) for Hospice – Liver Disease

1. Patient must have both:
- Prothrombin time prolonged more than 5 seconds over control or INR >1.5 (biosynthetic capacity of clotting factors I, II, V, VII, IX, X, XII, XIII), vitamin K does not correct
- Serum albumin <2.5gm/dl (protein biosynthesis), more common in chronic vs. acute

LDC for Hospice – Liver Disease

2. Patient must have at least one of the following:
- Ascites, refractory or non-compliant
- Spontaneous bacterial peritonitis
- Hepatorenal syndrome, elevated creatinine and BUN with oliguria (<400ml/day), and urine sodium <10mEq/L
- Hepatic encephalopathy, refractory or non-compliant
- Recurrent variceal bleeding, despite intensive therapy

LCD for Hospice – Liver Disease

3. Documentation of these factors supports eligibility:

- Progressive malnutrition
- Muscle wasting with reduced strength and endurance
- Continued active alcoholism (>80gm ethanol/day)
- Hepatocellular carcinoma
- HBsAg positive
- Hepatitis C refractory to interferon treatment

LCD for Hospice - Liver Disease

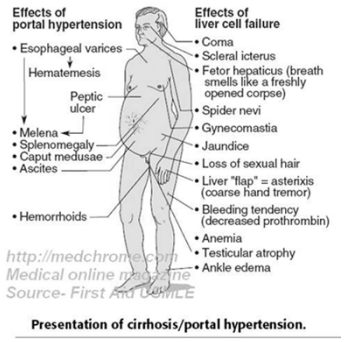
- Patients awaiting liver transplant who otherwise fit criteria may be certified for the Medicare hospice benefit, but if a donor organ is procured, the patient must be discharged from hospice.
- Notice: No mention of elevated aminotransferases (hepatocellular injury), alkaline phosphatase (cholestasis), or bilirubin (toxin clearance) because these to do not accurately reflect liver function

Symptoms and Complications

- Encephalopathy
- Variceal bleeding
- Ascites
- Spontaneous bacterial peritonitis
- Pruritus

Symptoms and Complications

- Hepatorenal syndrome
- Hepatopulmonary syndrome, portopulmonary hypertension, and hepatic hydrothorax
- Cardiovascular effects of liver disease
- Pain



Presentation of cirrhosis/portal hypertension.

Encephalopathy

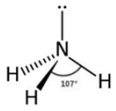
- Damaged liver is unable to remove toxins such as ammonia and manganese from the blood which then cross the blood-brain barrier and damage brain cells
- May be exacerbated by TIPS procedure which redirects blood around the liver

Encephalopathy

- Precipitants:
  - benzodiazepines
  - narcotics
  - alcohol
  - increased ammonia
  - excess protein intake
  - GI bleed
  - infection
  - constipation
  - metabolic alkalosis
  - dehydration
  - vomiting
  - diarrhea
  - hemorrhage
  - diuretics
  - paracentesis
  - shunt placement
  - spontaneous shunt
  - electrolyte disturbance
  - portal vein thrombosis
  - hepatic vein thrombosis
  - hepatocellular carcinoma

Encephalopathy

- Signs/Symptoms:
  - sleep disturbances
  - mood changes,
  - cognitive deficits
  - psychiatric disorders
  - coma
  - asterixis
  - hyperactive DTRs
  - motor disturbances
  - decerebrate posture

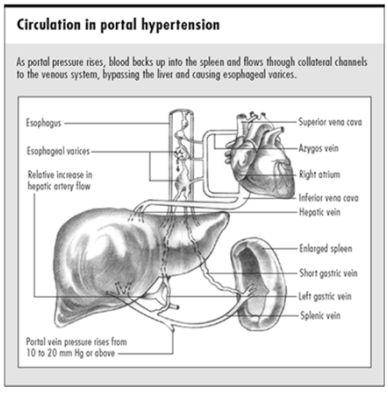


Encephalopathy

- Treatment:
- Treat precipitating factors
- Sugar molecules (lactulose) and antibiotics (neomycin) to reduce GI tract ammonia production
- L-ornithine L-aspartate converts ammonia into glutamine in muscle
- Experimental use of neuropharmacologic drugs
- Transplant and artificial livers

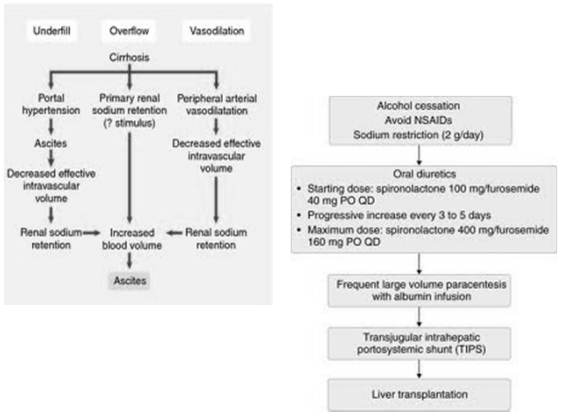
Variceal Bleeding

- Devastating complication, prior to current therapies, mortality was 30%
- Treatment: resuscitation, vasoconstrictors, sclerotherapy, band ligation, TIPS, variceal obliteration, surgical shunt
- Beta blockers as primary prophylaxis in compensated cirrhosis with varices
- Dark towels and education



Ascites

- Portal hypertension leads to fluid retention
- Sodium retention leads to volume expansion plus hypoalbuminemia which leads to low oncotic pressure
- 2 year survival of cirrhosis with ascites is 50% and decreases with diuretic resistant ascites
- Treatment:
  - Low sodium diet
  - Diuretics

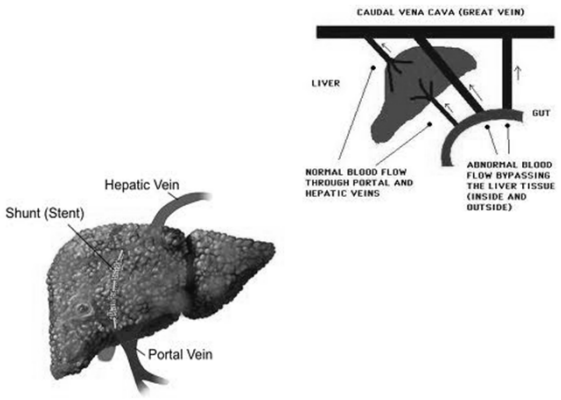


Ascites

- Treatment if diuretic resistant (10%):
  - Transplant
  - Large volume paracentesis (8.4L/2weeks +albumin 6-8g/L if following 2000mg sodium diet with no urine sodium)
  - TIPS
  - Peritoneovenous shunt (rare)
  - Midodrine (increases renal perfusion)

TIPS

- Transjugular Intrahepatic Portosystemic Shunt
- Hepatic encephalopathy occurs in ~ 30%
- Thrombosis and stenosis rates have decreased with coated stents
- Contraindications: encephalopathy, alcoholic hepatitis, MELD >18, advanced age, renal disease



Spontaneous Bacterial Peritonitis

- Infection of preexisting ascitic fluid without evidence of intra-abdominal source
- Signs/Symptoms: fever, abdominal pain, tenderness, AMS, positive fluid culture and/or elevated PMN leukocyte count >250cells/mm3
- High mortality
- Treatment: prophylaxis in high risk, early diagnostic paracentesis, IV antibiotics

Pruritus

- Interferes with quality of life including sleep deprivation and depression
- Intrahepatic itch is associated with HBV, HCV, cholestasis of pregnancy, PBC
- Extrahepatic itch is associated with obstructive tumor and PSC
- Itch seems to be much higher in PBC

Pruritus

- Usually generalized, intermittent, starts in palms/soles, and worse at night
- May lead to secondary lesions such as excoriations, hyper/hypopigmentation, lichenification, prurigo nodules, and scars
- Likely non-histaminergic pathway since most chronic itch does not respond to antihistamines

Pruritus

- May be related to hormones in females
- Consider endogenous opioids as source for itching, because they cause degranulation of cutaneous mast cells and activate mu receptors
- No direct correlation between level of bile salts etc. and itching

Pruritus

- Treatments:
  - SSRIs (sertraline)
  - SNRIs (mirtazapine)
  - neuroleptics (gabapentin)
  - sedating antihistamines (hydroxyzine)
  - opioid antagonist (naltrexone)
  - UV light
  - behavioral therapy
  - bile acid resin (cholestyramine)
  - bile acid (ursodeoxycholic acid)
  - rifampicin
  - molecular adsorbent recirculating system

Hepatorenal Syndrome

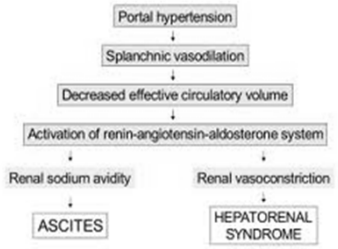
- Development of acute renal failure in setting of advanced liver disease
- Arterial splanchnic vasodilation leads decreased renal perfusion leads to decreased GFR
- Signs/Symptoms: oliguria, benign urine sediment, very low urine sodium, rising creatinine

Hepatorenal Syndrome

- Type I: more serious, creatinine clearance <20ml/min in 2 weeks or twofold increase in creatinine to >2.5mg/dL, oliguria
- Type II: less severe, ascites resistant to diuretics
- May occur in acute or chronic liver failure, may be precipitated by acute insult, and is least common in PBC

Hepatorenal Syndrome

- Criteria:
  - Chronic or acute liver failure and portal hypertension
  - Creatinine >1.5mg/dL that progresses over days to weeks
  - Absence of other apparent cause
  - Urine red cell excretion <50 and protein excretion <500mg/day
  - Lack of improvement with volume expansion with albumin for at least 2 days and withdrawal of diuretics



Hepatorenal Syndrome

- Treatment:
  - Vasopressin analogues + albumin can correct by causing constriction
  - Clonidine can raise GFR 25% by lowering renal sympathetic tone and vascular resistance, but benefit is not sustained
  - Midodrine + Somatostatin = vasoconstrictor + vasodilator inhibitor
  - Norepinephrine + Albumin = vasoconstrictor + protein replacement
  - TIPS and Dialysis and Transplant

Pulmonary

1. Hepatopulmonary Syndrome (20%):

- hepatic dysfunction + hypoxemia + intrapulmonary vascular dilations
- Type 1(improves with oxygen) and Type 2(true shunt)
- Etiology unknown, worsens cirrhosis prognosis
- Signs/Symptoms: cyanosis, clubbing, nail bed telangiectasias, orthodeoxia, platypnea, dyspnea, hypoxemia
- Treatment: transplant, medications give no benefit, TIPS (?), 5 year mortality is 20%

Pulmonary

2. Portopulmonary Hypertension (2-10%):

- cirrhosis leads to pulmonary artery hypertension
- Etiology unknown
- Signs/Symptoms: fatigue, edema, dyspnea, syncope, chest pain, JVD, increased P2 of the S2, TR, right heart failure
- Treatment: vasodilators (prostacyclin and sildenafil)
- Transplant contraindicated in most and only helps in very mild disease along with long term vasodilator therapy; 5 year mortality is 50-90%

Pulmonary

3. Hepatic Hydrothorax (10%):

- pleural effusion in cirrhosis without underlying cardiopulmonary disease resulting from ascites moving into pleural space (usually right side)
- Symptoms: dyspnea, cough, hypoxemia, chest discomfort
- Treatment: serial thoracenteses, fluid/sodium restriction, diuretics, draining catheters

Cardiovascular

"Cirrhotic Cardiomyopathy":

- Increased cardiac output
- Increased contractility at rest
- Decreased systemic vascular resistance
- Systemic hypotension
- Blunted response to stress

Pain in Liver Disease

Pain

- Most pain medications are metabolized by the liver
- Try to avoid complications including encephalopathy, hepatorenal syndrome, and bleeding
- Liver dysfunction = metabolism impairment
- Drug removal affected by hepatic blood flow, enzyme capacity, and plasma protein binding

Pain

- Low serum protein or albumin can cause increased levels of free drug if it is usually protein bound
- Severe cholestasis can affect some drug clearance
- Cirrhotic patients often have renal impairment, which may require dose adjustment of renal eliminated drugs

Pain

Acetaminophen:

- Doubled half-life
- In cirrhosis and no alcohol: maximum dose 2-3g/day for long term use
- In cirrhosis + alcohol: no long term studies, but consensus is <2g/day
- 3-4g/day short term use still safe despite FDA changes

Pain

NSAIDs:

- Increased serum levels due to liver metabolism and highly protein bound
- Renal impairment in cirrhosis due inhibition of prostaglandins leading to decreased renal perfusion, reduced GFR, and sodium retention
- Also cause increased bleeding in cirrhosis
- No studies for COX-2 inhibitors in cirrhosis

Pain

Opioids:

- No evidence based guidelines exist
- Mayo Clinic says opioids should be avoided due to increased encephalopathy
- In cirrhosis, decreased clearance, increased bioavailability, and prolonged half-life lead to drug accumulation
- Careful monitoring for side effects required

Pain

Opioids:

- Opioids should be adjusted for GFR
- Morphine is poorly excreted in renal insufficiency
- Hydromorphone and fentanyl seem to be the least affected by renal dysfunction
- Fentanyl has less hemodynamic disturbance due to lack of histamine release

Pain

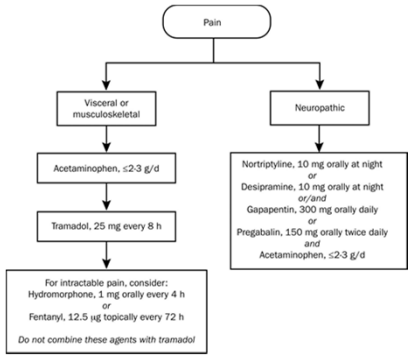
Opioids:

- High hepatic extraction (first pass metabolism): morphine and fentanyl have higher bioavailability in cirrhotic patients
- Liver dysfunction = decreased clearance
- Liver disease does not impact methadone bioavailability due to low hepatic extraction

Pain

Opioids:

- Metabolism of methadone, fentanyl, and hydromorphone does not yield toxic metabolites and may be better tolerated
- Methadone should be avoided with active alcohol use because alcohol inhibits metabolism of methadone



Pain

Others:

- Less potent TCAs should be used and started at very low doses and beware of side effects
- Anticonvulsants should also be started at low and less frequent doses
- Gabapentin is preferred because it is not metabolized by the liver or protein bound, but it is renally excreted (pregabalin is similar)

What Have We Learned?

- Common Causes of Liver Disease
- Hospice Criteria for Terminal Diagnosis of Liver Disease
- Treatment of Symptoms of Liver Disease

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