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



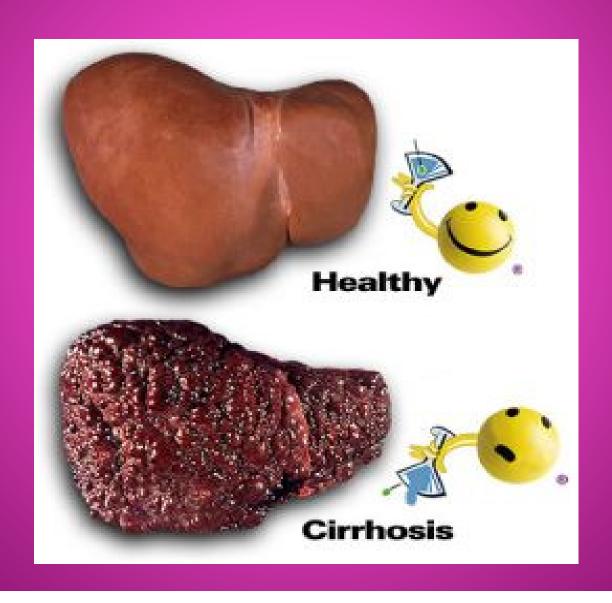
Common Causes of Liver Disease

- 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 (diunatic refractory)			
Bilirubin (mg/dL)	< 2	2-3	>3			
Albumin (gldL)	> 3.5	2.8-3.5	<2.8			
Profirembin time Seconds prolonged	+4	4-6	>6			
International normalized ratio	<1.7	1.7-2.3	>2.3			

Child-Turcette-Pugh Class obtained by adding score for each parameter (total points)

Class A = 5 to 6 points (least severe liver disease)

Class 8 = 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

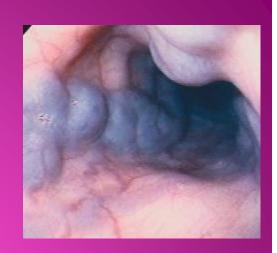
muscle cramps

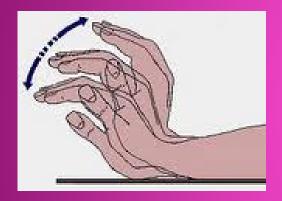
hypertrophic osteoarthropathy

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



Cirrhosis

Reminding you of your youth for years to come.

Alcoholic Liver Disease

Signs/Symptoms:

fever

jaundice

liver bruit

bleeding

gynecomastia

clubbing

neuropathy

ascites

hepatosplenomegaly

anorexia

encephalopathy

palmar erythema

caput medusa

Dupuytren's contractures

testicular atrophy

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



Signs/Symptoms:

fatigue jaundice

ascites encephalopathy

edema splenomegaly

Extrahepatic manifestations:

polyarteritis nodosa

glomerular nephropathy and nephritis aplastic anemia

- 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

- 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

Factors that increase risk of cirrhosis:

age male

Caucasian HIV

HBV schistosomal

infection alcohol

NASH iron overload

Signs/Symptoms:

fatigue

nausea

weakness

weight loss

dark urine

itching

RUQ pain

anorexia

musculoskeletal pain

abdominal swelling

fluid retention

Extra-hepatic manifestations of chronic HCV:

mixed cryoglobulinemia

B-cell non-Hodgkin's lymphoma

glomerulonephritis

seronegative arthritis

keratoconjunctivitis sicca

lichen planus

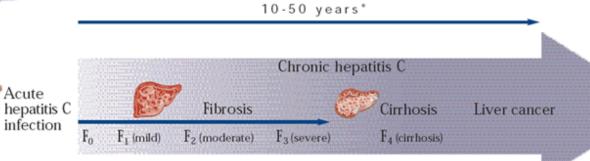
neuropathy cognitive disorders

porphyria cutanea tarda

thyroiditis autoantibodies diabetes mellitus

- 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

Progression of Hepatitis C



15-30% clear the virus without treatment.

Majority are asymptomatic (a few may have jaundice). At this stage, virus unlikely to clear without treatment. People may still be asymptomatic.

Symptoms:

- Fatigue
- Upper right quadrant discomfort
- Transient loss of appetite
- Itching
- Depression
- Impaired memory (last 3 symptoms end-stage)

Scarring can be mild to severe.

Extrahepatic complications :

- Cryoglobulinaemia
- Glomerulonephritis
- Keratoconjunctivitis sicca

Symptoms (due to hepatic insufficiency and portal hypertension):

- Ascites
- Oesophageal varices
- Hepatic encephalopathy

Consider OLT

Consider HCC screening.

Early stage HCC, 3 options:

- OLT
- Surgery
- Percutaneous Ablation

Intermediate HCC:

 TACE should be considered

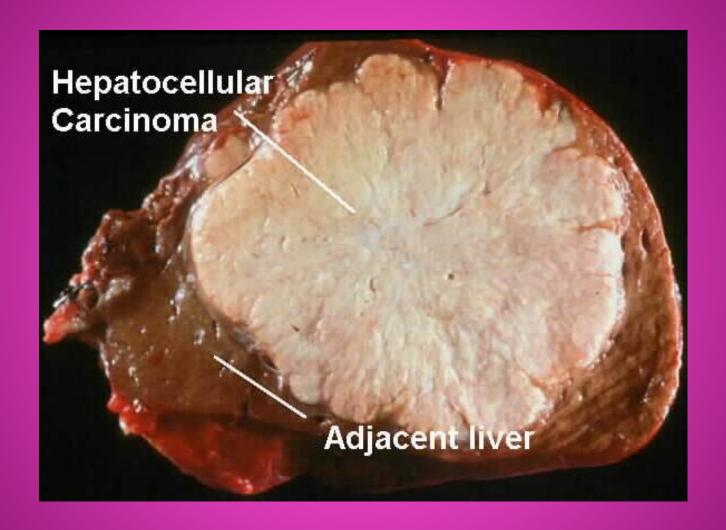
Terminal HCC:

 Institute a supportive programme

^{*} Biopsy scores describe extent of liver fibrosis and liver disease (ranging from mild fibrosis, moderate/severe fibrosis, to cirrhosis).

^{**} Speed of progression can vary according to host and environmental factors.

- 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



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

 Paraneoplastic manifestations: erythrocytosis, hypercalcemia, hypoglycemia, diarrhea

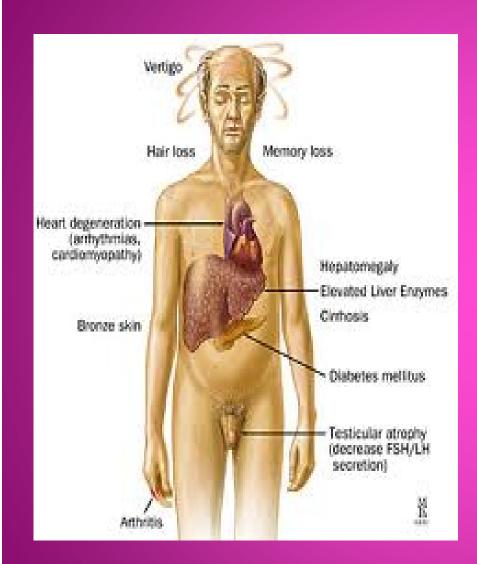
Treatments:

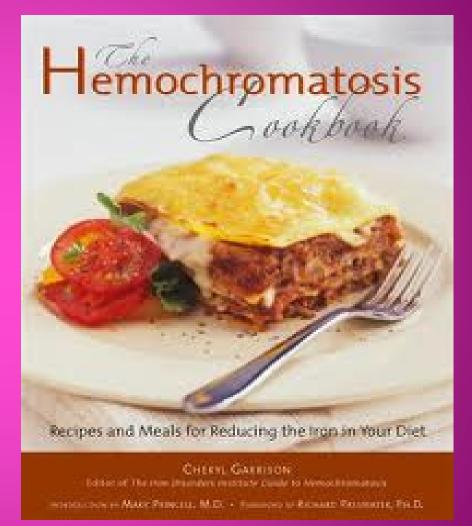
surgical resection
liver transplant
percutaneous ablation with ethanol
radiofrequency ablation
arterial embolization
chemotherapy
palliation

- 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



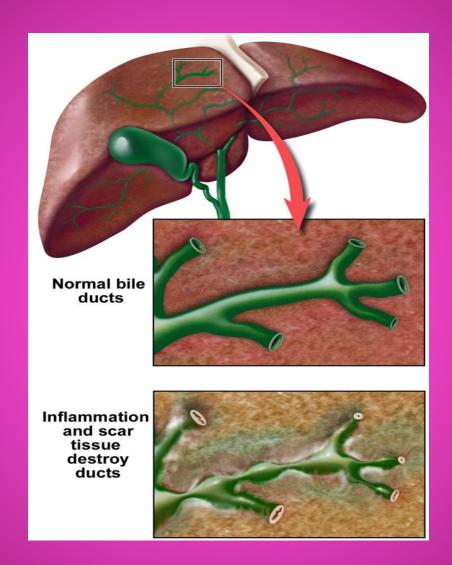


Hemochromatosis

- 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

itching
osteomalacia
hemorrhage
CREST syndrome
steatorrhea,
cytopenias
arthritis
RUQ pain

Primary Biliary Cirrhosis

 Labs: Elevated alkaline phosphatase, GGT, antimitochondrial antibodies and IgM, ANA, lipids, later elevated bilirubin

Treatment:

Ursodeoxycholic acid (bile acid replacement) turns off cycle, 30% respond

Budesonide

plasmapheresis with FFP

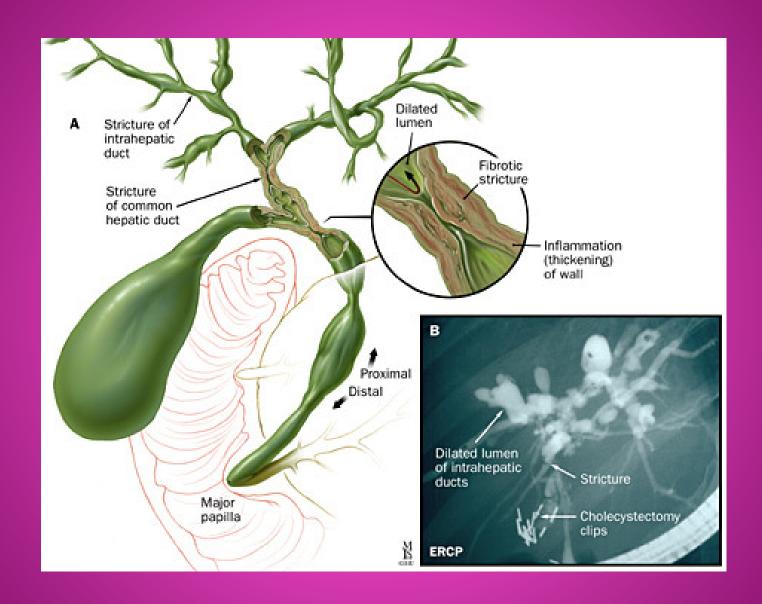
ion-exchange resins (questran)

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 vitamin deficiencies

abdominal pain hyperpigmentation

weight loss steatorrhea

fever/chills night sweats

fatigue metabolic bone disease

jaundice peristomal varices

gallstones bacterial cholangitis

polyps biliary strictures

IBD 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

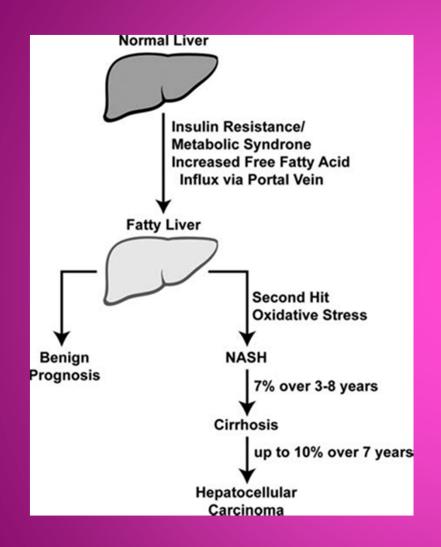
Alpha-1-Antitrypsin Deficiency

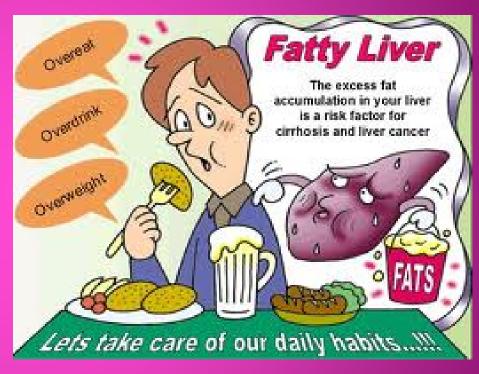
- Signs: Prolonged jaundice after birth, bleeding, and abnormal liver enzymes
- Cirrhosis/liver failure around age 50
- Emphysema in 30-40s with smoking and 50-60s if no smoking
- Panniculitis manifests as spontaneous necrosis
- Treatment: IV alpha-1-antitrypsin augmentation therapy, vaccines, bronchodilators,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

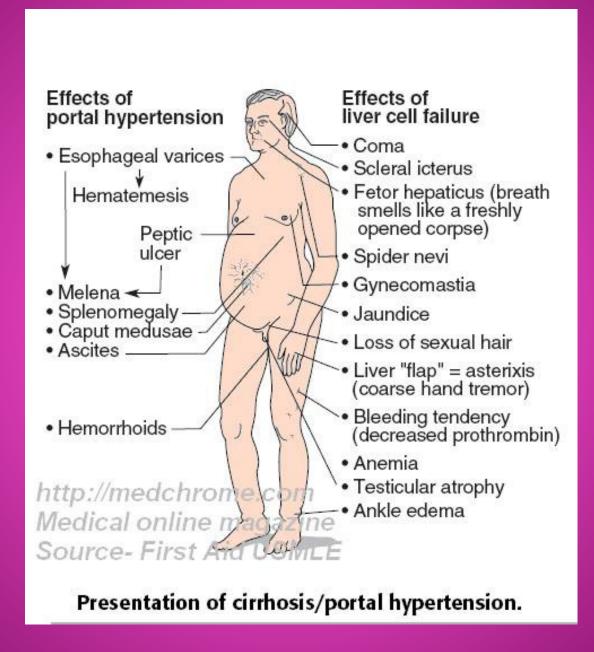
- Patients awaiting liver transplant who otherwise fit criteria may be certified for the Medicare hospice benefit, but if a donor organ is procured, the patient must be discharged from hospice.
- Notice: No mention of elevated aminotransferases (hepatocellular injury), alkaline phosphatase (cholestasis), 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



- 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

Precipitants:

benzodiazepines

alcohol

excess protein intake

infection

metabolic alkalosis

vomiting

hemorrhage

paracentesis

spontaneous shunt

narcotics

increased ammonia

GI bleed

constipation

dehydration

diarrhea

diuretics

shunt placement

electrolyte disturbance

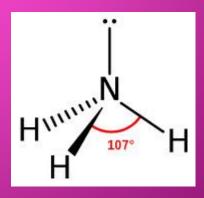
portal vein thrombosis hepatic vein thrombosis

hepatocellular carcinoma

Signs/Symptoms:

sleep disturbances
cognitive deficits
coma
hyperactive DTRs
decerebrate posture

mood changes,
psychiatric disorders
asterixis
motor disturbances



- 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

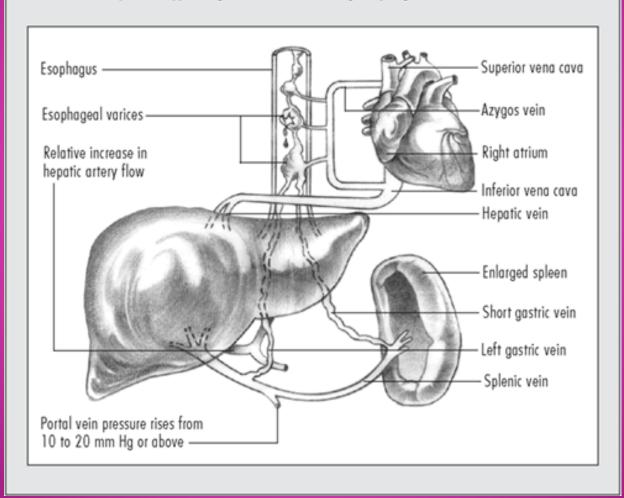


Variceal Bleeding

- 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

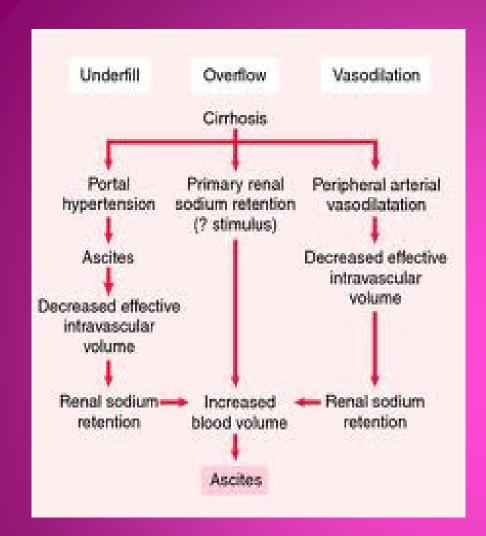
Circulation in portal hypertension

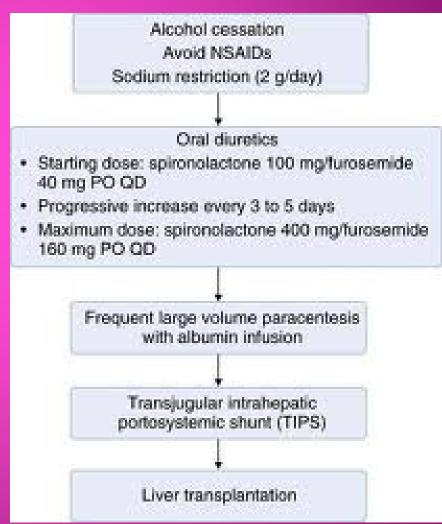
As portal pressure rises, blood backs up into the spleen and flows through collateral channels to the venous system, bypassing the liver and causing esophageal varices.



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



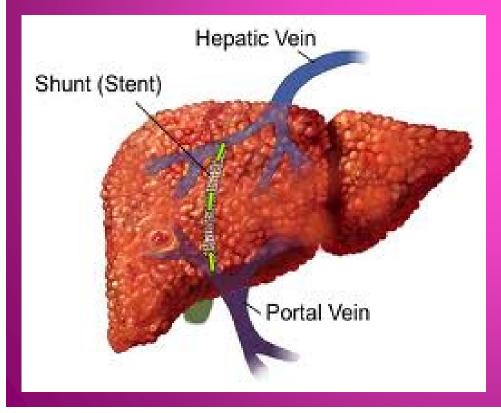


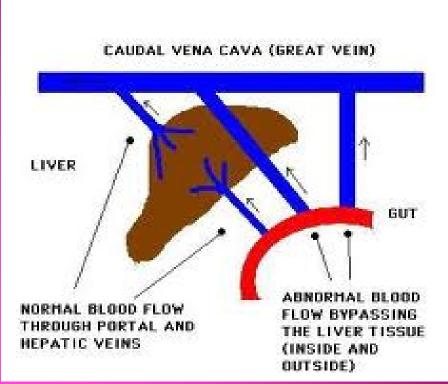
Ascites

- 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



- 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

- 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

Criteria:

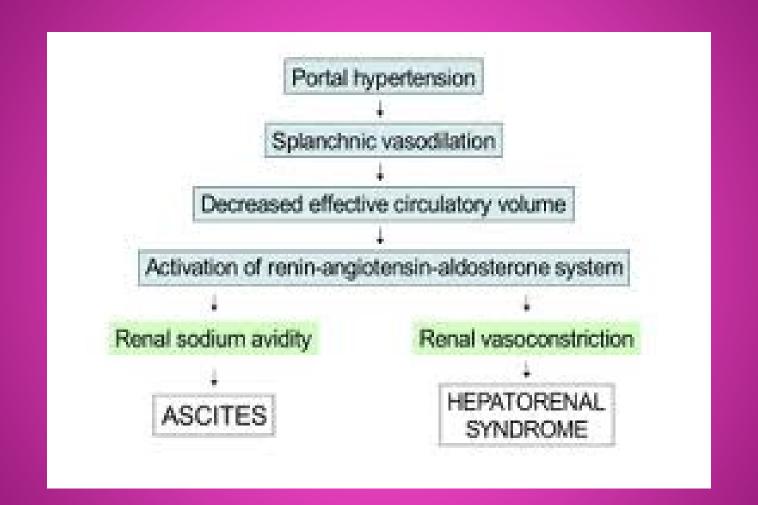
Chronic or acute liver failure and portal hypertension

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



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



- 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

- 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

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

NSAIDs:

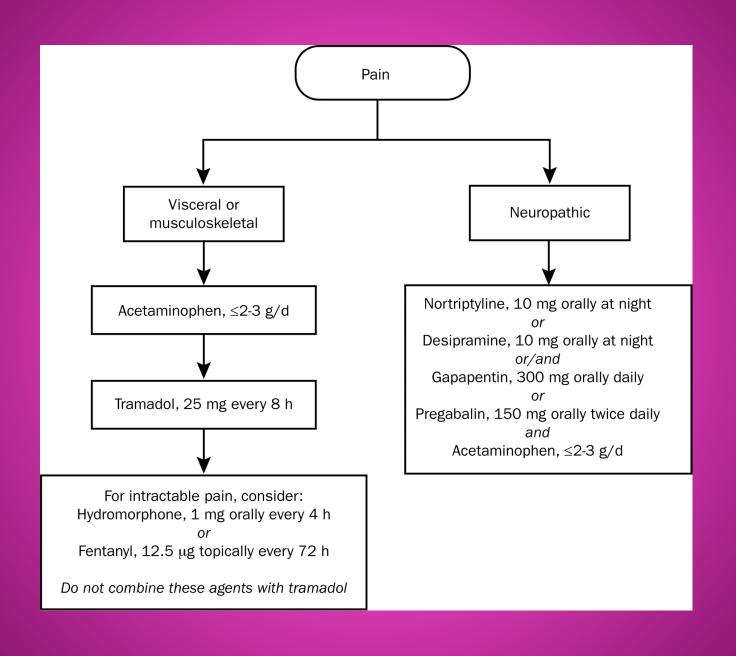
- Increased serum levels due to liver metabolism and highly protein bound
- Renal impairment in cirrhosis due inhibition of prostaglandins leading to decreased renal perfusion, reduced GFR, and sodium retention
- Also cause increased bleeding in cirrhosis
- No studies for COX-2 inhibitors in cirrhosis

- 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

- 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

- 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

- 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



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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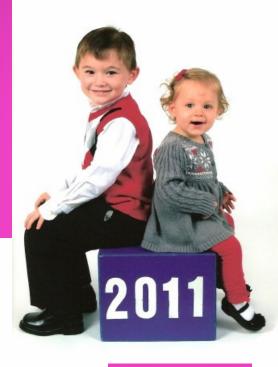
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