

# Liver Disease

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Medicine 3 Seminars in Medicine

October 2024

# Learning Objectives

- Understand key aspects on history and physical examination in approach to patients with liver disease.
- Understand rationale behind basic investigations for liver disease.
- Know the definition of cholestasis and the approach to a patient with jaundice.
- Understand the diagnostic approach to interpreting abnormal liver enzymes.
- Define and develop an approach to “fulminant” hepatic failure.
- Define cirrhosis and develop an approach to managing the common complications of cirrhosis

# THREE QUESTIONS ANYTIME YOU SEE LIVER INJURY

- **IS THE LIVER FUNCTIONING NORMALLY?**
  - **Abnormal functions (INR, Bilirubin, Albumin)**
  - **Signs of decompensation (Ascites, Esophageal variceal bleeding, Hepatic encephalopathy)**
- **IS THE INJURY ACUTE OR CHRONIC OR ACUTE-ON-CHRONIC?**
- **WHAT IS THE INJURY PATTERN?**
  - **Hepatitic, Cholestatic or Mixed**

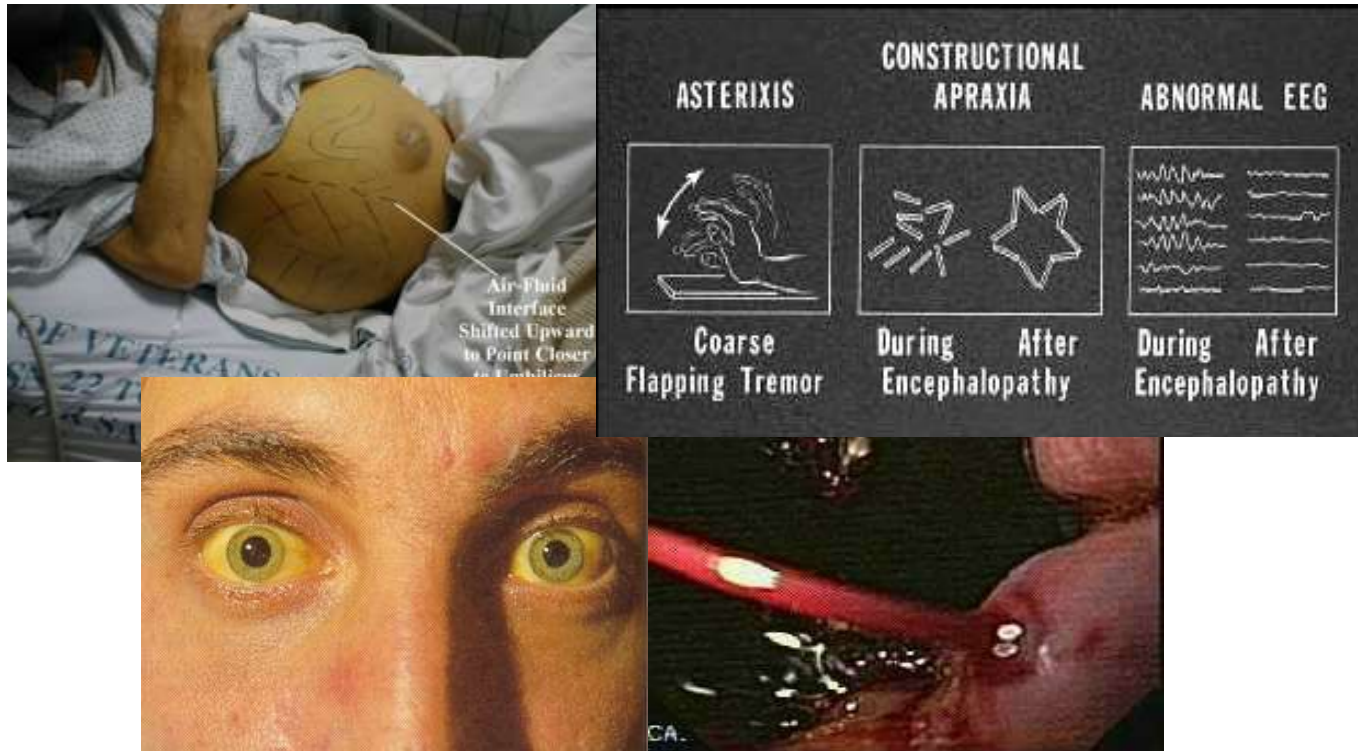
# Abnormal Function & Hepatic Decompensation

# Abnormal Liver Function



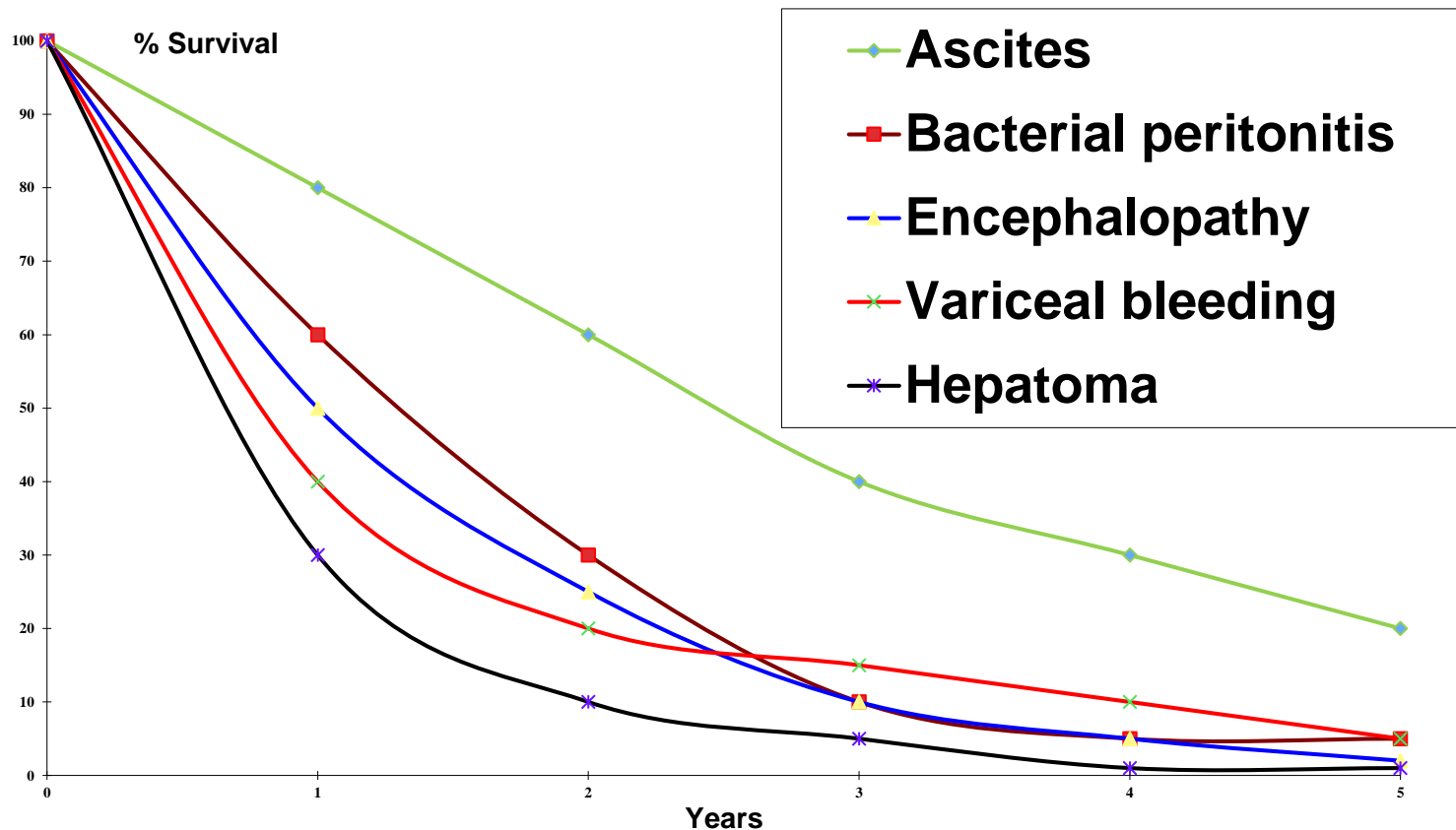
**LIVER IS AN ORGAN OF RESERVE**

# Hepatic “Alarm” Signs



These are also markers for transition from compensated to decompensated cirrhosis

# Why Hepatic “Alarm” Signs Matter?



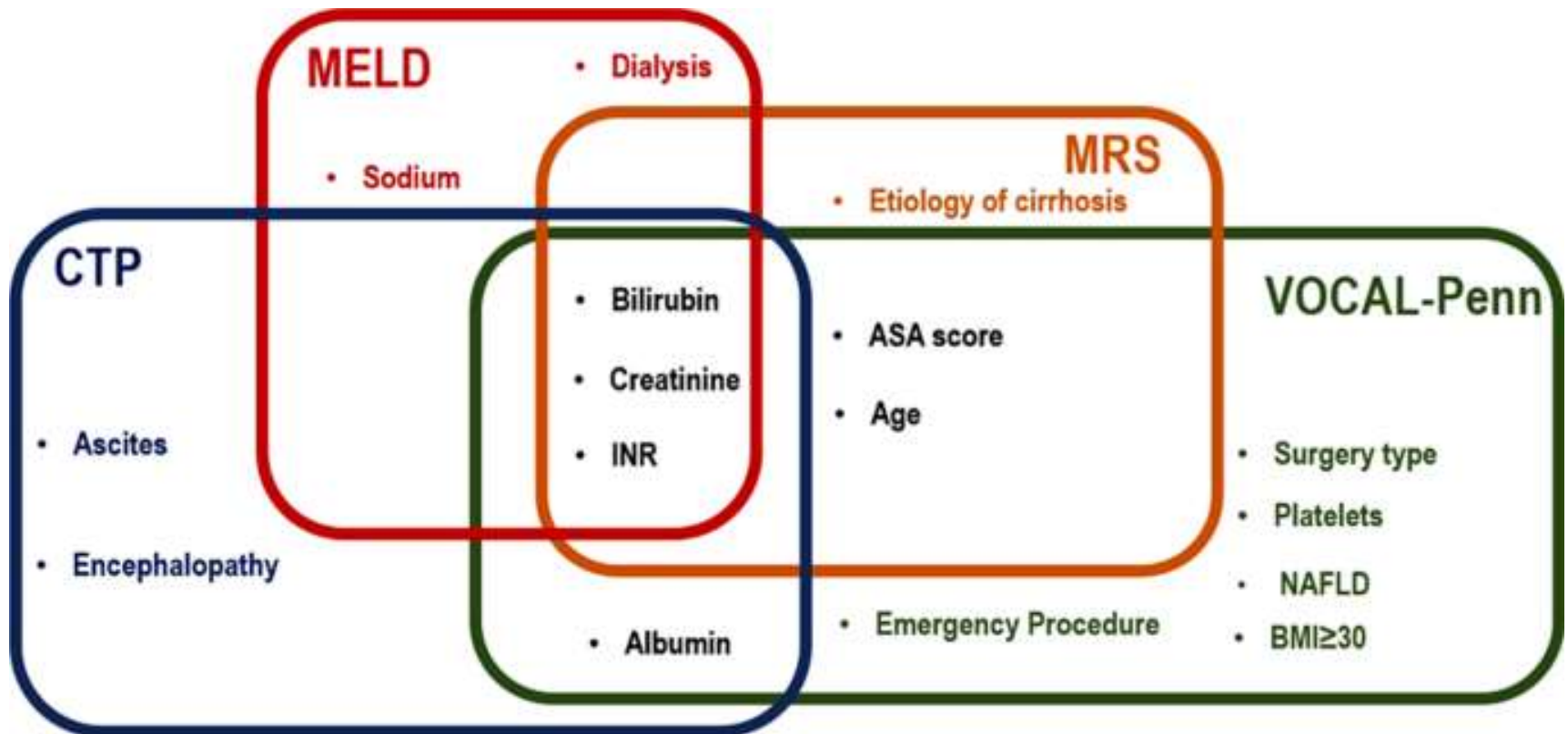
# Severity of Hepatic Dysfunction

2 Minute Medicine®		Child-Pugh Score		2minutemedicine.com
Factor	1 point	2 points	3 points	
Total bilirubin (μmol/L)	<34	34-50	>50	
Serum albumin (g/L)	>35	28-35	<28	
PT INR	<1.7	1.71-2.30	>2.30	
Ascites	None	Mild	Moderate to Severe	
Hepatic encephalopathy	None	Grade I-II (or suppressed with medication)	Grade III-IV (or refractory)	
	Class A	Class B	Class C	
Total points	5-6	7-9	10-15	
1-year survival	100%	80%	45%	

Table I. Child-Pugh score.



# Severity of Hepatic Dysfunction



# Severity of Hepatic Dysfunction

## Specific Scoring Systems: Glasgow Alcoholic Hepatitis Score

Score given	1	2	3
Age	<50	≥50	–
WCC ( $10^9/l$ )	<15	≥15	–
Urea (mmol/l)	<5	≥5	–
PT ratio or INR	<1.5	1.5–2.0	>2.0
Bilirubin ( $\mu\text{mol/l}$ )	<125	125–250	>250

GAHS  $\geq 9$  is associated with 40% 28-day survival vs GAHS < 9 has 80% survival

# THE THREE MANTRAS FOR LIVER INJURY

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# Acute or Chronic? Or Acute-on-chronic

# Acute versus Chronic

- Any abnormality that last less than 6 weeks
- Persistent or intermittent elevation of liver enzymes lasting more than 6 months

If lasts less than 6 months, acute process unlikely to cause permanent liver damage  
can lead to fulminant hepatic failure but potential for regeneration is not lost

# Chronicity

## On History:

Past history of jaundice/hepatitis

Family History

## On physical

Peripheral manifestations of chronic liver disease with more prominent findings in advanced cirrhosis

Physical findings of specific liver diseases

# Chronic Liver Disease on Physical Examination

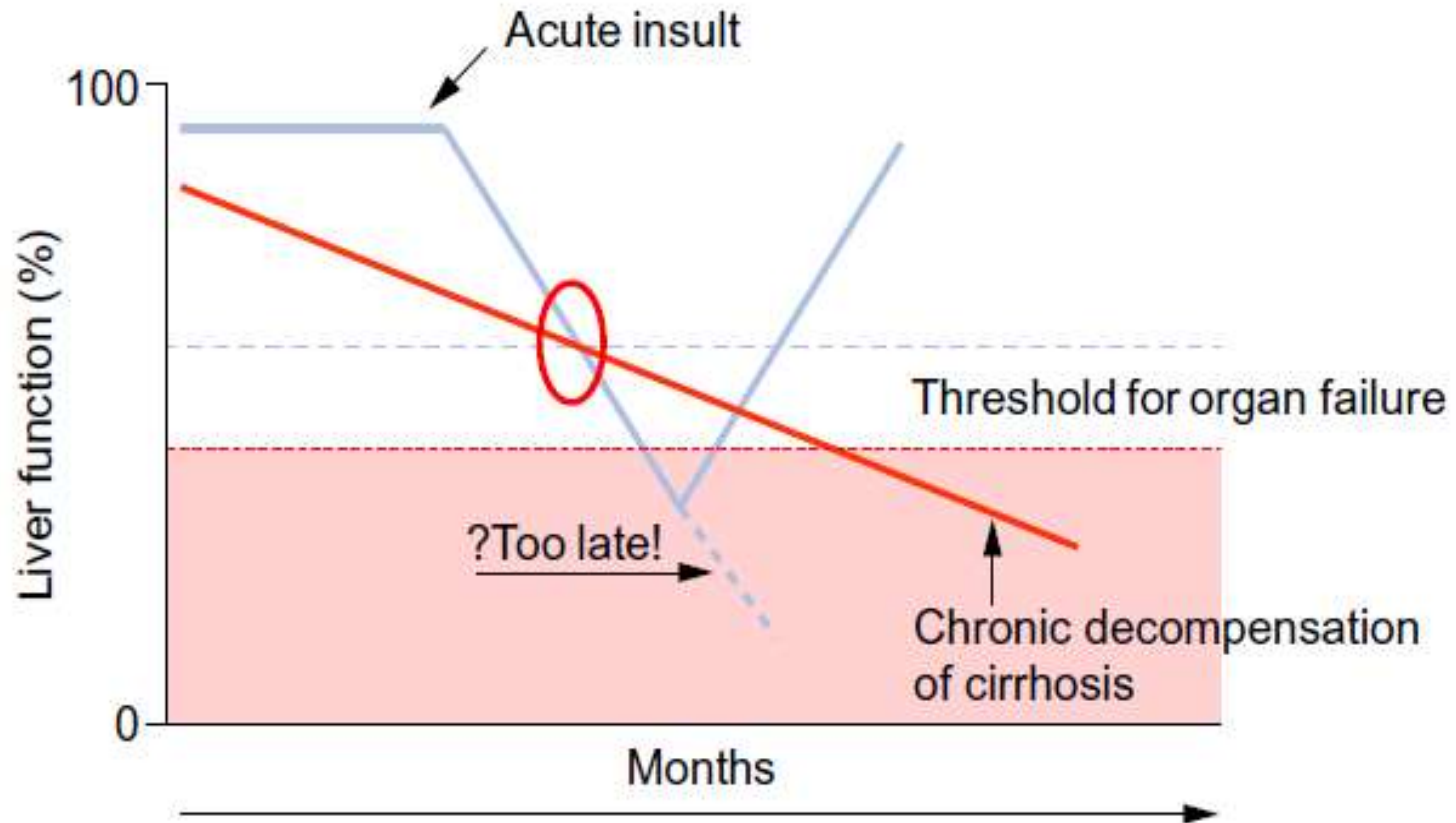
- Nail clubbing
  - Palmar erythema
  - Thenar/hypothenar wasting
  - Muscle wasting
  - Gynecomastia
  - Testicular atrophy
- Bronzing:  
Hemochromatosis
  - Kaiser-Fleisher rings:  
Wilson's disease
  - Dupuytren's contracture:  
EtOH
  - Tattoos, piercings:  
Hepatitis B, C, D
  - Vitiligo, psoriasis, goiter:  
Autoimmune liver diseases

# Chronicity on Investigations

- On Labs
  - Past abnormal liver enzymes – elevated MCV (especially with alcohol related liver disease)
  - High FIB-4 score based on Age, AST, ALT, Platelet count
- On imaging
  - Nodular liver on U/S, CT or MRI with Splenomegaly
  - Elastography (Fibroscan) with high liver stiffness >15 KPa
- On histology/pathology
  - Fibrosis on histology
  - Micronodular cirrhosis
  - Pathognomonic changes of diseases



# Acute-On-Chronic Liver Failure Syndrome



William Bernal, Rajiv Jalan, Alberto Quaglia, Kenneth Simpson, Julia Wendon, Andrew Burroughs

Lancet 2015; 386: 1576-87

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# Pattern of Injury

# Testing the liver

## For liver injury

AST (nl < 40 U/L)

ALT (nl < 40 U/L)

Alkaline

Phosphatase

(nl < 150 U/L)

## For liver function

INR (nl 0.8-1.2)

Albumin (nl 35-50 g/L)

Bilirubin (nl < 20  $\mu$ mol/L)

# Let's Do Cases Using The Three Questions

IS THE LIVER FUNCTIONING NORMALLY?

IS THE INJURY ACUTE OR CHRONIC OR  
ACUTE-ON-CHRONIC?

WHAT IS THE INJURY PATTERN?

# First Case: Jaundice and Fracture

- 58 year old man with chronic hepatitis C failed therapy, closely followed by nurse practitioner presents with L femur fracture
- He will need orthopedic surgery
- Laboratory Tests:
  - INR 2.0, Albumin 27, Protein 45, Bilirubin 69, LDH 540, Platelet count 65, AFP 28, Alk phos 300, GGT 88
- No lesions on hepatic ultrasound



# Approach to jaundice

***First step:*** direct or indirect?

If all or mostly indirect, think prehepatic and do appropriate workup

***Step two:*** if direct, or mostly direct, rule out obstruction with ultrasound

***Step three:*** if no obstruction, likely hepatic. Order appropriate tests.

# VOCAL-Penn for Cirrhosis Surgical Risk Score

Age: 58 years

Albumin: 27 g/L

Bilirubin (total): 69  $\mu\text{mol/L}$

Platelet Count:  $65 \times 10^9/\text{L}$

BMI  $\geq$  30: no

NAFLD: no

ASA score: 2

Emergency: yes

Type of Surgery: major  
orthopedic

30-day mortality: 9.5%

90-day mortality: 12.1%

180-day mortality: 13.5%

90-day decompensation:  
21.9%



# Second Case: Referred by PCP

- 53 year old with elevated liver enzymes
- No cardiopulmonary, renal or endocrine problems
- Non-smoker, no alcohol consumption
- Previous sigmoid resection for colon cancer 4 years ago
- No medications, no herbal therapies
- Incidentally, noted:
  - ALT 62, AST 160, ALP 152
  - Bilirubin 26, INR 0.9, Albumin 39
  - WBC 3.0, Platelet count 88, Hgb 109, MCV 105, GGT 48
  - Creatinine 132 umol/L

# Patterns of Abnormal Liver Enzymes

- Hepatocellular (AST, ALT)
- Cholestatic (Alk P with *GGT*)
- Mixed (Alk P, ALT, AST)

# Acute Hepatocellular Pattern

Drugs/toxins/alcohol

Acetaminophen

*Amanita phalloides* (mushroom)

Viral hepatitis

Hepatitis A, B or C or other

Autoimmune

Shock or ischemia

Wilson's disease

# Chronic Hepatocellular Pattern

Drugs/toxins

Steatohepatitis

- Alcohol-related liver disease

- Metabolic syndrome related fatty liver disease

Viral hepatitis

- Hepatitis B or C

Inherited liver diseases

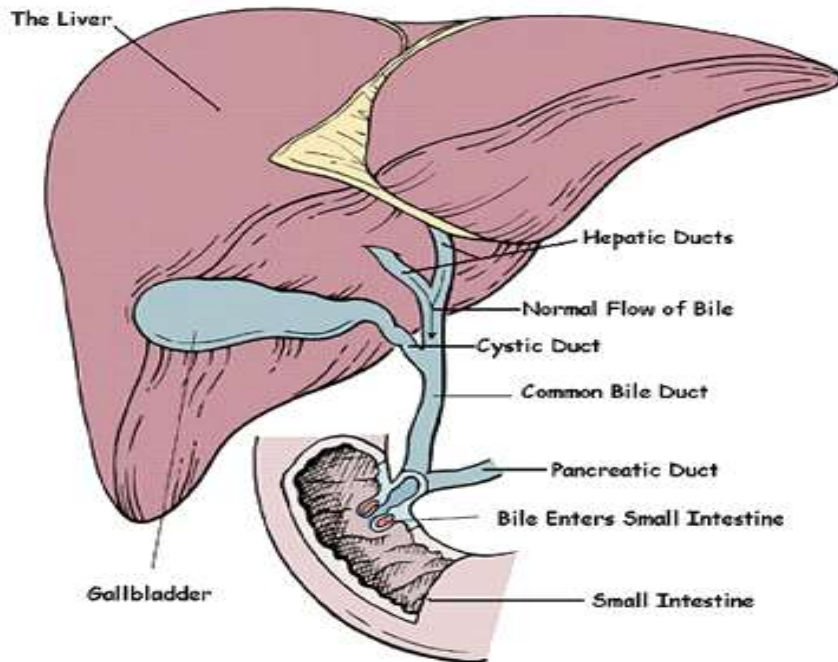
- Hemochromatosis,

- Alpha-1 anti-trypsin deficiency

- Wilson's disease

Autoimmune hepatitis

# Cholestasis



Large duct or small duct disease

Can be associated with elevation of bilirubin or not

Can be simply on basis of edema from most hepatocellular process

# Cholestasis: Approach

**Biliary tree  
on imaging**

**Normal:  
Intrahepatic**

**Dilated Ducts:  
Extrahepatic**

# Extrahepatic Cholestasis

- Cholelithiasis/ microlithiasis
- Stricture
  - Ischemic: post-cholecystectomy
  - Fibrotic: Primary Sclerosing Cholangitis
  - Malignant: cholangiocarcinoma
- External compression
  - Pancreatic mass/cancer
  - Lymph nodes of porta hepatis
- Ampulla of Vater
  - Dysfunction
  - Cancer
  - Stenosis
- Atresia

**“THINK OF THE ANATOMY ! ”**

# Intrahepatic Cholestasis

## Drugs

- Anti-psychotic medications
- Anabolic steroids/estrogens
- Antibiotics

## Infiltrative

- Malignancy
- Amyloid/granulomatous/mycobacterium
- Fatty liver

## Autoimmune

- Primary Biliary Cholangitis (previous known as Biliary Cirrhosis)
- Primary Sclerosing Cholangitis
- Autoimmune Cholangitis with or without high IgG4

## Sepsis

- Heart Failure (congestive hepatopathy)



# Trends to remember!

Alcohol: AST>ALT (2-3:1; less than 300...) with high MCV

Fatty liver disease: normal, hepatitic, cholestatic or mixed focus on long-standing diabetes and obesity

ALT most specific for liver disease

AST has other sources (muscle)

ALP has 5 sources (what are they?)

GGT too sensitive (helps discern 'source' of elevated ALP....)

# Third Case: Paracentesis

- Bedside procedure
- Cell count and differential:
  - WBC 900 and neutrophil count 80% (720)
- Fluid chemistry:
  - Albumin 8 g/L, Protein 15 g/L, LDH 200 IU/L
- 4 L fluid removed
- Serum chemistry:
  - Albumin 25 g/L, Protein 50 g/L, LDH 450 IU/L



# Spontaneous Bacterial Peritonitis

Fever, abdominal pain, encephalopathy or high white count may be present

Can be completely asymptomatic yet deadly

Always look for it – you cannot send patient with ascites home from emergency department without a diagnostic tap

# How Should We Interpret Serum to Ascites Albumin Gradient?

Gradient > 11 g/L

High JVP

Congestive heart failure, constrictive pericarditis (cardiac ascites)

Low JVP

Cirrhosis, alcoholic hepatitis, fulminant hepatic failure

Budd - Chiari syndrome (hepatic vein thrombosis) or veno occlusive disease

Myxedema

Massive liver metastasis

# How Should We Interpret Serum to Ascites Albumin Gradient?

Gradient < 11 g/L

Exudate (high protein, high LDH)

Peritoneal carcinomatosis

Tuberculosis, peritonitis

Pancreatic ascites

Transudate (low protein, low LDH)

Nephrotic syndrome

Malnutrition

Protein-losing enteropathy

# Treatment of Ascites

1. Low Na<sup>+</sup> diet (<2g/day)
2. Lasix 20-40 mg/Spironolactone 50 mg per day (double q 1-2 weeks to max. dose of 160mg/400mg....monitoring electrolytes and creatinine!)
3. Therapeutic paracentesis
4. Radiologic (TIPSS insertion)
5. Surgical (Transplant)

# What are the steps to resuscitation for Upper GI Bleeding?

1. ABC' s ALWAYS!
2. IV access (2 bore' s) and administer crystalloid (aim for BP systolic 90 mmHg)
2. IV pantoloc 80 mg, then 8 mg/h
3. Octreotide 50 mcg iv then 50 mcg/h
4. Correct INR, platelets
5. IV antibiotics (cefotaxime 2gm q12h)

# Encephalopathy Grading

## Grade 1 to 4

1. Reversal of sleep pattern
2. Asterixis
3. Confusion/lethargy
4. Coma

Ammonia may be useful to diagnose in liver failure but clinical picture usually enough



# Encephalopathy Checklist prior to Starting Specific Treatment

- If precipitant, find it and treat it if possible

Metabolic disturbance (including hyper/hypoglycemia)

Infection

GI bleed

Psychotropic drugs

PVT

HCC

Progression

# Treatment for Hepatic Encephalopathy

## *Empiric*

1. Lactulose 15 - 30 cc' s q1h until wake up
  - Alternative PEG 3353 (restoalax/laxaday)
  - If comatose: use lactulose retention enema with 300 cc in 700 cc water
2. Rifaximin 550mg po BID
  - Flagyl or Metronidazole IV or PO 250mg q12h
3. Raise head of bed >30 degrees in liver failure
4. Sodium benzoate in rare cases

## *Specific*

Treat the underlying cause

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# Any Other Questions



**#CoffeeGoodForLiver**



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