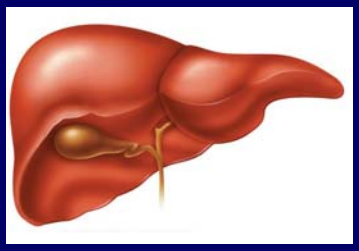
LIVER TESTS: HOW TO UTILIZE THEM



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I have no disclosures relevant to this presentation

OBJECTIVES

- Differentiate between hepatocellular and cholestatic liver disease
- Determine how to measure hepatic synthetic function
- Use common liver tests and exam findings to determine short and long-term survival
- * Recognize common adult liver disorders

LIVER TESTS: WHAT IS INCLUDED?

- SGPT (ALT): 8-66
- SGOT (AST): 13-44
- Alkaline phosphatase: 40-129
- Gamma-glutamyl transferase (GGT): 10-71
- Total bilirubin: 0.2-1.0
  - Direct bilirubin (conjugated): 0-0.3
  - Indirect bilirubin (unconjugated) = total - direct
- Prothrombin time, INR: 0.9-1.3
- Serum albumin: 3.8-5.0

QUESTION 1: TYPE OF LIVER DISEASE?

- **Hepatocellular: (ALT/AST)**
  - alcohol
  - viral hepatitis
  - autoimmune hepatitis
  - hemochromatosis
  - Wilson's Disease
  - Non-alcoholic fatty liver
  - alpha-1 antitrypsin deficiency
  - medications
- **Cholestatic/Obstructive: (alkaline phosphatase)**
  - stones
  - primary biliary cholangitis (PBC)
  - primary sclerosing cholangitis (PSC)
  - medications

INFILTRATIVE LIVER DISEASE

- Space occupying lesion
- Alkaline phosphatase elevation
- Occasional bilirubin elevation
- Examples: tumors, amyloid, sarcoid

LIVER TESTS: HELPFUL HINTS

- Bilirubin frequently not helpful in determining type of injury
  - Can become elevated due to hepatic as well as non-hepatic causes (hemolysis)
  - Can become elevated in hepatocellular, cholestatic as well as infiltrative disease
- ALT is more specific for liver disease than the AST
- Alkaline phosphatase; biliary, bone, placenta, intestine
- GGT is nonspecific
  - Helpful in determining the source of alkaline phosphatase elevation

LIVER TESTS: HELPFUL HINTS

- ALT > 500 = Hepatitis A, Hepatitis B, autoimmune hepatitis, medications, ischemia (shock liver)
- Alcoholic liver disease rarely has transaminases >300
  - AST:ALT > 2:1 is suggestive of alcoholic liver disease

QUESTION 2: ACUTE OR CHRONIC?

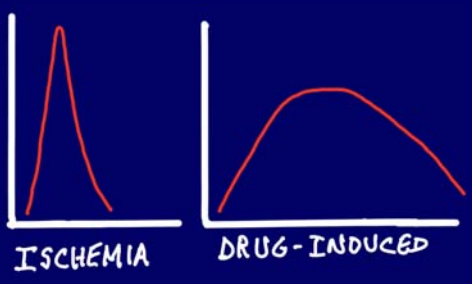
- INR, INR, INR
- Albumin

CASE 1

55-year-old male with recent cardioversion for atrial fibrillation.

- ALT 1614
- AST 1567
- ALK PHOS 145
- TOTAL BILI 10.3
- DIRECT BILI 7.6
- INR 1.2

TAKE HOME POINTS



CASE 2

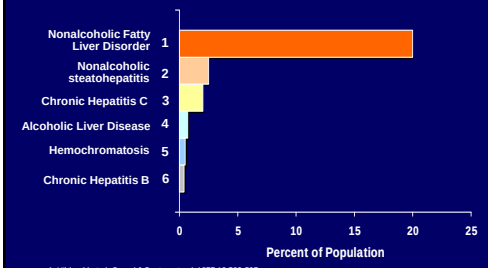
63-year-old asymptomatic female. BMI 33.
MEDS: amlodipine for HTN, glyburide for DM

- ALT 112
- AST 110
- ALK PHOS 102
- TOTAL BILI 0.9
- DIRECT BILI 0.5
- INR 0.9
- ALBUMIN 3.9

TAKE HOME POINTS

- Risk factors:
  - BMI > 30
  - Insulin resistance
  - Elevated triglycerides
- Hispanics > Caucasians > African Americans
- Diagnosis of exclusion
- Weight loss > 10%

Prevalence of Chronic Liver Disorders in the United States



1. Hilden M et al. *Scand J Gastroenterol*. 1977;12:593-597.
2. Ground KEU. *Aviat Spac Environ Med*. 1982;53:14-18.
3. Alter MF et al. *N Engl J Med*. 1999;341:556-562.
4. Venkataramani A et al. In: Maddrey WC, Feldman M, eds. *Atlas of the Liver*. Philadelphia: Current Medicine;1999:9.0.
5. Adapted from http://www.niddk.nih.gov/new/press/01/09 -25.htm. Accessed 11/01/02.
6. McQuillan GM et al. *Am J Public Health* 1999;89:14-18.

CASE 3

46-year-old male with jaundice. EGD shows large varices.

- ALT 31
- AST 119
- ALK PHOS 98
- TOTAL BILI 3.4
- DIRECT BILI 1.9
- INR 1.6

TAKE HOME POINTS

- Transaminases < 300, AST:ALT > 2:1
- Vitamin K not beneficial in hepatocellular injury and coagulopathies
- All patients with cirrhosis should undergo EGD to evaluate for varices
  - If normal, repeat in three years

CASE 4

A 40-year-old woman is found to have abnormal liver tests during an evaluation for pruritus of 1 year duration. Denies alcohol and takes no medications.

- ALT 143
- AST 110
- ALK PHOS 741
- TOTAL BILI 3.2
- DIRECT BILI 2.9
- INR 2.0

TAKE HOME POINTS

- Primary biliary cholangitis
  - 90% of affected are women
  - Anti-mitochondrial antibody (AMA)
  - Microscopic bile ducts
- Pruritus = cholestasis (cholestyramine)
- Sicca syndrome
- Bone disease
- Hypercholesterolemia (xanthelasma)
- Vitamin K beneficial for coagulopathies

Xanthelasma

Tuberous Xanthomata

Tuberous Xanthomata

emedicine.com

CASE 5

35-year-old male with abnormal liver tests noted during routine labs for health insurance. He is asymptomatic.

- ALT 26
- AST 21
- ALK PHOS 78
- TOTAL BILI 2.9
- DIRECT BILI 0.2
- INR 0.9

TAKE HOME POINTS

- Elevated total bilirubin
- Conjugated (direct) versus unconjugated (indirect)
- Unconjugated
  - Gilbert's versus hemolysis

CASE 6

60-year-old male with fatigue and dyspnea on exertion. Father died of cirrhosis.
MEDS: sildenafil, insulin, ibuprofen for knee pain

- ALT 86
- AST 65
- Alkaline Phosphatase 97
- Total bilirubin 1.1
- Direct bilirubin 0.4
- INR 1.4

TAKE HOME POINTS

- Hereditary hemochromatosis (primary)
  - All chronic liver diseases raise iron levels (secondary)
- Homozygous 1/200 (Caucasian patients)
- Darkening of skin, DM, CHF, arthropathy
- Elevated ferritin (usually greater than 1000)
- Transferrin saturation (iron/TIBC) > 45%
- HFE gene positive in 75-80%
- Treat with phlebotomy until ferritin approx. 50

CASE 7

37-year-old female with generalized malaise and fatigue.
MEDS: methotrexate for rheumatoid arthritis

- ALT 589
- AST 712
- Alkaline Phosphatase 158
- Total bilirubin 2.0
- Direct bilirubin 1.6
- INR 1.3

TAKE HOME POINTS

- Autoimmune hepatitis
- > 75 % are female
- Anti-smooth muscle antibody positive
- Anti-nuclear antibody positive
- Elevated IgG or gamma globulins
- Treated with immunosuppressive therapy
  - Corticosteroids, azathioprine

CASE 8

29-year-old male with fatigue and dyspnea on exertion.

- ALT 76
- AST 62
- Alkaline Phosphatase 99
- Total bilirubin 1.6
- Direct bilirubin 0.9
- INR 1.2

TAKE HOME POINTS

- Alpha-1 antitrypsin deficiency
- Homozygous in 1/1600
- More frequently presents in childhood
- Check A1AT level (pathology seen at 15-20% of normal values)
- Phenotype
  - normal MM
  - liver disease seen in ZZ
- No treatment

CASE 9

- 38-year-old male with jaundice and malaise.
- ALT 29
- AST 96
- ALK PHOS 98
- TOTAL BILI 12
- DIRECT BILI 8
- PT 19 SEC
- CONTROL PT 12 SEC

TAKE HOME POINTS

- Alcoholic hepatitis
- Transaminases < 300, AST:ALT > 2:1
- Discriminant function

  4.6(PT-PT control) + total bilirubin
  - Values > 32 at high risk for 30-day mortality
- May benefit from steroids if no infectious contraindications

4.6(19-12)+12
Discriminant Fct: 44

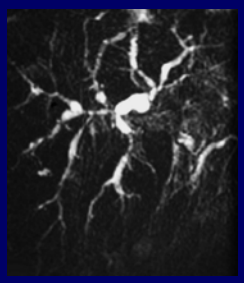
CASE 10

- 40-year-old male with jaundice, pruritus and diarrhea.
- AST 52
- ALT 58
- ALK PHOS 516
- TOTAL BILI 6.3
- DIRECT BILI 4.1
- INR 1.8

TAKE HOME POINTS

- Primary sclerosing cholangitis (PSC)
- Two-thirds with inflammatory bowel disease
- Large duct disease
- No associated autoantibody
- Imaging with MRCP/ERCP

PRIMARY SCLEROSING CHOLANGITIS ON MRCP



Radiology Assistant

PRIMARY SCLEROSING CHOLANGITIS

Child-Pugh Scoring Criteria

	POINTS		
	1	2	3
Albumin (g/dL)	>3.5	2.8 – 3.5	<2.8
Bilirubin (mg/dL)	<2	2 – 3	>3
INR (PT prolongation)	<1.70 (<3 seconds)	1.71 – 2.20 (>3 – < 5 seconds)	>2.20 (>5 seconds)
Ascites	None	Easily controlled with diuretics	Poorly controlled with diuretics
Encephalopathy	None	Easily controlled with lactulose	Poorly controlled with lactulose
Child-Pugh Class	A= 5-6 Compensated	B= 7-9 Decompensated	C= >9 Decompensated

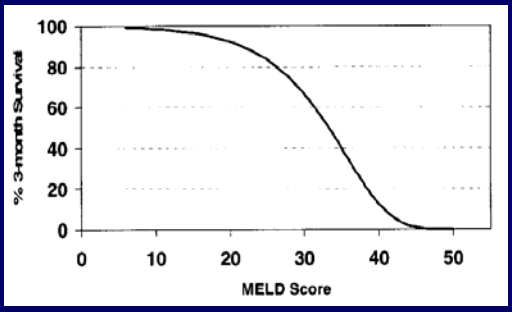
Ghany et al. In: Kasper et al, eds. *Harrison's Principles of Internal Medicine*. 16th Edition. McGraw-Hill; New York. 2004:1812-1813.

CHILD-TURCOTTE-PUGH CLASSIFICATION

- 5-YEAR SURVIVAL
  - A = 70-75%
  - B = 40-45%
  - C = 10-15%

MODEL FOR END-STAGE LIVER DISEASE (MELD)

MELD AND 3-MONTH SURVIVAL



Wiesner et al. Gastroenterology 2003

BONUS

PREDICTING MORTALITY IN PATIENTS WITH CIRRHOSIS UNDERGOING SURGERY

MELD SCORE AS A PREDICTOR OF POST-OPERATIVE MORTALITY

MELD score	7 Days	30 Days	90 Days
0-7 (n = 351)	1.9 (314)	5.7 (301)	9.7 (287)
8-11 (n = 257)	3.3 (236)	10.3 (219)	17.7 (200)
12-15 (n = 106)	7.7 (94)	25.4 (78)	32.3 (69)
16-20 (n = 35)	14.6 (29)	44.0 (19)	55.8 (15)
21-25 (n = 13)	23.0 (7)	53.8 (4)	66.7 (3)
≥26 (n = 10)	30.0 (6)	90.0 (1)	90.0 (1)

Modified from Ray Kim et al; GASTROENTEROLOGY 2007;132:1261–1269

THANK YOU !!!