# Approach to Elevated Liver Tests

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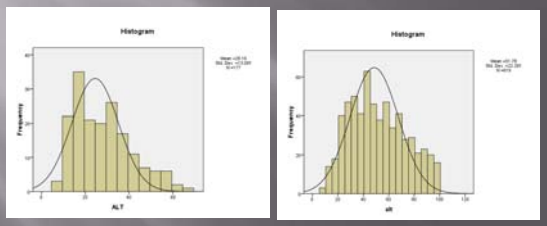
## Lecture Objectives

- At the conclusion the audience should have a better understanding of
  - What constitutes an abnormal aminotransferase
  - How to make an initial evaluation of an abnormal test
  - Understand disease specific serologic tests
  - Understand laboratories which are prognostic in chronic liver disease

## Clinical Scenario

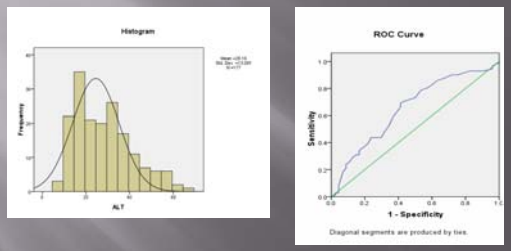
- You follow a 65 year old male at VA clinic
- His ALT is 58 IU/ml (within normal limits)
- On a rotation through cardiology, you see him at LUMC
- He is to be started on a statin, his ALT at LUMC is 55 IU/ml (H)
- He asks you what this means?

## Defining Normal




The left depicts 177 overweight patients undergoing routine surgery
The right depicts 629 patients undergoing evaluation for HCV

## Defining Normal




For obese persons undergoing bariatric surgery 2 SD above the mean was an ALT of 60 IU/mL
The right is the ability of ALT to discriminate the presence of fatty liver disease in patients undergoing bariatric surgery (AUC = 0.653)

## Refining Normal

- Population of persons donating blood
  - Selected those at lowest risk for liver disease (normal BMI, normal lipids and glucose, no medications)
  - Median ALT was 11 U/L
  - Value at the 95$^{th}$ percentile for
    - Women was 19 U/L
    - Men was 30 U/L
- Applied this to a population with HCV RNA
  - Reference of lab "abnormal" was 55% sensitive and 97% specific
  - The above criteria was 76% sensitive and 89% specific

Prati Ann Intern Med 2002;137:1-9

## Significant disease can occur at "normal"

- Data from Italy-patients at risk for NAFLD
- 63/458 patients had a liver biopsy with an ALT < 40 U/L (long standing steatosis)
- Mean ALT was 28 ± 7 U/L
- Fibrosis ≥ 2 (moderate) was seen in 22% with "normal" ALT and 34% with increased ALT (p=ns)
- 5/63 (8%) persons had cirrhosis
- Of 37% of persons with NASH and a normal ALT, 27% met more stringent criteria for normal
  - Fracanzani Hepatology 2008 ;48:792-798

## Conclusions

- Most laboratories use > 2 SD to define abnormal
  - The differences in clinical laboratories abnormal is based on the health of the reference population
- There is difficulty defining "normal" so your clinical suspicion for disease should must supersede labs
- A "normal" ALT does not exclude liver disease or histologic damage

## Who to test?

- No recommendation to routinely test healthy, asymptomatic persons
- Screened disease
  - Medically important
    - Yes
  - Relatively high prevalence
    - Yes
  - Natural history of disease should be known
    - Limited data (Lack of population based data)
  - Effective intervention should exist
    - Limited interventions for some diseases (NAFLD)

## Prevalence of abnormal aminotransferases

- NHANES III data
- Used ALT > 40 for men and > 31 for women as abnormal
- Prevalence of abnormal aminotransferases was 7.9%
- Men 9.3%, women 6.6%
- Hispanic 14.9%, African American 8.1% and non-Hispanic white 7.1%
- Only 31% of cases had an etiology for abnormal aminotransferases (viral hepatitis, alcohol, iron overload)
- If more stringent criteria for abnormal ALT used 26% had an elevated ALT, of which 21.2% had no explanation

Clark Am J Gastroenterol 2003

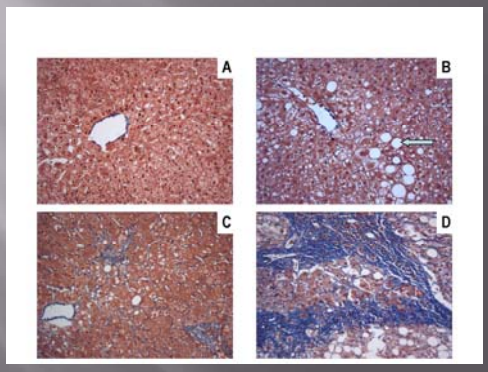
## LFTS: Worrisome?

- 20 yo male
  - TB 1.8
  - AP 180
  - AST 2789
  - ALT 6239
  - Alb 3.0
  - PT 20
- 29 yo female
  - TB 22.0
  - AP 99
  - AST 560
  - ALT 901
  - Alb 2.1
  - PT 66

Listing for fulminant hepatic failure requires onset of encephalopathy within 8 weeks of onset of liver disease symptoms and one of the following: 1) ventilator dependence, 2) requiring renal replacement therapy or 3) INR > 2.0

## Interpretation of Liver Tests

- True "liver function tests"
  - What does the liver do?
- Hepatocellular damage
- Cholestasis
- Are the abnormalities noted acute or chronic?




## True Liver Function Tests

- Albumin
  - Low albumin: edema, anasarca
  - Nephrotic syndrome, malnutrition, protein losing enteropathy
- Prothrombin time
  - High PT/INR: increased risk of bleeding
  - Vitamin K deficiency, consumptive coagulopathy
- **Bilirubin**
  - **Jaundice (total bilirubin > 2-3 mg/dL)**
- **Cholesterol**

## Prolonged PT

- Machines are calibrated to activated thromboplastins for patients on warfarin
  - There is significant variation in INR from lab to lab in cirrhotic patients
- Common clinical dilemma- vitamin K deficiency, consumptive coagulopathy or cirrhosis

| Factor | Cirrhosis | Vit K def | Consumption |
|---|---|---|---|
| Abnormal V | Yes | No | Yes |
| Abnormal VII | Yes | Yes | Yes |
| Abnormal VIII | No | No | Yes |

## Markers of Hepatocyte Damage

- ALT (alanine aminotransferase--SGPT)
  - Cytosol of hepatocytes
  - More hepatocyte specific
- AST (aspartate aminotransferase--SGOT)
  - Cytosol and mitochondria
  - Muscle, intestine, brain, kidney, pancreas, red blood cells
  - Mitochondrial induction/damage by alcohol explains higher AST levels in persons consuming excessive ETOH, vitamin deficiency leads to lower ALT
- **Lactate dehydrogenase (LDH)**
  - **Can be markedly elevated in shock liver**

## Causes of Markedly Elevated Aminotransferase Levels (> 1,000 U/L)

- Drug/toxin induced injury
  - Acetaminophen
  - NOT alcohol alone
- Acute viral hepatitis
- Shock liver
- **Autoimmune hepatitis**
- **Common bile duct stone**

## ALT/AST ratios

- In most liver diseases ALT > AST
- Exceptions:
  - Alcoholic liver disease
  - >2:1 ratio Wilson's disease
  - Accompanying hemolytic anemia
  - Advanced fibrosis
    - AST/ALT ratio >1 had a sensitivity of 41%, a specificity of 78% to identify advanced fibrosis
      - Unpublished data

## Markers of Cholestasis

- Alkaline phosphatase
  - Localized in microvilli of bile canaliculus
  - Hepatic synthesis ⇑ in cholestasis
  - Fractionation can help
  - Bone, intestine, placenta
- Gamma glutamyl transferase (GGT)
  - Induced by alcohol, medications
- 5′-Nucleotidase
  - Specific to liver
- Bilirubin

## Cholestasis

| Unconjugated hyperbilirubinemia | Conjugated hyperbilirubinemia | Elevated Alkaline phosphatase |
|---|---|---|
| Gilbert's syndrome<br>Crigler-Najjer syndrome<br>Hemolysis<br>Hematoma resorption | Bile duct obstruction<br>Severe hepatitis<br>Cirrhosis<br>Medication/Toxin<br>PBC<br>PSC<br>Sepsis<br>TPN<br>Benign recurrent cholestasis<br>Vanishing bile duct syndrome<br>Dubin-Johnson syndrome<br>Rotor syndrome | Hepatobiliary<br>Bile duct obstruction<br>PBC<br>PSC<br>Medications<br>Hepatic metastasis<br>Severe hepatitis<br>Cirrhosis<br>Vanishing bile duct syndrome<br>Benign recurrent cholestasis<br>Infiltrating diseases<br>Sarcoid<br>TB<br>Fungal<br>Amyloidosis<br>Heme malignancy |

## Bilirubin Metabolism

- Bilirubin is a normal heme degredation product
  - Predominant excretion is in bile
  - Unconjugated (indirect) is taken up by hepatocytes
  - Conjugated (direct) by the endoplasmic reticulum using enzyme bilirubin UDP-glucuronyltransferase
  - Water soluble bilirubin glucuronides secreted across canicular membrane into bile
- Clinical correlate**: Gilbert's syndrome**
  - Diminshed expression of bilirubin UDP-glucuronyltransferase
  - Up to 5% of population
  - Benign, unconjugated hyperbilirubinemia
  - Can be worsened by stress, fasting

## First Approach

- Repeat abnormal tests(?????)
  - Many will normalize without intervention, **ONLY** consider if no risk factors are present
  - Discontinue alcohol, potential hepatotoxins
  - Would not wait however if there are signs of synthetic dysfunction
    - Elevated bilirubin, PT prolongation
- Continued Elevation
  - Work up is based on pattern of abnormalities
    - Hepatocellular injury versus cholestatic
    - Acute versus Chronic

## Clinical scenario

- A 55 year old man is admitted overnight, he is new to LUMC and presents with melena
- On US he has a nodular appearing liver with possible fatty infiltration
- Relevant labs ALT 55, AST 77, TB 0.9, AP 88, PLT 55, HGB 8.9
- He undergoes endoscopy finding recently bleeding varices which were banded

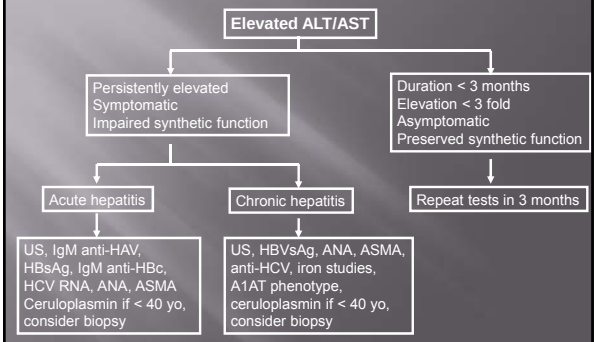
## Continued

- Which of the following labs sent over night are unnecessary?
- Acute hepatitis panel (hep A IgM, HB S AG, Anti-HBV core AB total, Anti-HCV)
- ANA, ASMA, AMA
- Ceruloplasmin
- Alpha-1 antitrypsin
- Ferritin, iron, TIBC
- Tylenol level
- Serum alcohol

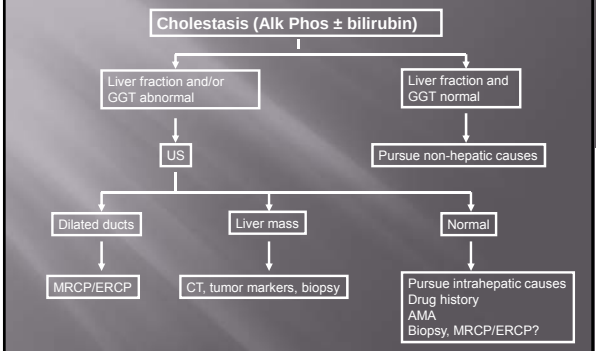
## The "shotgun" approach

- Liver consult
  - HAV IgM ← Chronic hepatitis?
  - HBV s Ag, core IgM
  - Anti-HCV
  - AMA ← Is there cholestasis?
  - ANA, ASMA
  - Ceruloplasmin ← Patient age?
  - Alpha-1 antitrypsin
  - Iron, TIBC, ferritin
  - Tox screen
  - RUQ US
  - Consider Biopsy

## General Approach to Abnormal LFTs




## General Approach to Abnormal LFTs




## Patient Characteristics

- Sex:
  - Female (AIH, PBC)
  - Male (PSC)
- Age:
  - Neonatal (A1AT)
  - < 40 (Wilson's, AIH)
  - > 40 (viral, HFE)
- Medications:
  - Antiepileptics
  - HAART
  - INH
- Risk factors (HCV):
  - IVDA (viral, EtOH)
  - Blood transfusions
  - Tattoos
- Comorbidities:
  - DM/obesity: NASH
  - CHF: HFE
- Family Hx
  - A1AT deficiency
  - Hemachromatosis
- Country of Birth
  - HBV

## Historical Clues

| History Component | Disease Correlation |
|---|---|
| Remote history of jaundice | Viral hepatitis |
| Medical history of autoimmune diseases | AIH |
| Hypothyroidism | AIH, PBC |
| History of liver disease as a newborn | Alpha-1 antitrypsin deficiency |
| Family history of liver disease | HBV, hemochromatosis |
| History of alcohol abuse, DUI | Alcohol |
| History of IVDA, blood transfusion prior to 1990 | HCV |
| Diabetes | Hemochromatosis, NAFLD |
| Components of Metabolic Syndrome | NAFLD |
| Medications, CAM therapy | Drug induced liver injury |
| Pruritis | PBC |
| Ulcerative Colitis | PSC |
| Arthritis | Hemochromatosis, HCV |

## Physical Clues

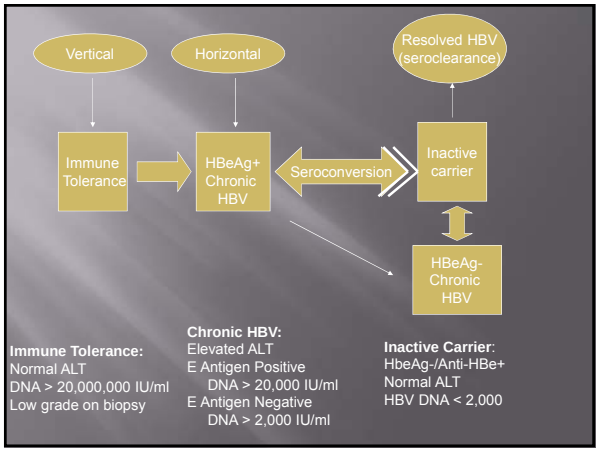
| Physical Exam Findings | Disease Correlates |
|---|---|
| Spider angiomas | Cirrhosis |
| Palmar erythema | Cirrhosis |
| Splenomegaly | Portal hypertension |
| Jaundice | Cirrhosis, Biliary obstruction, hemolysis, Gilbert's |
| Hyperpigmentation | Hemochromatosis |
| Kayser-Fleisher rings | Wilsons disease |
| Emphysema/Lung disease | Alpha-1 antitrypsin deficiency |
| Ascites | Portal hypertenson, cirrhosis |
| Asterixis | Portal hypertension |
| Xanthalasma | PBC |

## Liver Disease

- A clinician is better able to understand the evaluation of liver disease with a basic understanding of each individual disease
- The next section will focus on serology of chronic liver diseases

## Hepatocellular causes

| Disorder | Acute | Chronic |
|---|---|---|
| Hepatitis A | + | |
| Hepatitis B | + | + |
| Hepatitis C | + | + |
| Hepatitis E | + | (rare) |
| Autoimmune hepatitis | + | + |
| Wilson Disease | + | + |
| Hemochromatosis | | + |
| Alpha-1 AT deficiency | (neonatal) | + |
| NAFLD | | + |
| Alcohol | + | + |
| Medication/Toxin | + | + |




## Diagnosis of HBV

| | HBsAg | HBc | HBe | HBsAb | HBV DNA |
|---|---|---|---|---|---|
| Acute | HBsAg | HBcIgM | | | + |
| Chronic (immune tolerant or active) | HBsAg | HBcIgG | HBeAg+ or eAg- | | $>10^4$-$10^5$ |
| Inactive Carrier | HBsAg | HBcIgG | eAb+ | | $<10^4$ |
| Immune | | HBcIgG | | HBsAb | |
| Vaccinated | | | | HBsAb | |

## HCV lab tests

| HCV test | Comment |
|---|---|
| Anti-HCV | Seropositive in past and current infection |
| HCV RIBA | Seldom used<br>Can distinguish false positive AB from past infection |
| HCV RNA | Viremia indicates current infection<br>Viral load does not correlate with severity of liver disease |
| HCV genotype | Measure if considering interferon based therapy<br>Genotype 1 predominates in US |

## Hemochromatosis

- **LABS: iron/TIBC, ferritin, genotype**
- Clinical suspicion
  - Fatigue, arthralgia, diabetes mellitus, hyperpigmentation, impotence
- Transferrin saturation and ferritin
  - TS > 45%
    - Sensitivity >97%
    - Specificity 45%
  - Ferritin > 1000 mg/ml marker of significant disease
- Genotype
  - C282Y (prevalence 5/1000 if Northern European descent)
    - Accounts for 80-85% of typical hemochromatosis
    - Only 10% of C282Y homozygotes will have end organ damage
  - Other mutations: ie H63D, S65C controversial

## Autoimmune Hepatitis

- **LABS: ANA, ASMA, anti-LKM (kids), immunoglobulins**
- Type 1 AIH
  - Women (4:1), peak 20's to 40's
    - All ages and ethnic groups susceptible
  - ANA (67%), SMA (87%)
    - ANA found in PBC, PSC, viral hepatitis, drug related hepatitis, NASH, ETOH
    - pANCA common
  - Hyperglobulinemia (high IgG)
- Type 2 AIH (young women)
  - Anti-LKM1
  - Less hyperglobulinemia
  - Tends to be more severe at onset and more likely to progress to cirrhosis

## Wilson's

**LABS: ceruloplasmin, 24 urine copper, serum copper, genetic testing**

| Test | WD | Comments |
|---|---|---|
| Ceruloplasmin | <20 mg/dl | 95% homozygotes<br>20% heterozygotes |
| Slit-lamp | KF rings | Absent early<br>F(+) cholestatic disease |
| 24 hour urine | >100 ug | F(-) early<br>F(+) cholestatic disease |
| Hepatic copper | >250 ug/g | F(+) cholestatic disease<br>F (-) sampling error |

Genetic testing by whole-gene sequencing exists, but can be difficult as most persons with WD are compound heterozygotes and there are roughly 300 mutations

## Alpha-1 Antitrypsin Deficiency

- **LABS: alpha1-antitrypsin level, phenotype**
- Serine protease inhibitor for which liver disease results from failure to export
- History
  - 10% develop neonatal hepatitis or obstructive jaundice
- Serum levels
  - Low
- Phenotyping
  - PiZZ
- Liver histology
  - A1AT globules in ER of periportal hepatocytes
  - PAS positive, diastase-resistant

## NAFLD

- NAFLD
  - 20-30% in US
- NASH
  - 3% of general population
  - 20% of obese individuals
- Disease associations
  - Metabolic syndrome
    - Visceral obesity, insulin resistance, dyslipidemia (HDL, TG), elevated blood pressure
- Asymptomatic transaminase elevation
  - ALT > AST
  - GGT may be increased
  - Alk phos usually < 2x ULN
  - Elevated ferritin—60% (marker for IR)

## Alcoholic Hepatitis

- Diagnosis-History
  - Ask about DUI
  - AST>>ALT (both typically < 300 U/L)
  - Elevated bilirubin and prolonged PT
  - Alkaline phosphatase often normal
- Calculate discriminant function
  - Serum bilirubin + 4.6*(patient PT- control PT)
- DF > 32 is important
  - Designates poor prognosis, high mortality
  - Marker for therapy consideration
    - Prednisolone, pentoxifylline

## Hepatotoxic Medications

- Commonly prescribed Medication
  - Augmentin
  - Anti-Epileptics
  - Azole (antifungal)
  - Isoniazid
  - Anesthetics
    - Halothane
  - Nicotinic acid
  - Nitrofurantion
  - Propylthiouricil
  - Oral hypoglycemics
    - Glyburide
    - TZDs
  - HMG CoA reductase inhibitors
  - Protease inhibitors
- OTC, CAM, illicit
  - Acetaminophen
  - NSAIDs
  - Ephedra
  - Kava
  - Chaparral
  - Black Cohosh
  - Ecstasy
  - Hydrofluorocarbons
  - Chloroform
  - Toluene

## LFT's and Statins

- Chronic aminotransferase elevation and histological injury has never been convincingly proven
- Significant hepatotoxicity attributable to statins is very rare
- Use of lower doses and highly lipophilic (cerivastatin, lovastatin, simvastatin) may reduce hepatotoxicity

| Agent | RR | CI |
|---|---|---|
| Highly Lipophilic | 1.58 | 0.81, 3.05 |
| Mildly Lipophilic | 3.54 | 1.72, 5.58 |

Argo et al Hepatology 2008;48:662

## Incidence of Aminotransferase Elevation with Statin Use for Cardiovascular Disease

**Table 1. Incidence of Aminotransferase Elevation with Statin Use for Cardiovascular Disease**

| Study | Year | Agent | Multiple Assessments of AST or ALT | Statin (%) | Placebo (%) | Total (%) |
|---|---|---|---|---|---|---|
| EXCEL | 1991 | Lovastatin | Yes | 45/6,582 (0.6) | 2/1,663 (0.1) | 47/8,245 (0.6) |
| 4S | 1994 | Simvastatin | No | 49/2,221 (2.2) | 33/2,223 (1.5) | 82/4,444 (1.8) |
| ACAPS | 1994 | Lovastatin | No | 6/460 (1.3) | 6/459 (1.3) | 12/919 (1.3) |
| CRISP | 1994 | Lovastatin | Yes | 0/289 (0) | 0/142 (0) | 0/431 (0) |
| Oxford | 1994 | Simvastatin | No | 0/414 (0) | 2/207 (1.0) | 2/621 (0.3) |
| WOSCOPS | 1995 | Pravastatin | No | 16/3,302 (0.5) | 12/3,293 (0.4) | 28/6,595 (0.4) |
| KAPS | 1995 | Pravastatin | No | 4/224 (1.8) | 3/223 (1.3) | 7/447 (1.6) |
| CARE | 1996 | Pravastatin | No | 66/2,081 (3.2) | 73/2,078 (3.5) | 139/4,159 (3.3) |
| LCAS | 1997 | Fluvastatin | Yes | 2/214 (0.9) | 0/215 (0) | 2/419 (0.5) |
| AFCAPS-TEXCAPS | 1998 | Lovastatin | Yes | 18/3,242 (0.5) | 11/3,248 (0.3) | 29/6,490 (0.4) |
| LIPID | 1998 | Pravastatin | No | 95/4,512 (2.1) | 85/4,502 (1.9) | 180/9,014 (2.0) |
| LIPS | 2002 | Fluvastatin | Yes | 10/844 (1.2) | 3/833 (0.4) | 15/1,677 (0.9) |
| PROSPER | 2002 | Pravastatin | No | 1/2,891 (0) | 1/2,913 (0) | 2/5,804 (0) |
| Total | | | | 312/27,276 (1.1) | 231/21,999 (1.1) | 543/49,275 (1.1) |
| Odds ratio | | | | 1.26 (NS) | 1.00 | |

This table was adapted from de Denus et al.[7]
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; NS, not significant.

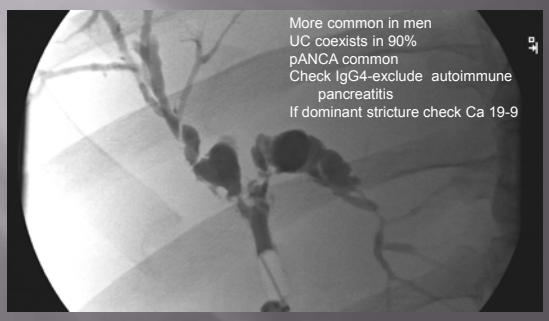
## Cholestatic Liver Disease

| Disorder | Acute | Chronic |
|---|---|---|
| PBC | | + |
| PSC | | + |
| Obstructive Jaundice | +(pain) | + |
| Medications/Toxins | + | + |

## PBC

- **LABS: AMA, immunosglobulins**
- Serologic
  - Anti-mitochondrial antibody (AMA)
    - 95% positive in PBC
    - 1% general population
    - 5% PBC patients AMA negative
    - Targets mitochondrial specific complexes
  - High levels of IgM
  - Alkaline phosphatase elevation > aminotransferases
  - Increased bilirubin associated with worsened disease severity
  - High cholesterol (especially HDL)

## PSC



More common in men
UC coexists in 90%
pANCA common
Check IgG4-exclude autoimmune pancreatitis
If dominant stricture check Ca 19-9

## Medicines that Cause Cholestasis

- Anabolic steroids
- Allopurinol
- Amoxicillin-clavulanic acid
- Atazanavir
- Diltiazem
- Erythromycin
- Estrogens
- Indinavir
- Nevirapine
- Methyltestosterone
- Quinidine
- Total parenteral nutrition
- Trimethoprim-sulfamethoxazole

## Surveillance for HCC

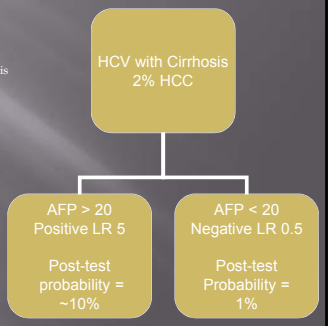
AASLD recommends US (and AFP*) every 6-12 months for surveillence

- Hepatitis B carriers
  - Asian males ≥ 40
  - Asian females ≥ 50
  - Cirrhosis at any age
  - Positive family history
  - Africans ≥ 20
- *For those not listed above HCC risk varies; consider HBV viral load and grade of inflammation*
- Non-hepatitis B Cirrhosis
  - Hepatitis C
  - Alcohol
  - Hemochromatosis
  - PBC
  - Alpha-1 antitrypsin
  - NASH
  - Autoimmune hepatitis

Bruix Hepatology 2010 (AASLD position paper)
*AFP was dropped from 2010 guidelines

## Alpha-Fetoprotein

- AFP is a marker of liver rejeneration
  - It is often elevated in viral hepatitis
- AFP can be used for surveillance and diagnosis
- AFP > 20 ug/dl
  - Sensitivity 41-65%
  - Specificity 80-94%
  - Positive LR 3.1-6.8
  - Negative LR 0.4-0.6
    - Gupta Ann Intern Med 2003



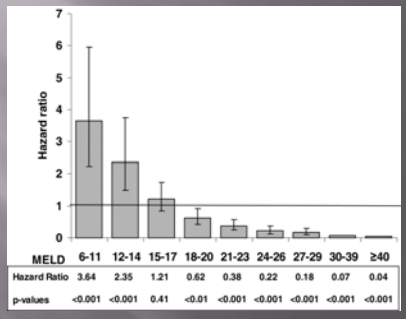

## Clinical scenario

- A 45 year old woman sees you in follow up.
- She has HCV and alcohol cirrhosis, but stopped drinking 2 years ago
- Her labs include CR 0.8, TB 0.9 and INR 1.1, AST 66, ALT 48
- She recently saw hepatology and was told she did not need transplant
- As her primary care doctor she asks if you agree

## Severity of Liver Disease

- Child-Turcotte-Pugh System (CTP)
  - Not formally validated as prognostic tool
  - Useful means to rapidly assess prognosis
  - Also useful for pre-operative risk assessment
  - Semi-Subjective
- Model for End stage Liver Disease (MELD)
  - Currently used for transplant listing
  - Based on creatinine, INR, total bilirubin (Cr and INR more heavily weighted)
  - Objective values comprise score
  - Validated to predict survival
    - 3 month survival for a MELD of
      - 6 >90%
      - 40 7%
      - Malinchoc Hepatology 2003

## Cirrhosis ≠ Transplant




Merion Am J Transplant 2005

## CTP score

| | 1 point | 2 points | 3 points |
|---|---|---|---|
| Grade encephalopathy | None | 1-2 | 3-4 |
| Ascites | Absent | Slight | Moderate or more |
| Bilirubin | 1-2 | 2-3 | >3 |
| Bilirubin (for PBC patients) | 1-4 | 4-10 | >10 |
| Albumin | >3.5 | 2.8-3.5 | <2.8 |
| INR | <1.7 | 1.7-2.3 | >2.3 |

Score ≤6 Class A, 7-9 Class B, ≥10 Class C

## Important Disease Assocations

- Emphysema and Liver disease
- Cirrhosis, DM, arthritis, AFIB
- IBD and elevated alkaline phosphatase
- Viral hepatitis associated with liver failure in pregnancy
- Liver disease, with anemia and psychosis
- ALT greater than 5000 in someone with alcoholism
- Elevated alkaline phosphatase with itching and fatigue seen in a 50 year old woman

## Case 1

- A 25 year old presents 3 days after a significant acetaminophen ingestion
- There is AMS and they are intubated early in the course- NAC is started

| Lab | Day 1 | Day 2 | Day 3 |
|---|---|---|---|
| TB | 3.2 | 4.1 | 4.8 |
| AST | 12000 | 13000 | 9000 |
| ALT | 9000 | 10000 | 8500 |
| INR | 3.0 | 4.1 | 5.3 |

By Day 3 is the course better, worse or stable?

## Case 2

- A person is referred for initial elevation in ALT (52)- synthetic function is normal and there are no prior available liver tests
- Ultrasound one year prior suggested a fatty liver
- Clinical history includes a blood transfusion in 1988 for a trauma, DM, BMI 29 and a family history of cancer in the liver but might have been metastatic
- Medications include metformin, losartan and atorvastatin

## Conclusions

- When evaluating suspected liver disease
  - Realize that aminotransferases are imperfect markers of disease state
  - Following synthetic function is of vital importance
  - Remember medications and complementary medicines
  - Approach patients based on risk factors and pattern of liver injury (hepatocellular or cholestatic)
  - Use models to assess severity of liver injury