Approach to Elevated Liver Tests

Eric R Kallwitz, MD
Associate Professor of Medicine
Loyola University Medical Center
Section of Hepatology

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
- 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 95th 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

For obese persons undergoing bariatric surgery ± 3SD 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)
**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

<table>
<thead>
<tr>
<th>Factor</th>
<th>Cirrhosis</th>
<th>Vit K def</th>
<th>Consumption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal V</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Abnormal VII</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Abnormal VIII</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**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 ETOL, 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

<table>
<thead>
<tr>
<th>Unconjugated hyperbilirubinemia</th>
<th>Conjugated hyperbilirubinemia</th>
<th>Elevated Alkaline phosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gilbert’s syndrome</td>
<td>Bile duct obstruction</td>
<td>Hepatobiliary pathology</td>
</tr>
<tr>
<td>Crigler-Najjer syndrome</td>
<td>Severe hepatitis</td>
<td>Bile duct obstruction</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>Cirrhosis</td>
<td>PBC</td>
</tr>
<tr>
<td>Hematoma resection</td>
<td>Medication/Toxin</td>
<td>PSC</td>
</tr>
<tr>
<td></td>
<td>Septic</td>
<td>Medications</td>
</tr>
<tr>
<td></td>
<td>TPN</td>
<td>Hepatic metastases</td>
</tr>
<tr>
<td></td>
<td>Benign recurrent cholestasis</td>
<td>Severe hepatitis</td>
</tr>
<tr>
<td></td>
<td>Vanishing bile duct syndrome</td>
<td>Carcinoma</td>
</tr>
<tr>
<td></td>
<td>Dubin-Johnson syndrome</td>
<td>Vanishing bile duct syndrome</td>
</tr>
<tr>
<td></td>
<td>Rotor syndrome</td>
<td>Benign recurrent cholestasis</td>
</tr>
</tbody>
</table>

Bilirubin Metabolism

- Bilirubin is a normal heme degradation 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 canalicular membrane into bile

Clinical correlate: Gilbert’s syndrome

- Diminished 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 Evaluation
    - 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
  - HBV s Ag, core IgM
  - Anti-HCV
  - AMA
  - ANA, ASMA
  - Ceruloplasmin
  - Alpha-1 antitrypsin
  - Iron, TIBC, ferritin
  - RUQ US
  - Consider Biopsy

General Approach to Abnormal LFTs

<table>
<thead>
<tr>
<th>Cholestasis (Alk Phos ± bilirubin)</th>
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<tbody>
<tr>
<td><img src="image1" alt="Liver fraction and/or GGT abnormal" /></td>
</tr>
<tr>
<td><img src="image3" alt="Pursue non-hepatic causes" /></td>
</tr>
<tr>
<td><img src="image5" alt="Diabetic diabetes" /></td>
</tr>
<tr>
<td><img src="image7" alt="MRC/ERCP" /></td>
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</tbody>
</table>

Patient Characteristics
- **Sex:**
  - Female (AIH, PBC)
  - Male (PSC)
- **Age:**
  - Neonatal (A1AT)
  - ≤ 40 (Wilson’s, AIH)
  - > 40 (viral, HFE)
- **Medications:**
  - Antiepileptics
  - HAART
  - INH

Historical Clues

<table>
<thead>
<tr>
<th>History Component</th>
<th>Disease Correlation</th>
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<tbody>
<tr>
<td>Remote history of jaundice</td>
<td>Viral hepatitis</td>
</tr>
<tr>
<td>Medical history of autoimmune diseases</td>
<td>AIP</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>AIP, PBC</td>
</tr>
<tr>
<td>History of liver disease as a newborn</td>
<td>Alpha-1 antitrypsin deficiency</td>
</tr>
<tr>
<td>Family history of liver disease</td>
<td>HBV, hemochromatosis</td>
</tr>
<tr>
<td>History of alcohol abuse, DUI</td>
<td>Alcohol</td>
</tr>
<tr>
<td>History of IVDA, transfusion prior to 1990</td>
<td>HCV</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Hemochromatosis, NAFLD</td>
</tr>
<tr>
<td>Components of Metabolic Syndrome</td>
<td>NAFLD</td>
</tr>
<tr>
<td>Medications, CAM therapy</td>
<td>Drug induced liver injury</td>
</tr>
<tr>
<td>Pruritis</td>
<td>PBC</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>PSC</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Hemochromatosis, HCV</td>
</tr>
</tbody>
</table>

Physical Clues

<table>
<thead>
<tr>
<th>Physical Exam Findings</th>
<th>Disease Correlates</th>
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</thead>
<tbody>
<tr>
<td>Spider angiomas</td>
<td>Cirrhosis</td>
</tr>
<tr>
<td>Palmar erythema</td>
<td>Cirrhosis</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>Portal hypertension</td>
</tr>
<tr>
<td>Jaundice</td>
<td>Cirrhosis, bilary obstruction, hemolysis, Gilbert’s</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>Hemochromatosis</td>
</tr>
<tr>
<td>Kayser-Fleisher rings</td>
<td>Wilson’s disease</td>
</tr>
<tr>
<td>Empysema/Lung disease</td>
<td>Alpha-1 antitrypsin deficiency</td>
</tr>
<tr>
<td>Ascites</td>
<td>Portal hypertension, cirrhosis</td>
</tr>
<tr>
<td>Asteatosis</td>
<td>Portal hypertension</td>
</tr>
<tr>
<td>Xanthelasmas</td>
<td>PBC</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Acute</th>
<th>Chronic</th>
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</thead>
<tbody>
<tr>
<td>Hepatitis A</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hepatitis E</td>
<td>+</td>
<td>(rare)</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Wilson Disease</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hemochromatosis</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Alpha-1 AT deficiency</td>
<td>(neonatal)</td>
<td>+</td>
</tr>
<tr>
<td>NAFLD</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Medication/Toxin</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

### Diagnosis of HBV

- **Acute**
  - HBsAg
  - HBc:
  -HBcAg
  - HBeAg
  - HBV DNA

- **Chronic**
  - (immune tolerant or active)
  - HBsAg
  - HBeAg
  - HBeAg+ or eAg-

- **Inactive Carrier**
  - HBsAg
  - HBeAg
  - eAb+

- **Immune**
  - HBsAg
  - HBeAg
  - HBcAb

- **Vaccinated**
  - HBsAb

### Hemochromatosis

- **LABS:** iron/TIBC, ferritin, genotype
- **Clinical suspicion**
  - Fatigue, arthralgia, diabetes mellitus, hyperpigmentation, impotence
- **Transferrin saturation and ferritin**
  - TS > 45%
  - Sensitivity 99%
  - Specificity 45%
- **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 (87%), SMA (87%)
  - ANA found in PBC, PSC, viral hepatitis, drug related hepatitis, NASH, DTDH
  - pANCA common
  - Hyperglobulinemia (high IgG)
- Type 2 AIH (young women)
  - Anti-LKM
  - 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
  - 20% heterozygotes
  - Slit-lamp KF rings Absent early
  - F(+) cholestatic disease
  - 24 hour urine >100 ug F(-) early
  - F(+) cholestatic disease
  - Hepatic copper >250 ug/g F(-) early
  - F(+) cholestatic disease
  - 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 Medications
  - Aspirin
  - Anti-Epileptic
  - Acute (antifungil)
  - Isoniazid
  - Metronidazole
  - Sertraline
  - Nortriptiline
  - Propylthiouracil
  - 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

<table>
<thead>
<tr>
<th>Agent</th>
<th>RR</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highly Lipophilic</td>
<td>1.58</td>
<td>0.81, 3.05</td>
</tr>
<tr>
<td>Mildly Lipophilic</td>
<td>3.54</td>
<td>1.72, 5.58</td>
</tr>
</tbody>
</table>

Argo et al Hepatology 2008;48:662

Incidence of Aminotransferase Elevation with Statin Use for Cardiovascular Disease

<table>
<thead>
<tr>
<th>Year</th>
<th>Agent</th>
<th>Multiple Incr of AST in %</th>
<th>Systolic (mm Hg)</th>
<th>Plasma (mg %)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>Lovastatin</td>
<td>Yes</td>
<td>49.383 (2.8)</td>
<td>21.140 (2.7)</td>
<td>47.192 (4.1)</td>
</tr>
<tr>
<td>2004</td>
<td>Simvastatin</td>
<td>No</td>
<td>38.221 (1.7)</td>
<td>30.444 (2.2)</td>
<td>27.207 (2.0)</td>
</tr>
</tbody>
</table>

Medications/Toxins

LABS: AMA, immunoglobulins

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)

PBC

Cholestatic Liver Disease

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBC</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PSC</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Obstructive Jaundice</td>
<td>+ (pain)</td>
<td>+</td>
</tr>
<tr>
<td>Medications/Toxins</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

PSC

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

Medicines that Cause Cholestatic

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

This table was adapted from de Heus et al. 2

References: 1. de Heus et al. 2. de Heus et al.
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

Alpha-Fetoprotein
- AFP is a marker of liver regeneration
- 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

HCV with Cirrhosis
- 2% HCC
- AFP > 20
  - Positive LR 5
  - Post-test probability = ~10%
- AFP < 20
  - Negative LR 0.5
  - Post-test Probability = 1%

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
  - Absorbed 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%
    - 4-5 >7%
    - >6 <2%
- Merion Hepatology 2003
- Malinchoc Hepatology 2003

Cirrhosis ≠ Transplant

CPT score

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<tr>
<th>Grade</th>
<th>Score</th>
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<tbody>
<tr>
<td>None</td>
<td>1 point</td>
</tr>
<tr>
<td>1-2</td>
<td>2 points</td>
</tr>
<tr>
<td>&gt;3</td>
<td>3 points</td>
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<table>
<thead>
<tr>
<th>Ascites</th>
<th>Score</th>
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<tbody>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Slight</td>
<td>1</td>
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<tr>
<td>Moderate or more</td>
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<table>
<thead>
<tr>
<th>Bilirubin</th>
<th>Score</th>
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<tbody>
<tr>
<td>&lt;1.5</td>
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<tr>
<td>1.5-3.5</td>
<td>1</td>
</tr>
<tr>
<td>&gt;3.5</td>
<td>2</td>
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<table>
<thead>
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<th>Albumin</th>
<th>Score</th>
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<tr>
<td>&gt;1.7</td>
<td>0</td>
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<tr>
<td>1.7-2.3</td>
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<tr>
<td>&gt;2.3</td>
<td>2</td>
</tr>
</tbody>
</table>

Score 0-6 Class A, 7-9 Class B, 10-11 Class C
Important Disease Associations

- 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

<table>
<thead>
<tr>
<th>Lab</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB</td>
<td>3.2</td>
<td>4.1</td>
<td>4.8</td>
</tr>
<tr>
<td>AST</td>
<td>12000</td>
<td>13000</td>
<td>9000</td>
</tr>
<tr>
<td>ALT</td>
<td>9000</td>
<td>10000</td>
<td>8500</td>
</tr>
<tr>
<td>INR</td>
<td>3.0</td>
<td>4.1</td>
<td>5.3</td>
</tr>
</tbody>
</table>

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