A, B, C’s of Elevated LFT’s

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Gastroenterology Care
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Clinical Use of Serum Enzymes in Liver Disease

- ALT – Alanine Amino Transferase
- AST – Aspartate Amino Transferase
- Alk P04 – Alkaline Phosphatase
- GGT – Gamma Glutamyl Transpeptidase

Financial Costs of Selective Serologic Tests for Assessing Hepatic Diseases

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Fiscal Charges</th>
<th>Medicaid/ Medicare</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT, AST, Alk P04, Bb</td>
<td>60-104</td>
<td>51</td>
</tr>
<tr>
<td>ALT</td>
<td>28-58</td>
<td>15</td>
</tr>
<tr>
<td>Bb</td>
<td>26-104</td>
<td>9</td>
</tr>
<tr>
<td>Protime</td>
<td>29-44</td>
<td>33</td>
</tr>
<tr>
<td>Albumin</td>
<td>27-49</td>
<td>8</td>
</tr>
<tr>
<td>CBC</td>
<td>41-82</td>
<td>31</td>
</tr>
<tr>
<td>GGT</td>
<td>28-65</td>
<td>40</td>
</tr>
<tr>
<td>AMA</td>
<td>88</td>
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</tr>
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</table>

Financial Costs (cont.)

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Charge 2016</th>
<th>Reimbursement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A IgM</td>
<td>79-111</td>
<td>6-56</td>
</tr>
<tr>
<td>Hepatitis B Surface Ag</td>
<td>55-58</td>
<td>14</td>
</tr>
<tr>
<td>Hepatitis C Antibody (Elisa)</td>
<td>92-104</td>
<td>18</td>
</tr>
<tr>
<td>Hepatitis C RNA Qualitative</td>
<td>250-276</td>
<td>442</td>
</tr>
<tr>
<td>Hepatitis C genotype</td>
<td>578-590</td>
<td>430</td>
</tr>
<tr>
<td>Hepatitis Screen</td>
<td>380</td>
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</table>

Financial Costs (cont.)

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Charge 2016</th>
<th>Reimbursement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron</td>
<td>29-57</td>
<td>55</td>
</tr>
<tr>
<td>Ferritin</td>
<td>69-120</td>
<td>90</td>
</tr>
<tr>
<td>ANA</td>
<td>58-113</td>
<td>66</td>
</tr>
<tr>
<td>Alpha-1 antitrypsin</td>
<td>83-99</td>
<td>89</td>
</tr>
<tr>
<td>Ceruloplasmin</td>
<td>65-78</td>
<td>65</td>
</tr>
<tr>
<td>Abd. Ultrasound</td>
<td>600</td>
<td>80</td>
</tr>
<tr>
<td>Liver Biopsy U/S (total)</td>
<td>1500</td>
<td>63-113</td>
</tr>
<tr>
<td>CT Scan Liver</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1,124 consecutive patients referred for chronic increase ALT’s

In 81 patients with no definable cause...
-Liver biopsy done

RESULTS:
1. Stenosis – 41 patients
2. Steatohepatitis – 26 patients
3. Fibrosis – 4 patients
4. Cirrhosis – 2 patients
5. “Normal biopsy” – 9 patients
19,877 Air Force Trainees
(*) all volunteered to donate blood

- Results:
  - 99 trainees (0.5%) had elevated ALT’s
    - causes found in only 12 patients
      1. Hepatitis B – 4
      2. Hepatitis C – 4
      3. Autoimmune hepatitis – 2
      4. Cholelithiasis – 1
      5. Appendicitis – 1

100 consecutive blood donors with elevated ALT levels

- Causes:
  1. 48% related to alcohol use
  2. 22% with fatty liver
  3. 17% had hepatitis C
  4. 4% with another identified problem
  5. 9% without specific diagnosis

Consideration of increased LFT’s (asymptomatic)

- Magnitude – (% elevation above normal)
- History and Physical examination
- The “Ratio”
- Trends with time
- Patient/Physician concern

Etiology of Severe ALT and AST Elevations: Greater than 15x normal

- Acute viral hepatitis (A-E, herpes)
- Medications/toxins (Acetaminophen)
- Ischemic hepatitis
- Autoimmune hepatitis
- Wilson’s disease
- Acute bile duct obstruction
- Acute Budd-Chiari syndrome
- Hepatic artery ligation
- HELLP Syndrome

Causes of Chronically Elevated Aminotransferase Levels

- Hepatic Causes:
  - Alcohol abuse
  - Medication
  - Chronic hepatitis B and C
  - Steatosis and nonalcoholic steatohepatitis
  - Autoimmune hepatitis
  - Hemochromatosis
  - Wilson’s disease (in patients ≤ 40 years old)
  - Alpha 1- antitrypsin deficiency
Causes of Chronically Elevated Aminotransferase Levels

• Nonhepatic causes:
  • Celiac sprue
  • Inherited disorders of muscle metabolism
  • Acquired muscle disease
  • Strenuous exercise
  • Thyroid disease

Elevated ALT and AST < 5 times normal

- History and Physical Examination: Discontinue hepatotoxic medications
- Confirm abnormality if an error is suspected
- Liver chemistries, PT, Albumin, CBC with platelets, Hepatitis A, B, and C Serologies
- **Fe, TIBC, Ferritin
- Consider ultrasound, ANA, anti-smooth muscle AB, ceruloplasmin, alpha 1-antitrypsin

Abnormal results
- Liver biopsy

Medications

• Antibiotics
  • Synthetic penicillins
  • Ciprofloxacin
  • Nitrofurantoin
  • Ketoconazole and fluconazole
  • Isoniazid

• Antiepileptic drugs
  • Phenytoin
  • Carbamezine
  • Amiodarone

Medications (cont.)

• Inhibitors of hydroxymethylglutaryl-coenzyme A reductase
  • Simvastatin
  • Pravastatin
  • Lovastatin
  • Atorvastatin

• Nonsteroidal anti-inflammatory drugs
• Sulfonylureas for hyperglycemia
  • Glipizide

Herbs and Homeopathic Treatments

• Chaparral
• Chinese Herbs
  • Ji bu huan
  • Ephedra (ma huang)
  • Gentian
  • Alchemilla (lady’s mantle)
  • Senna
  • Shark cartilage
  • Scutellaria (skullcap)

Table 3: Medications, Herbs, and Drugs or Substances of Abuse Reported to Cause Elevations in Liver-Enzyme Levels
Drugs and Substances of Abuse

- Anabolic steroids
- Cocaine
- 5-Methoxy-3, 4-methylenedioxyamphetamine (MDMA, "ecstasy")
- Phencyclidine ("angel dust")
- Glues and solvents
  - Glues containing toluene
  - Trichloroethylene, chloroform

Elevated ALT and AST < 5 times normal

- History and Physical Examination: Discontinue hepatotoxic medications
- Confirm abnormality if an error is suspected
- Liver chemistries, PT, Albumin, CBC with platelets, Hepatitis A, B, and C Serologies
- Fe, TIBC, Ferritin

Negative serology, asymptomatic patient without hepatic decompensation

Positive serology

- Positive Hepatitis A IgM serology
- Follow clinically, Serial Liver Chemistries
- Clinical improvement: Liver chemistries normal + 6 months
- Persistent Liver Chemistries: Abnormality + 6 months
- Liver biopsy (or ultrasound, volumetry, Fibriscan+)

Positive Hepatitis B or C Infection

- Observation
- Persistent ALT elevation, Increased Fe with phlebotomy
- Liver biopsy +/- phlebotomy

No iron supplements

Fe saturation < 45%, elevated Ferritin

Lifestyle Modification

- Discontinue alcohol
- Stop hepatotoxic medications
- Weight loss
- Diabetic control
- Repeat Liver chemistries
- Ultrasound and serologic evaluation: ANA, Anti-smooth muscle AB, Ceruloplasmin, Alpha 1 AT, Anti-gliadin, Anti-endomysial AB, TSH, Free T4, Free T3
Elevated Alk P04

- Hepatobiliary
  - Bile duct obstruction (stone, stricture, tumor)
  - Primary biliary cirrhosis
  - Medications
  - Infiltrating diseases of the liver
  - Hepatic metastasis
  - Hepatitis
  - Cirrhosis
  - Vanishing bile duct syndromes
  - Benign recurrent cholestasis

- Nonhepatic
  - Bone disease
  - Pregnancy
  - Chronic renal failure
  - Lymphoma and other malignancies
  - Congestive heart failure
  - Childhood growth
  - Infection/inflammation

Age & Sex-Related Upper Limits for Serum Alkaline Phosphatase

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Serum Concentration (IU/liter)</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>10</td>
<td>275</td>
</tr>
<tr>
<td>11</td>
<td>275</td>
</tr>
<tr>
<td>12</td>
<td>245</td>
</tr>
<tr>
<td>13</td>
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<td>20</td>
<td>215</td>
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<td>30</td>
<td>155</td>
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<tr>
<td>50</td>
<td>95</td>
</tr>
<tr>
<td>70</td>
<td>85</td>
</tr>
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</table>

Infiltrating Diseases of the Liver causing elevations of Alk P04

- Sarcoidosis
- Tuberculosis
- Fungal infection
- Other granulomatous diseases
- Amyloidosis
- Lymphoma
- Metastatic malignancy
- Hepatocellular carcinoma
Percutaneous liver biopsy (without ultrasound)

- Complications
  - Fatal complication (death)
  - Severe bleeding
  - Bile leakage
  - Pain (minor, major)
  - Other
  - Risk
    - Less than 1/2000
    - Less than 1/100
    - Less than 1/500
    - Rather common
    - (More rare than any previous complication)

Grading of disease activity in chronic hepatitis

<table>
<thead>
<tr>
<th>Grading Termology</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Semiquantitative</td>
</tr>
<tr>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>Minimal</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
</tr>
<tr>
<td>4</td>
<td>Severe</td>
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</tbody>
</table>

Staging of chronic hepatitis

<table>
<thead>
<tr>
<th>Staging termology</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>No fibrosis</td>
</tr>
<tr>
<td>1</td>
<td>Portal fibrosis</td>
</tr>
<tr>
<td>2</td>
<td>Periportal fibrosis</td>
</tr>
<tr>
<td>3</td>
<td>Septal fibrosis</td>
</tr>
<tr>
<td>4</td>
<td>Cirrhosis</td>
</tr>
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