Asymptomatic Elevated Liver Function Tests: Physiology, Chemistry, and Workup

James T. Sing, Jr., D.O., FACG, AGAF
Scott & White Clinic
Assistant Professor
Department of Internal Medicine
Division of Gastroenterology
Director, Endoscopy
Director, GI Oncology
Lecture Outline

- Introduction
- Interpretation of Abnormal Liver Chemistry Values
- Biological Basis of Liver Chemistries
- Initial Approach to the Evaluation of Abnormal Liver Chemistries Tests
- Evaluation of Abnormalities of the Serum ALT and AST Levels
- Evaluation of Abnormalities of the Serum Bilirubin and Alkaline Phosphatase Levels
- Serum Albumin and Prothrombin Time
Introduction

- Liver chemistry tests are commonly used for periodic health screening, blood banking, and insurance physicals and during hospitalization for medical, surgical, or psychiatric illnesses unrelated to hepatic disorders.

- Abnormal elevations of serum liver chemistries may occur in 1% to 4% of the asymptomatic population*

* Kundrotas et al, Dig Dis Sci 1993
Introduction

• Therefore, to provide high-quality, cost-effective health care, a rational approach for the appropriate evaluation of serum liver chemistries is essential.

• Interpretation of liver chemistries must be performed within the context of the patient’s risk factors for disease, symptoms, historical, and physical examination process.
Lecture Outline

• Introduction
• Interpretation of Abnormal Liver Chemistry Values
• Biological Basis of Liver Chemistries
• Initial Approach to the Evaluation of Abnormal Liver Chemistries Tests
• Evaluation of Abnormalities of the Serum ALT and AST Levels
• Evaluation of Abnormalities of the Serum Bilirubin and Alkaline Phosphatase Levels
• Serum Albumin and Prothrombin Time
Interpretation of Abnormal Liver Chemistry Values

- Normal laboratory values are defined as the mean of the distribution +/- 2 standard deviations of the "normal" population.
- By definition, 5% of normal patients will have abnormalities of any given test.
- The "normal" population may not be reflective of normal values for a given patient.

![Diagram showing the normal distribution with standard deviations and their corresponding percentages.]

- About 68% of the values fall within 1 standard deviation of the mean.
- About 95% of the values fall within 2 standard deviations of the mean.
- About 99.7% of the values fall within 3 standard deviations of the mean.
Interpretation of Abnormal Liver Chemistry Values

- All laboratory abnormalities must be interpreted within the clinical context of the patient
  - Alkaline phosphatase in pregnancy
  - Hepatic decompensation (ascites, encephalopathy, coagulopathy, and portal hypertension)
  - Lab error

- A normal liver chemistry test does not ensure that the patient is free of liver disease
Interpretation of Abnormal Liver Chemistry Values

- Hepatocellular Injury
  - AST and ALT abnormalities

- Cholestatic Pattern
  - Alkaline phosphatase and/or bilirubin abnormalities

- Overlapping Patterns (common)
Interpretation of Abnormal Liver Chemistry Values

• “Infiltrative” diseases of the hepatic parenchyma
  ✓ Elevated alkaline phosphatase with minimal or no elevation of serum ALT, AST, or bilirubin

• Hepatic synthetic function
  ✓ Albumin and prothrombin time (not specific for hepatic disease)
Lecture Outline

- Introduction
- Interpretation of Abnormal Liver Chemistry Values
  - Biological Basis of Liver Chemistries
- Initial Approach to the Evaluation of Abnormal Liver Chemistries Tests
- Evaluation of Abnormalities of the Serum ALT and AST Levels
- Evaluation of Abnormalities of the Serum Bilirubin and Alkaline Phosphatase Levels
- Serum Albumin and Prothrombin Time
Biological Basis of Liver Chemistries

- Do not effectively assess the actual function of the liver
- **AST** (aspartate aminotransferase) & **ALT** (alanine aminotransferase) are abundant hepatic enzymes that catalyze the transfer of amino groups to form the hepatic metabolites pyruvate and oxaloacetate
  - ALT found in the cytosol of the liver
  - Two AST isoenzymes are located in the cytosol and mitochondria
Biological Basis of Liver Chemistries

- ALT & AST are released from damaged hepatocytes into the blood after injury or death
  - AST is also abundantly expressed in several nonhepatic tissues (liver > heart > skeletal muscle > blood)
  - AST is cleared more rapidly than ALT
  - ALT is found in low concentrations in other tissues
    - Specific for hepatocellular injury but not absolute (myopathic diseases)
Biological Basis of Liver Chemistries

To secrete bilirubin into bile, unconjugated bilirubin must be taken up into the hepatocyte

Conjugated into the glucuronide form by the E.R. enzyme bilirubin UDP-glucuronyltransferase (bilirubin-UGT)

Water-soluble bilirubin glucuronides must be secreted across the canalicular membrane into bile
Biological Basis of Liver Chemistries

- Bilirubin-UGT is expressed shortly after birth
- Highly expressed and preserved even in severe liver disease and cirrhosis
- Diminished expression of this enzyme can lead to Gilbert’s syndrome
  ✓ Benign, unconjugated hyperbilirubinemia (< 4 mg/dl)
  ✓ 5% of the normal population
Biological Basis of Liver Chemistries

• Unconjugated hyperbilirubinemia (other causes)
  ✓ Hemolysis
  ✓ Crigler-Najjar syndrome (rare genetic disease)

• Conjugated hyperbilirubinemia [(after neonatal period) impaired secretion into bile]
  ✓ Extrahepatic obstruction
  ✓ Intrahepatic cholestasis
  ✓ Hepatitis
  ✓ Cirrhosis
Causes of an Isolated Unconjugated Hyperbilirubinemia

- Gilbert’s syndrome
- Neonatal jaundice
- Hemolysis
- Blood transfusion (hemolysis)
- Resorption of a large hematoma
- Shunt hyperbilirubinemia
- Crigler-Najjar syndrome
- Ineffective erythropoiesis
Biological Basis of Liver Chemistries

- Alkaline Phosphatase family of enzymes are zinc metalloenzymes that are present in nearly all tissues
  - Localized to the microvilli of the bile canaliculus
  - Primarily liver and bone isoenzymes
  - Intestinal enzymes ~ 20% of total activity
Biological Basis of Liver Chemistries

- Elevated caused by
  - Cholestatic or infiltrative diseases of the liver (PBC, amyloidosis, etc.)
  - Obstruction of the biliary system
  - Bone diseases (Paget’s disease)
  - Medications (ex. tegretol)
  - Tumors of hepatic and nonhepatic origin
Biological Basis of Liver Chemistries

- **Pregnancy**
  - Alkaline phosphatase activity begins to rise by the late first trimester (placental isoenzymes)
  - May reach levels of twice normal by term
  - May remain elevated several weeks after delivery
An important clinical issue is whether the alkaline phosphatase abnormality is of hepatobiliary or nonhepatic origin

- Liver = heat stable, Bone = heat labile
- Considerable inaccuracy
- γ- Glutamyltransferase (GGT) activity can be used to confirm the liver-specific origin
  - Highest levels are found in cholestatic conditions (PBC & PSC)
  - Not found in bone
Lecture Outline

- Introduction
- Interpretation of Abnormal Liver Chemistry Values
- Biological Basis of Liver Chemistries
- Initial Approach to the Evaluation of Abnormal Liver Chemistries Tests
  - Evaluation of Abnormalities of the Serum ALT and AST Levels
  - Evaluation of Abnormalities of the Serum Bilirubin and Alkaline Phosphatase Levels
- Serum Albumin and Prothrombin Time
Initial Approach to the Elevation of Abnormal Liver Chemistries Tests

- Asymptomatic elevation of one or more liver chemistry test, we must decide what initial additional evaluation, if any, is clinically indicated?
  - Findings of the history and physical exam
  - Data are lacking on the cost-effectiveness of testing these individuals and long-term prospective studies to define the natural history of the potential liver disease
Initial Approach to the Elevation of Abnormal Liver Chemistries Tests

- Study of 19,877 presumably healthy Air Force recruits*
  - 99 (0.5%) had confirmed ALT elevations
  - 12% had identifiable causes
    - HBV-4, HCV-4, Autoimmune-2, Cholelithiasis-1, GI infection-1
  - Suggest that the majority of asymptomatic individuals may not have significant liver disease ?????

Initial Approach to the Elevation of Abnormal Liver Chemistries Tests

- Scandinavian study of 151 consecutive patients who were referred for mild to moderate elevation of serum aminotransferase levels (42-300 U/L) for > 6 months and who had liver biopsy*
  
  - Identifiable cause of liver disease was more common
    - HCV 15.3%, Alcoholic liver disease 8%, Autoimmune hepatitis, hepatitis and PBC in 1.3%, and non-alcoholic steatohepatitis and/or steatosis 42%
    - 36 (24%) had chronic hepatitis of unknown origin

Initial Approach to the Elevation of Abnormal Liver Chemistries Tests

- The incidence of hepatic disease in selective high-risk populations is, not surprisingly, significantly higher than in screening populations.

- Thus, a decision to observe an asymptomatic patient closely and repeat a liver chemistry test, versus proceeding with an additional evaluation, must be made in the context of clinical scenario.
Initial Approach to the Elevation of Abnormal Liver Chemistries Tests

- All liver chemistry abnormalities are not indicative of progressive chronic liver disease
- Must also appreciate the prompt diagnosis and therapy of many common liver disease can prevent progression to end-stage liver disease
Lecture Outline

- Introduction
- Interpretation of Abnormal Liver Chemistry Values
- Biological Basis of Liver Chemistries
- Initial Approach to the Evaluation of Abnormal Liver Chemistries Tests
  - Evaluation of Abnormalities of the Serum ALT and AST Levels
  - Evaluation of Abnormalities of the Serum Bilirubin and Alkaline Phosphatase Levels
- Serum Albumin and Prothrombin Time
Evaluation of Abnormalities of the Serum ALT and AST Levels

- Both the magnitude and relative level of elevation of the ALT and AST may be useful in diagnosing possible liver disease
  - ALT and AST elevations < 5x normal, with either a predominant ALT or AST elevation
  - ALT and AST elevations > 15x normal
  - Intermediate range elevations can be caused by numerous disease processes that fall into both of the above categories and thus are less useful for limiting the differential diagnosis
Evaluation of Abnormalities of the Serum ALT and AST Levels

- Detailed history and physical to determine potential causes
  - Lifestyle modifications (alcohol, wt. loss, etc..)
  - Discontinuation of medications
- The pt. should be evaluated initially for common causes of liver injury
Etiology of Mild ALT or AST Elevations:
Less Than 5 Times Normal

Hepatic: ALT-predominant
  Chronic hepatitis C
  Chronic hepatitis B
  Acute viral hepatitis (A–E, EBV, CMV)
  Steatosis/steatohepatitis
  Hemochromatosis
  Medications/toxins
  Autoimmune hepatitis
  Alpha\textsubscript{1}-antitrypsin deficiency
  Wilson’s disease
  Celiac disease

Hepatic: AST-predominant
  Alcohol-related liver injury
  Steatosis/steatohepatitis
  Cirrhosis

Nonhepatic
  Hemolysis
  Myopathy
  Thyroid disease
  Strenuous exercise
  Macro-AST
Etiology of Mild ALT and AST Elevations < 5x ULN (ALT Predominant)

- Chronic viral hepatitis remains one of the most common causes of abnormal liver chemistries
- Hepatitis C virus affecting nearly 2% of American population
  - Need to question IVDA, intranasal drug abuse, blood transfusion, exposure to unsterile needles (piercing, tattoo, etc..), sexual exposure to an infected individual
Etiology of Mild ALT and AST Elevations < 5x ULN (ALT Predominant)

- Hepatitis B virus significant cause worldwide
  - Prevalence of HBsAg-carrier rate
    - 0.1%-0.2% in USA, Australia, and Western Europe
    - 10% to 20% in Southeast Asia and Sub-Saharan Africa
- Most medications, although some more frequently than others
## Medications, Herbs, and Toxins That Can Cause Elevations of Aminotransferases

<table>
<thead>
<tr>
<th>Medications and drugs</th>
<th>Herbs/Alternative medications</th>
<th>Illicit drugs</th>
<th>Toxins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Chaparral leaf</td>
<td>Anabolic steroids</td>
<td>Carbon tetrachloride</td>
</tr>
<tr>
<td>Alpha-methyldopa</td>
<td>Ephedra</td>
<td>Cocaine</td>
<td>Chloroform</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>Gentian</td>
<td>Ecstasy (MDMA)</td>
<td>Dimethylformamide</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Germander</td>
<td>Phencyclidine (PCP)</td>
<td>Hydrazine</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Jin Bu Huan</td>
<td></td>
<td>Hydrochlorofluorocarbons</td>
</tr>
<tr>
<td>Dantrolene</td>
<td>Senna, Kavakava</td>
<td></td>
<td>2-Nitropropane</td>
</tr>
<tr>
<td>Disulfiram</td>
<td>Scutellaria (skullcap)</td>
<td></td>
<td>Trichloroethylene</td>
</tr>
<tr>
<td>Etretinate</td>
<td></td>
<td></td>
<td>Toluene</td>
</tr>
<tr>
<td>Fluconazole</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glyburide</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Halothane</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heparin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HMG-Co A reductase inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketoconazole</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Labetolol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicotinic acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenytoin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propylthiouricil</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protease inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulfonamides</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trazadone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Troglidazone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valproic acid</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Etiology of Mild ALT and AST Elevations < 5x ULN (ALT Predominant)

- Over-the-counter medications and herbal preparations, can lead to liver failure
- **Take an accurate medication history!!**
- Hepatotoxicity often occurs within 1-2 months when a medication is initiated, this is not universally true
- All nonessential medications discontinued and liver chemistries monitored
- With many medications, liver enzyme elevations are mild and essential medications must be continued
Etiology of Mild ALT and AST Elevations < 5x ULN (ALT Predominant)

• If liver enzyme elevations continue to rise, the suspect medication should be stopped because liver failure potentially can occur.
Etiology of Mild ALT and AST Elevations < 5x ULN (ALT Predominant)

- Hepatic steatosis/steatohepatitis (fatty infiltration of the liver with or without inflammation) may be the most common cause of mild liver enzyme elevations
  - Nonalcoholic steatohepatitis (NASH) is asymptomatic in 48% to 100% of patients
  - No available blood test to confirm diagnosis
  - Diagnosis of exclusion (viral hepatitis and etc..)
  - Imaging tests can be suggestive
  - If liver chemistry remains elevated > 6 to 12 months, or if the ALT remains elevated despite successful lifestyle modifications, liver biopsy should be considered
Etiology of Mild ALT and AST Elevations
< 5x ULN (ALT Predominant)

- Hereditary Hemochromatosis (HH) is one of the most common genetic diseases (1:250)
  - Considered with mildly elevated ALT or AST levels
  - HFE-gene (C282Y and H63D)
  - Autosomal recessive inheritance
  - Symptoms of weakness, fatigue, abdominal pain, arthralgias, and impotence
  - Extrahepatic manifestations like: CHF, DM, and darkening of skin pigmentation can occur late in the disease
  - Transferrin saturation > 45% (screening test)
Etiology of Mild ALT and AST Elevations
< 5x ULN (ALT Predominant)

- Autoimmune Hepatitis
  - Female gender predisposition
  - Prevalence of 1:6k to 1:7k
  - Often associated with thyroid disease and other autoimmune disorders
  - (+) anti-nuclear antibody, anti-smooth muscle antibody
  - Elevated serum IgG fraction
  - Liver biopsy is recommended
Etiology of Mild ALT and AST Elevations < 5x ULN (ALT Predominant)

- ALT elevations of unknown origin
  - Wilson’s disease (autosomal recessive)
    - Prevalence 1:30,000 to 1:300,000
    - Check ceruloplasmin level and if (+) 24 hour urinary copper level, slit-lamp exam for Kayser-Fleischer rings, and liver biopsy for copper measurement
  - A-1-antitrypsin deficiency (autosomal recessive)
    - Prevalence 1:1500 to 1:7,600
    - Check protease inhibitor phenotype analysis (Pi-type)
    - Liver biopsy
  - Celiac Disease
Etiology of Mild ALT or AST Elevations: Less Than 5 Times Normal

Hepatic: ALT-predominant
  Chronic hepatitis C
  Chronic hepatitis B
  Acute viral hepatitis (A–E, EBV, CMV)
Steatosis/steatohepatitis
Hemochromatosis
Medications/toxins
Autoimmune hepatitis
Alpha_{1}-antitrypsin deficiency
Wilson’s disease
Celiac disease
Hepatic: AST-predominant
  Alcohol-related liver injury
  Steatosis/steatohepatitis
  Cirrhosis
Nonhepatic
  Hemolysis
  Myopathy
  Thyroid disease
  Strenuous exercise
  Macro-AST

Don’t forget about these players!!
<table>
<thead>
<tr>
<th>Virologic test</th>
<th>Usual clinical implication of a positive test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A–IgM</td>
<td>Positive in acute hepatitis A</td>
</tr>
<tr>
<td>Hepatitis A–IgG</td>
<td>Positive in response to previous hepatitis A infection or vaccination</td>
</tr>
<tr>
<td>Hepatitis B surface antigen</td>
<td>Positive during active hepatitis B infection</td>
</tr>
<tr>
<td>Hepatitis B surface antibody</td>
<td>Positive in response to previous hepatitis B infection or vaccination</td>
</tr>
<tr>
<td>Hepatitis B core antibody–IgM</td>
<td>Positive during active hepatitis B infection</td>
</tr>
<tr>
<td>Hepatitis B core antibody–IgG</td>
<td>Positive in response to current or prior hepatitis B infection</td>
</tr>
<tr>
<td>HBV-DNA</td>
<td>Positive during active hepatitis B infection</td>
</tr>
<tr>
<td>Hepatitis B e antigen</td>
<td>Positive tests indicates replicative state of wild-type hepatitis B infection</td>
</tr>
<tr>
<td>Hepatitis B e antibody</td>
<td>Positive after replicative state of wild-type hepatitis B infection</td>
</tr>
<tr>
<td>HCV-antibody ELISA</td>
<td>Positive during or after hepatitis C infection</td>
</tr>
<tr>
<td>HCV-RIBA</td>
<td>Positive during or after hepatitis C infection</td>
</tr>
<tr>
<td>HCV-RNA</td>
<td>Positive during hepatitis C infection</td>
</tr>
</tbody>
</table>

ELISA, enzyme-linked immunosorbent assay.
Etiology of Mild ALT and AST Elevations < 5x ULN (AST Predominant)

- Alcohol abuse
  - Thorough history of quantity and length of time consumed
- Alcohol-related liver injury
  - Hepatic steatosis 9% to 100%
  - Hepatitis 10% to 35%
  - Cirrhosis 8% to 20%
  - Alcoholic hepatitis commonly AST:ALT ratio of 2:1
    - AST rarely exceeds 300IU/dL
- If higher enzyme levels, additional cause of liver injury (viral hepatitis, acetaminophen, etc..)
Etiology of Mild ALT and AST Elevations < 5x ULN (AST Predominant)

- AST elevations often predominate in patients with cirrhosis
- DDx (Non-alcoholic steatohepatitis & drug-induced)
- AST levels may be reduced in renal failure patients*
- Nonhepatic diseases can present with mild elevations of AST
  - Hemolysis
  - Myopathy (creatine phosphokinase)

Etiology of Mild ALT or AST Elevations: Less Than 5 Times Normal

Hepatic: ALT-predominant
- Chronic hepatitis C
- Chronic hepatitis B
- Acute viral hepatitis (A–E, EBV, CMV)
- Steatosis/steatohepatitis
- Hemochromatosis
- Medications/toxins
- Autoimmune hepatitis
- Alpha₁-antitrypsin deficiency
- Wilson’s disease
- Celiac disease

Hepatic: AST-predominant
- Alcohol-related liver injury
- Steatosis/steatohepatitis
- Cirrhosis

Nonhepatic
- Hemolysis
- Myopathy
- Thyroid disease
- Strenuous exercise
- Macro-AST
The differential diagnosis of moderately elevated liver aminotransferases (5-15 times the upper limits of normal) encompass a wide range of hepatic diseases (mild or severe aminotransferase elevations), and ALT and AST elevations in this range may therefore be less useful in determining likely causes of liver disease.
Etiology of Severe ALT and AST Elevations > 15x ULN

- Relatively limited
  - Marked hepatocellular injury or necrosis
  - Drug-induced hepatotoxicity
    - OTC, Acetaminophen esp. with chronic alcohol consumption
  - Primary hepatotrophic hepatitis viruses (A-E)
    - Initial HCV antibody testing may be negative during acute viral hepatitis C

Etiology of Severe ALT and AST Elevations: Greater Than 15 Times Normal

- Acute viral hepatitis (A–E, herpes)
- Medications/toxins
- Ischemic hepatitis
- Autoimmune hepatitis
- Wilson’s disease
- Acute bile duct obstruction
- Acute Budd-Chiari syndrome
- Hepatic artery ligation
Etiology of Severe ALT and AST Elevations > 15x ULN

- Hepatitis E is acquired by contaminated food or water in endemic areas
  - Can present with fulminant hepatic failure in pregnant females
- Ischemic hepatitis causes marked elevations in liver enzymes
  - Hypotension, sepsis, cardiac arrhythmia, myocardial infarction, and hemorrhage
Lecture Outline

- Introduction
- Interpretation of Abnormal Liver Chemistry Values
- Biological Basis of Liver Chemistries
- Initial Approach to the Evaluation of Abnormal Liver Chemistries Tests
- Evaluation of Abnormalities of the Serum ALT and AST Levels
  - Evaluation of Abnormalities of the Serum Bilirubin and Alkaline Phosphatase Levels
- Serum Albumin and Prothrombin Time
Conjugated Hyperbilirubinemia and Elevated Hepatic Alkaline Phosphatase

• Cholestatic conditions (ex. PBC & PSC)
  ✓ Bilirubin elevations and jaundice develop late in the natural history and may indicate impending hepatic failure or malignancy (hepatocellular carcinoma or cholangiocarcinoma)

• Conjugated hyperbilirubinemia
  ✓ Hepatocellular diseases
  ✓ Biliary obstruction
  ✓ Toxins
  ✓ Drugs
## Causes of Conjugated Hyperbilirubinemia

- Bile duct obstruction
- Hepatitis
- Cirrhosis
- Medications/toxins
- Primary biliary cirrhosis
- Primary sclerosing cholangitis
- Sepsis
- Total parenteral nutrition
- Intrahepatic cholestasis of pregnancy
- Benign recurrent cholestasis
- Vanishing bile duct syndromes
- Dubin-Johnson syndrome
- Rotor syndrome

---

**Toxin**
Conjugated Hyperbilirubinemia and Elevated Hepatic Alkaline Phosphatase

- Isolated hepatic alkaline phosphatase elevations may be the sole abnormality in PBC or other cholestatic diseases, or with infiltrative diseases of the liver
Ciprofloxacin should be added to this group

<table>
<thead>
<tr>
<th>Medications That Can Cause Elevations of the Serum Bilirubin or Alkaline Phosphatase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anabolic steroids</td>
</tr>
<tr>
<td>Allopurinol</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
</tr>
<tr>
<td>Captopril</td>
</tr>
<tr>
<td>Carbamazepine</td>
</tr>
<tr>
<td>Chlorpropamide</td>
</tr>
<tr>
<td>Cyproheptadine.</td>
</tr>
<tr>
<td>Diltiazem</td>
</tr>
<tr>
<td>Erythromycin</td>
</tr>
<tr>
<td>Estrogens</td>
</tr>
<tr>
<td>Floxuridine</td>
</tr>
<tr>
<td>Flucloxacillin</td>
</tr>
<tr>
<td>Fluphenazine</td>
</tr>
<tr>
<td>Gold salts</td>
</tr>
<tr>
<td>Imipramine</td>
</tr>
<tr>
<td>Indinivir</td>
</tr>
<tr>
<td>Iprindole</td>
</tr>
<tr>
<td>Nevirapine</td>
</tr>
<tr>
<td>Methyltestosterone</td>
</tr>
<tr>
<td>Methylenedioxymethamphetamine</td>
</tr>
<tr>
<td>Oxaprozin</td>
</tr>
<tr>
<td>Pizotyline</td>
</tr>
<tr>
<td>Quinidine</td>
</tr>
<tr>
<td>Tolbutamide</td>
</tr>
<tr>
<td>Total parenteral hyperalimentation</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
</tr>
</tbody>
</table>
Causes of Elevated Serum Alkaline Phosphatase

Hepatobiliary
- Bile duct obstruction
- Primary biliary cirrhosis
- Primary sclerosing cholangitis
- Medications
- Infiltrating diseases of the liver
- Hepatic metastasis

Hepatitis
Cirrhosis
Vanishing bile duct syndromes
Benign recurrent cholestatic

Nonhepatic
- Bone disease
- Pregnancy
- Chronic renal failure
- Lymphoma and other malignancies
- Congestive heart failure
- Childhood growth
- Infection/inflammation
Infiltrating Diseases of the Liver That Can Cause Elevations of the Serum Alkaline Phosphatase

- Sarcoidosis
- Tuberculosis
- Fungal infection
- Other granulomatous diseases
- Amyloidosis
- Lymphoma
- Metastatic malignancy
- Hepatocellular carcinoma
Lecture Outline

• Introduction
• Interpretation of Abnormal Liver Chemistry Values
• Biological Basis of Liver Chemistries
• Initial Approach to the Evaluation of Abnormal Liver Chemistries Tests
• Evaluation of Abnormalities of the Serum ALT and AST Levels
• Evaluation of Abnormalities of the Serum Bilirubin and Alkaline Phosphatase Levels
  • Serum Albumin and Prothrombin Time
Serum Albumin and Prothrombin Time

- The liver synthesizes both albumin and many of the blood coagulation factors that are required to be in adequate concentrations in order for the prothrombin time to be normal
  - Poor nutritional status
  - Severe illness
  - Nephrosis
  - Malabsorption
Serum Albumin and Prothrombin Time

- In the absence of other nonhepatic etiologies, serum albumin and prothrombin time can be useful in assaying hepatic synthetic function
  - Album half-life 19 – 21 days
  - Coagulation factors half-life < day
  - Tests can be used in tandem to assess both acute and chronic components of hepatic function or impairment
Serum Albumin and Prothrombin Time

• The prothrombin time may be a better indicator of coagulation in liver disease than the INR

• ALT, AST, and alkaline phosphatase are not true indicators of hepatic function

• Hepatic function assessment
  ✓ Serum albumin
  ✓ Prothrombin time
  ✓ Physical exam (encephalopathy + coagulopathy = acute liver failure)
  ✓ Use in the context of abnormal liver chemistries
Thank You!!