

## Interpretation of Abnormal Liver Injury Tests

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## Interpretation of Abnormal Liver Injury Tests

- Clinical manifestations of liver disease:
  - Fatigue, anorexia, malaise, weight loss, fevers, fetor hepaticus, spider angiomas, palmar erythema, jaundice, pruritis, xanthomas, testicular atrophy, gynecomastia, RUQ pain, GI bleeding, ascites, hepatosplenomegaly, encephalopathy

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## Interpretation of Abnormal Liver Injury Tests

- Liver Injury Tests:
  - Aminotransferases (AST/ALT)
  - Alkaline Phosphatase
  - Gamma-glutamyl Transpeptidase (GGT)
  - Bilirubin
  - Total Protein/Albumin/Globulin
  - Prothrombin Time (INR)

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## Interpretation of Abnormal Liver Injury Tests

- Liver Injury Tests commonly used as Liver Function Tests (LFT's)
- Not a direct measure of liver function
- May be abnormal in the healthy liver
- May be normal in the diseased liver (cirrhosis)

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## Abnormal Liver Injury Tests

- Air Force Recruit Study
  - 99/19877 (0.5%) had abnormal LIT's
    - 12/99 had a specific cause found
    - 87/99 had no specific diagnosis
  - Dig. Dis. Sci. 1993, p. 2145.

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## Interpretation of Abnormal Liver Injury Tests

- Epidemiology of Abnormal LIT's:
  - 249 blood donors with abnormal LIT's
    - Alcoholic liver disease, NAFLD (NASH), HCV
    - 2%-8% had no specific diagnosis
  - Ann. Int. Med. 1991, p.882.

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## Interpretation of Abnormal Liver Injury Tests

- Epidemiology of Abnormal LIT's:
  - Liver Biopsy Studies
    - 81/1124 biospies in abnormal LIT's
    - 84% has steatosis/steatohepatitis
    - 6 had fibrosis/cirrhosis
    - 8 had normal histology
  - Am. J. Gastro: 1999, 94: p. 3010.

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## Interpretation of Abnormal Liver Injury Tests

- Epidemiology of Abnormal LIT's:
  - European Study
    - 151 pts. With abnormal LIT's > 6 months had a liver biopsy performed
      - Chronic HCV – 15.3%
      - NASH (NAFLD) – 45.2%
      - Chronic hepatitis – 24%
      - AIH/PBC – 1.5%
      - Alpha-1 antitrypsin deficiency – 0.7%
  - Scand. J. Gastro: 1999; p.85.

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## Interpretation of Abnormal Liver Injury Tests

- In the majority of patients, non-invasive testing will suggest the diagnosis
- In the majority of patients, the diagnoses will be: alcoholic liver disease, steatosis, steatohepatitis
- Most of these study were done before the HCV testing era

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## Interpretation of Abnormal Liver Injury Tests

- Evaluation of the pt. with abnormal LIT's:
  - Detailed history
  - Accurate physical examination
  - Laboratory testing
  - Pattern of the abnormal IIT's
  - Isolated hyperbilirubinemia??

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## Interpretation of Abnormal Liver Injury Tests

- History
  - Medication (prescription/OTC's/illicit drugs/herbal preparations)
  - ETOH use (CAGE questions where indicated)
  - Bloos tranfusions?/tattoos?/travel?
  - Occupation, past/present
  - Family history

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## Interpretation of Abnormal Liver Injury Tests

- Physical Examination:
  - Stigmata of chronic liver disease
  - Muscle wasting/testicular atrophy
  - Hepato-splenomegaly
  - Pleural effusions
  - Ascites

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## Interpretation of Abnormal Liver Injury Tests

- Patterns of abnormal LIT's:
  - Hepatocellular: AST/ALT (levels/ratio)
  - Cholestatic: Alkaline Phosphatase, GGT, Direct Bilirubin
  - Mixed

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## Interpretation of Abnormal Liver Injury Tests

- Liver enzymes:
  - ALT: cytosol (liver, muscle)
  - AST: cytosol/mitochondria (liver, heart, skeletal muscle, blood cells)
  - Alk. Phos: microvilli of bile canaliculus (bone, intestine kidney, placenta)
  - GGTP: membrane of cells (liver, kidney, pancreas, intestine, prostate)

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## Interpretation of Liver Injury Tests

- Hepatocellular causes of abnormal LIT's:
  - Chronic viral hepatitis
  - Hemochromatosis, Wilson's, alpha-1 antitrypsin deficiency
  - Autoimmune hepatitis
  - Celiac Disease
  - NAFLD/steatohepatitis
  - ETOH related liver diseases

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## Interpretation of Liver Injury Tests

- Non-hepatic causes of abnormal LIT's:
  - Hemolysis
  - Myopathies
  - Thyroid disease
  - Strenuous exercise

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## Interpretation of Abnormal Liver Injury Tests

- Viral Hepatitis:
  - HBV/HCV positive serology
  - Viral load can be determined (copies/ml)
  - AST/ALT >1000 IU/l indicates acute hepatitis or acute toxicity such as acetaminophen
  - AST/ALT >2000 IU/l –fulminant failure
  - AST/ALT may be normal in advanced cirrhosis

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## Interpretation of Abnormal Liver Injury Tests

- Cholestatic causes of abnormal LIT's:
  - PBC/PSC
  - Drugs
  - Viral hepatitis
  - Extra-hepatic biliary obstruction
  - Infiltrative liver disease (high AP)
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  - TPN
  - Familial cholestasis

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## Interpretation of Abnormal Liver Injury Tests

- Cholestatic LIT's in Biliary Obstruction:
  - AST/ALT - 1-5x nl
  - Alk. Phos. - 2-20x nl
  - Bilirubin - 1-30x nl
  - Pro-time (INR) - prolonged

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## Interpretation of Abnormal Liver Injury Tests

- Role of Liver Biopsy:
  - Diagnostic and prognostic information
  - Safe as an out-patient procedure
  - Complications - 0.1% - 0.3%
    - Bleeding/pneumothorax/bile peritonitis
  - Mortality: 9/100,000
  - Transjugular biopsy

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## Interpretation of Abnormal Liver Injury Tests

- Frequently encountered clinical problems:
  - Asymptomatic ALT/AST elevation
    - common problem, frequently sent from screened blood donors
    - elevation of bilirubin and AP increases likelihood of liver disease
    - Far East/Egypt/Africa: HBV, schisto, malaria
    - USA: CAH, steatosis, ETOH, drugs, metabolic

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## Interpretation of Abnormal Liver Injury Tests

- Approach to pt with asymptomatic elevation of aminotransferases:
  - Evaluation guided by clinical history, physical examination, and pattern of LIT's
  - Focus on medication (OTC/Rx), ETOH use, occupational exposure, risk factors for hepatitis, family history of liver disease
  - Focus on treatable etiologies: viral, Cu, Fe

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## Interpretation of Abnormal Liver Injury Tests

- Cholestatic liver disease:
  - Differentiating intra vs extra hepatic cholestasis can be difficult at times.
  - Medical vs surgical cholestasis can be difficult to differentiate from routine biochemical tests and clinical history/physical examination
  - Indirect tests: CT, US
  - Direct tests: ERCP, PTC, Liver biopsy

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## Interpretation of Abnormal Liver Injury Tests

- Isolated hyperbilirubinemia
- Unconjugated:
  - Gilbert's syndrome
  - Hemolysis
- Conjugated:
  - Dubin-Johnson syndrome
  - Rotor syndrome
- Extra-hepatic causes

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## Interpretation of Abnormal Liver Injury Tests

- Summary:
  - Take a *detailed* history that includes all risks for hepatic disease.
  - Perform an *accurate* physical examination
  - Order appropriate laboratory
  - Perform indicated imaging studies
  - Consider liver biopsy if definitive diagnosis can not be established from non-invasive testing

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