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Assessment of Hepatic Function

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Disclosure

- No real or potential conflict of interest to disclose.
- No off-label, experimental or investigational use of drugs or devices will be presented.

Objectives

- At the end of this presentation, the participant will be able to:
  - Identify the appropriate use of laboratory testing as part of the evaluation process of the person with or at risk for hepatic dysfunction.

Objectives (continued)

- At the end of this presentation, the participant will be able to: (cont.)
  - Discuss the clinical utility of commonly ordered hepatic laboratory tests such as hepatic enzymes, albumin, INR, bilirubin, and others, as part of the differential diagnosis process.

References

Found within and at End of Presentation
The Liver

- Largest solid internal organ
- Critical to drug metabolism

Multiple Hepatic Roles

- Glucose homeostasis
  - Low BS in liver disease, heavy alcohol use, w/fasting
- 19- yo in ED at 6 AM
  - “My blood sugar is too low.”
  - Awoke at 5 AM feeling dizzy, thirsty
  - BS= 55 mg/dL (3.05 mmol/L) as checked by mom who has T2DM

Multiple Roles

Synthesis of Plasma Proteins

- Albumin
  - Level low in chronic liver disease, as well as severe protein malnutrition
  - Maintenance of colloid osmotic pressure
  - Exhibits effect on vascular permeability
  - Binds, transports drugs and other substances
  - Free radical scavenging
  - Role in acid-base balance

Low Albumin as a Result of Hepatic Dysfunction

Image source: James Heilman, MD, author; CC BY-SA 3.0
https://en.wikipedia.org/wiki/Hypoalbuminemia

Multiple Roles

Synthesis of Plasma Proteins (continued)

- Prothrombin
  - Glycoprotein (carbohydrate-protein compound) that is an essential component of blood-clotting mechanism
  - Transformed into thrombin by clotting factor X

Multiple Roles

- Lipoprotein synthesis
  - Substrate for sex hormones
- Bile acid production
  - LDL synthesis
- Vitamin B₁₂, A, D, E, K storage
  - Water- and fat-soluble vitamins
Multiple Roles (continued)

- Detoxification and excretion
  - Exogenous toxins
    - Including medications
  - Endogenous substances
    - By-products of metabolism

Multiple Roles (continued)

- Biotransformation or metabolism of drugs
  - Primarily by way of the cytochrome P-450 enzyme
  - Fat- to water-soluble conversion for renal elimination and to be in a form that can get to the drug site of action
  - Conversion of prodrug to active metabolite

Substances Needed for Hepatic Detoxification Actions

- Sulfate
- Glucuronic acid
- Acetate
- Glycine
- Glutathione

What question are you trying to answer when you order "LFTs?"

Do "LFTs" really exist?
Better terms- Liver tests, liver chemistries


Hepatocellular Injury

- Defined
  - Disproportionate elevation of AST and ALT levels compared with alkaline phosphatase levels

Hepatic testing for what?

- Is there hepatocellular damage?
  - Elevation of alanine aminotransferase (ALT, formerly known as SGPT), aspartate aminotransferase (AST, formerly known as SGOT)
    - Enzymes held within the liver, increase in amount in circulation when liver cells injured
- How severe is the injury?
ACG Practice Guideline
What is the lab normal value?
• “A true healthy normal ALT level ranges from 29 to 33 units/L for males, 19 to 25 units/L for females and levels above this should be assessed.”
• Most labs=0–40 units/L as norm

Ethnic-specific Lab Norms
• African ancestry
  – ~15% higher AST
  – ~10% higher Cr
• Exercisers
  – Higher AST, CK, ? higher Cr
  – Source: http://www.kidney.org/professionals/kld/pdf/12-10-4004_KBB_FAQs_AboutGFR-1.pdf

Why?
• Greater muscle mass
  – Creatinine derived from muscle creatine
    • Production=Renal excretion
  – AST
    • Fraction in skeletal muscle
    • Other fractions=Myocardium, liver

AST vs. ALT
• AST/SGOT
  \( T_{1/2}=12–22 \text{ h} \)
  • With hepatic injury
    • Also found in skeletal muscle, RBC
      – Rapid rise
    • With recovery
      – Quick to resolve

• ALT/SGPT
  \( T_{1/2}=37–57 \text{ h} \)
  • More liver-specific
    • Intrahepatic injury
    • With hepatic injury
      – Slower peak
    • With recovery
      – Slower clearance

AST/ALT Ratios
• Chronic hepatitis B, C
  – ALT >AST
  – AST=67 units/L
    • NL 0–40
  – ALT=82 units/L
    • NL 0–40

• Alcohol-related
  – In absence of other hepatic problems
    • Often AST >ALT
    – AST=83 units/L
    • NL 0–40
    – ALT=50 units/L
    • NL 0–40

Alcohol Consumption and Elevated Hepatic Enzymes
• Threshold for women
  – More than 140 g alcohol per week
    – >10 drinks per week
  – 12 oz (0.35 L) beer, 5 oz (0.15 L) wine, 1.5 oz (0.04 L) 80-proof liquor= Approx. 14 g

• Threshold for men
  – More than 210 g alcohol per week
    – >15 drinks per week

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Kenneth – 10-year Hx
Substance Use Disorder (Alcohol)
AST:ALT >1
• AST=83 units/L
  – NL 0–40
• ALT=50 units/L
  – NL 0–40
• H/H=15 g/dL and 45%
  (150 g/L and 0.45 proportion)
• MCV=105 fL
  – NL 80–96 fL
• HDL=58 mg/dL
  (1.5 mmol/L)
• LDL=120 mg/dL
  (3.1 mmol/L)
• TG=320 mg/dL
  (3.6 mmol/L)
  – <150 mg/dL
  (1.7 mmol/L)

Samuel
AST:ALT Ratio ≤1
ALT:AST Ratio ≥1
• IDU hx
• No use × 5 y
• AST=25 units/L
• ALT=88 units/L
• + anti-HCV with positive HCV viral load
• Hepatic biopsy = Inflammatory, fibrosis

Enrique
• 32-year-old w/chronic hepatitis C
  • Baseline ALT=78 units/L
  – Contracts hepatitis A
    • AST=778 units/L (0–40)
    • ALT=1,300 units/L (0–40)
    – ALT > AST
  • Why drop in AST/ALT?
    – Drop possible when few remaining hepatic cells to damage

Enrique (continued)
• Condition deteriorates
  – AST=68 units/L (0–40)
  – ALT=132 units/L (0–40)
  • ALT > AST
• Why drop in AST/ALT?
  – Drop possible when few remaining hepatic cells to damage

Evaluation of Hepatocellular Injury
• Health history, physical exam
  – OTC meds
    • Frequency, amount
  – Herbal products
    • In particular, kava, unregulated products
  – Alcohol intake

With persistently unexplained elevated AST/ALT...
• Consider screening.
  – Autoimmune hepatitis
    • 70% women, age 15–40 y, other autoimmune conditions such as T1DM, vitiligo, RA, SLE
  – Next step testing
    • ANA, ASMA, and globulin level
With persistently unexplained elevated AST/ALT...
(continued)
- Consider screening. (cont.)
  - Hereditary hemochromatosis
    - Iron overload, often seen with T2DM, OA, thyroid disorder, usually European ancestry
  - Next step testing
    - Iron level, transferrin saturation, serum ferritin, genetic testing if positive

• Consider screening. (cont.)
  - Hereditary hemochromatosis
    - Iron overload, often seen with T2DM, OA, thyroid disorder, usually European ancestry
  - Next step testing
    - Iron level, transferrin saturation, serum ferritin, genetic testing if positive

With elevated AST/ALT...
• Screen for alpha-1 antitrypsin deficiency.
  - Seen with European ancestry w/ personal and family early onset COPD, severe asthma NAFLD
  - Panniculitis
    - Inflammation of panniculus, layer of fatty and fibrous tissue just beneath skin’s outer layers

Suspected Alpha-1 Antitrypsin Deficiency
• Next step testing
  - Quantitative alpha-1 anti-trypsin
  - Genotype testing for PiZZ mutation

True or false?
In autoimmune hepatitis, hepatic enzymes are typically modestly elevated, for example, AST 127 units/L, ALT 198 units/L (0–40 units/L).

Evaluation of Alkaline Phosphatase
• Is there cholestatic injury?
  - Disproportionate elevation of alkaline phosphatase level as compared with AST and ALT levels
### Cholestasis/Cholestatic Injury

- **Defined**
  - Decrease in bile flow due to impaired secretion by hepatocytes or to obstruction of bile flow through intra- or extrahepatic bile ducts

### Alkaline Phosphatase (ALP)

- **Rises in response to hepatocyte injury, cholestasis, damage to biliary tree**
- **T_{1/2} = Approx. 7 d**
  - Slow increase post injury, slow clearance post injury resolution

### True or false?

**ALP is physiologically produced by placenta and is therefore elevated during pregnancy.**

**During childhood, normally growing bone releases ALP.**

### Alkaline Phosphatase (ALP) (continued)

- **Present in all human cells**
  - Concentrated in liver, bile duct, kidney, bone, placenta

### GGT

**Gamma-glutamyl Transferase**

- **Enzyme found in liver, kidney**
  - Rises in response to hepatocyte injury, cholestasis, damage to biliary tree
- **In hepatic disease**
  - Increase parallels ALP

### GGT Clinical Utility

- **Major clinical utility**
  - To exclude ALP elevation as bone source
    - Chronic elevation possible with phenytoin, barbiturate use
- **T_{1/2} = 26 days**
  - Not as helpful a marker of alcohol use as once thought
    - Might detect remote rather than recent ingestion
43-yr Woman w/RUQ Tenderness + Murphy’s Sign

- AST = 25 units/L  
  0–40
- ALT = 45 units/L  
  0–40
- ALP = 355 units/L  
  0–125
- GGT = 245 units/L  
  0–45
- UA = + bilirubin

Kenneth ≥6 Alcoholic Drinks per Day × 10 Y

- AST = 83 units/L  
  0–40
- ALT = 50 units/L  
  0–40
- GGT = 100 units/L  
  7–33
- ALP = 170 units/L  
  0–125
- MCV = 104 fl
- TG = 320 mg/dL  
  (3.6 mmol/L)
- HDL = 48 mg/dL  
  (1.2 mmol/L)
- LDL = 136 mg/dL  
  (3.5 mmol/L)

Hepatic testing for what? Do LFTs exist?

- Can the liver synthesize plasma protein?  
  - Albumin (longer T½, 20 days)
  - Prothrombin (shorter T½, 60 hours)
  - Markers of hepatocellular function
- How is the liver’s excretion function?  
  - Bilirubin

Kenneth 10 Years Later

- Continues to drink heavily
  - Develops stigmata of alcohol abuse
  - Painful breast enlargement
  - Testicular atrophy
  - Erectile dysfunction

- INR = 1.6 g/L (22.2 mmol/L)
  - Not on warfarin
- Albumin = 3.2 g/dL (3.5–5.5) (32 g/L [35–55])
  - Reasonable nutrition
Kenneth 10 years later (continued)

- Blood alcohol level (BAL)=355 mg/dL (77.1 mmol/L)
  - BAL >300 mg/dL (76 mmol/L) can be fatal in person without alcohol tolerance or dependence.
  - BAL 80–100 mg/dL (17.4–21.7 mmol/L)= DWI=~4 drinks/hour for 70-kg adult
  - 1 drink=12 oz (0.35 L) of beer, 5 oz (0.15 L) of wine, 1.5 oz (0.04 L) of 80-proof liquor

With Sobriety

- AST/ALT
  - WNL in ~3 mo, if no underlying hepatic disease
- GGT
  - WNL in 1–2 wks
- TG WNL
  - In ~1 mo
- MCV
  - WNL in 2–4 mo

When measuring serum bilirubin, you are asking the question...

- Is the liver capable of...
  - Uptake?
  - Conjugation?
  - Excretion?
- Heme degradation product
  - 85–90% from hemoglobin
  - 10–15% from myoglobin

Bilirubin Production

- Reticuloendothelial cells
  - Take in haptoglobin
  - Haptoglobin=Protein that binds with hemoglobin from aged RBCs
  - Serum haptoglobin drops in hemolysis.
  - Remove Fe from hemoglobin for recycling.

Bilirubin

- Released into circulation
  - Binds to albumin, transported to liver
- Hepatocytes detach bilirubin from albumin
  - Water-soluble, AKA conjugated or direct

Bilirubin (continued)

- Conjugated bilirubin loosely attached to albumin
  - Easily detaches in kidney
  - Gives urine its yellow color
  - When bilirubin is found in urine, direct or water-soluble form
Bilirubin (continued)

- Remaining substances then degraded to bilirubin
  - Unconjugated or indirect form
  - Not water-soluble
- Excess occurs when liver cannot keep up with conversion demand.

Image source: James Heilman MD, AuPhD, CC BY 3.0; https://en.wikipedia.org/wiki/Jaundice#/media/File:Jaundice08.jpg

Bilirubin (continued)

- Conjugated bilirubin not excreted
  - Reabsorbed by small intestine
- Converted to urobilinogen by bacterial action in the gut
  - Reabsorbed into circulation
  - Excess amount in urine

High Bilirubin

- Caramel colored, carbonated sweetened soft drink (Coca-Cola™) urine
- ? Increase free drug w/highly-protein bound meds
  - ≥80% protein binding including many older AEDs, warfarin

Hanna Reasonable Nutrition, End-stage Liver Disease, Cirrhosis

- Albumin=2.6 g/dL (3.4–4.8)
  - 26 g/L (34–48)
- INR=2.8
  - No warfarin use
- Alk phos=229 units/L
  - 39–117

Model for End-stage Liver Disease (MELD) Calculator

- What is it?
  - Scoring system for assessing severity of chronic liver disease
- How is it used?
  - Determining prognosis
  - Prioritizing for liver transplantation

Hanna (continued)

- Cr=1.4 mg/dL (123.8 μmol/L)
  - eGFR=49 mL/min/1.73 m², stage 3A CKD
- Bili direct=1.33 mg/dL (0–0.3)
  - 22.7 μmol/L (0–5.1)
  - Conjugated or water-soluble form
- Total protein=10 g/dL (5.9–8.4)
  - 100 g/L (59–84)
  - Often elevated in chronic liver disease

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• MELD=22
  - Model for end-stage liver disease
  - Average MELD score for person undergoing liver transplant=20
  - Higher score, the more severe liver damage, greater need for transplant, if a candidate
    - Source: https://liverfoundation.org/for-patients/about-the-liver/the-progression-of-liver-disease/liver-transplant/?gclid=Cj0KCQjwtLT1BRD9ARIsAMH3BtVY9M0t6wK4wU]

MELD Score
Assessing Severity of Liver Disease

- Average MELD score for person undergoing liver transplant=20
- Higher score, the more severe liver damage, greater need for transplant, if a candidate

MELD Scores and 90-day Mortality

<table>
<thead>
<tr>
<th>Score Range</th>
<th>Mortality</th>
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<tbody>
<tr>
<td>≥40 or more</td>
<td>71.3% mortality</td>
</tr>
<tr>
<td>30–39</td>
<td>52.6% mortality</td>
</tr>
<tr>
<td>20–29</td>
<td>19.6% mortality</td>
</tr>
<tr>
<td>10–19</td>
<td>6.0% mortality</td>
</tr>
<tr>
<td>&lt;9</td>
<td>1.9% mortality</td>
</tr>
</tbody>
</table>

Child-Pugh Scoring System

- Designed to predict mortality in patients with cirrhosis
- Occasional mention in medication prescribing

Child-Pugh Scoring System

<table>
<thead>
<tr>
<th>Total serum bilirubin</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 mg/dL (&lt;34.2 μmol/L)</td>
<td>1 point</td>
</tr>
<tr>
<td>2–3 mg/dL (34.2–51.3 μmol/L)</td>
<td>2 points</td>
</tr>
<tr>
<td>&gt;3 mg/dL (&gt;51.3 μmol/L)</td>
<td>3 points</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Serum albumin</th>
<th>Points</th>
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</thead>
<tbody>
<tr>
<td>&gt;3.5 g/dL (&gt;35 g/L)</td>
<td>1 point</td>
</tr>
<tr>
<td>2.8–3.5 g/dL (28–35 g/L)</td>
<td>2 points</td>
</tr>
<tr>
<td>&lt;2.8 g/dL (&lt;28 g/L)</td>
<td>3 points</td>
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</table>

<table>
<thead>
<tr>
<th>INR</th>
<th>Points</th>
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<tbody>
<tr>
<td>&lt;1.70</td>
<td>1 point</td>
</tr>
<tr>
<td>1.71 to 2.20</td>
<td>2 points</td>
</tr>
<tr>
<td>&gt;2.20</td>
<td>3 points</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ascites</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>No ascites</td>
<td>1 point</td>
</tr>
<tr>
<td>Ascites controlled medically</td>
<td>2 points</td>
</tr>
<tr>
<td>Ascites poorly controlled</td>
<td>3 points</td>
</tr>
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<table>
<thead>
<tr>
<th>Encephalopathy</th>
<th>Points</th>
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<td>No encephalopathy</td>
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<tr>
<td>Encephalopathy poorly controlled</td>
<td>3 points</td>
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Hanna’s Score=11

<table>
<thead>
<tr>
<th>Points</th>
<th>Class</th>
<th>One-year survival</th>
<th>Two-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>5–6</td>
<td>A</td>
<td>100%</td>
<td>85%</td>
</tr>
<tr>
<td>7–9</td>
<td>B</td>
<td>80%</td>
<td>60%</td>
</tr>
<tr>
<td>10–15</td>
<td>C</td>
<td>45%</td>
<td>35%</td>
</tr>
</tbody>
</table>
Non-hepatic Reasons for GGT Elevation

- Renal failure
- Recent myocardial infarction
- Pancreatic disease
- Diabetes mellitus, esp. with fatty liver disease

Case Study

- 55-year-old female
  - Recently started taking an herbal product bought online, "I heard it was good for your nerves."
  - Has been taking herb for 3–4 months
  - Presents with malaise, RUQ abd pain for p 2–3 weeks

What was the herb?

- AST 2054 units/L
  - NL 0–40
- ALT 3056 units/L
  - NL 0–40
- Alk. phos. 186 units/L
  - NL 43–122
- Total bili. 26.2 mg/dL
  - NL 0.2–1.3
  - 448.02 µmol/L (0.342–22.23)
- Direct bili. 17.1 mg/dL
  - NL 0–0.4
  - 292.4 µmol/L (0–6.84)
- Albumin 2.7 g/dL
  - NL 3.4–5.0
  - 27 g/L (34–50)
- INR 1.93
  - NL 0.79–1.21

Case Study

- 51-year-old male
  - Drinks approximately 6-mixed drinks per day, each with 1.5 oz (44.4 mL) whiskey, pattern × 6+ years
  - Now presents with a 2-week history mild RUQ tenderness and fatigue
  - Recently "pulled my back out" at work and is taking "pain medicine" multiple times a day

What was the pain medication?

- AST 21687 units/L
  - NL 0–40
- ALT 9501 units/L
  - NL 0–40
- Alk. phos. 112 units/L
  - NL 43–122
- Total bili. 7.0 mg/dL
  - NL 0.2–1.3
  - 119.7 µmol/L (3.4–22.23)
- Direct bili. 4.1 mg/dL
  - NL 0–0.4
  - 70.11 µmol/L (0–6.84)
- Albumin 3.5 g/dL
  - NL 3.4–5.0
  - 35 g/L (34–50)
- INR 2.88
  - NL 0.79–1.21

Resources for Hepatitis A, B, C

https://www.cdc.gov/hepatitis/hbv/profresourcesb.htm
Includes Guidelines for Populations Most at Risk and Testing
Testing for Viral Hepatitis – Acute vs. Chronic Infection

- Hepatitis A?
- Hepatitis B?
- Hepatitis C?

Match the viral hepatitis type with the most common method of acquisition. An option can only be used once.

<table>
<thead>
<tr>
<th>Acquisition method</th>
<th>Hepatitis type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecal-contaminated food or water</td>
<td>A. Hepatitis A</td>
</tr>
<tr>
<td>Injection drug use</td>
<td>B. Hepatitis B</td>
</tr>
<tr>
<td>Sexual contact</td>
<td>C. Hepatitis C</td>
</tr>
</tbody>
</table>

Hepatitis A

- Incubation period
  - Between 2 and 6 weeks with an average of 28 days
- Onset of symptoms
  - Approx. 70% of adults symptomatic
  - At end of incubation period
  - Usually last from less than 2 months to as long as 6 months

Hepatitis type: A

Q and A

- About ___ of children with acute hepatitis A do not have symptoms during the illness.
  - A. 20%
  - B. 40%
  - C. 60%
  - D. 90%

Clinical Criteria per CDC – Hepatitis A

- Defined
  - An acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, abdominal pain, or dark urine)
  - And

Laboratory Criteria per CDC – Hepatitis A

- Jaundice or elevated total bilirubin levels ≥3.0 mg/dL (51.3 μmol/L)
  - Or
- Elevated ALT levels >200 units/L
  - And
- Absence of a more likely diagnosis
Laboratory Criteria per CDC – Hepatitis A (continued)

- Required
  - Immunoglobulin M (IgM) antibody to hepatitis A virus (anti-HAV) positive
    - IgM=M=Miserable, acute disease marker
  - Or
  - Nucleic acid amplification test (NAAT), PCR or genotyping) for hepatitis A virus RNA
  - Viremic stage of illness

Hepatitis B

- Incubation period
  - 1.5 to 6 months (average 4 months)

- Acute phase
  - 1st 6 months after infection
  - Clinical presentation from asymptomatic to mild to fulminant illness
    - Source: https://emedicine.medscape.com/article/177632-clinical

Common Presentation of Symptomatic Acute Hepatitis B

- Anorexia
- Nausea, vomiting
- Low-grade fever
- Myalgia
- Fatigability
- Aversion to food and cigarettes
- Right upper quadrant and epigastric pain
  - Intermittent, mild to moderate

Q and A

Preventing Development of Chronic Hepatitis B

- When babies become infected at birth or during infancy, what percentage will go on to develop chronic hepatitis B?
  - A. 10%
  - B. 25%
  - C. 50%
  - D. 90%

- When otherwise healthy adults become infected with hepatitis B, what percentage go on to develop chronic hepatitis B?
  - A. 10%
  - B. 25%
  - C. 50%
  - D. 90%
Q and A
Duration of Viral Carriage with Acute Hepatitis B

- The duration of carriage of the hepatitis B virus in the person who develops acute hepatitis B without development of chronic hepatitis B can be up to:
  A. 2 months.
  B. 4 months.
  C. 6 months.
  D. 8 months.

Hepatitis B Serology
- Hepatitis B surface antigen (HBsAg)
  - Ag=Always growing
  - Surface protein on HBV
  - Detected in serum during acute or chronic HBV infection
  - Indicates
    - Presence of hepatitis B virus

Acute vs. Chronic Hepatitis B – Clinical Presentation

- ALT=3510 units/L
  - NL=0–40
- AST=2243 units/L
  - NL=0–40
- Fatigue
- Myalgia
- RUQ abd tenderness

- ALT=98 units/L
  - NL=0–40
- AST=55 units/L
  - NL=0–40
- No complaints
- Abd exam unremarkable

Hepatitis B Serology (continued)
- Hepatitis B e antigen (HBeAg)
  - E=Extra growing
  - Presence=HBV replicating
  - Usually w high levels of HBV

Serologic Markers in Acute Hepatitis B

- IgM antibody to hepatitis B core antigen
  - IgM anti-HBc
  - Usually indicates acute (<6 months) as opposed to chronic hepatitis B infection
Serologic Markers in Acute Hepatitis B

Hepatitis B Serology (continued)

- **Total hepatitis B core antibody**
  - **Anti-HBc**
    - Appears at onset of symptoms in acute hepatitis B infection
    - Persists for life
    - **Anti-HBc** = Previous or ongoing infection with HBV

Serologic Markers in Acute Hepatitis B

Hepatitis B Serology (continued)

- **Hepatitis B e antibody**
  - **HBeAb or anti-HBe**
    - Spontaneous conversion from “e” antigen to “e” antibody
    - “e” seroconversion = Predictor of long-term clearance of HBV in patients undergoing antiviral therapy or in naturally acquired infection

Serologic Markers in Acute Hepatitis B

Hepatitis B Serology (continued)

- **Hepatitis B surface antibody**
  - **Anti-HBs**
  - **Anti-HBs** = Recovery from/immunity to HBV infection
  - Immunity whether from vaccine or wild/naturally acquired infection

Assessment of Hepatic Function
Hepatitis C

- Incubation period
  - 14–184 days
  - Average=14–84 days
- Testing
  - Anti HCV
  - HCV RNA

True or false?
About 80% of people are without symptoms during initial or acute HCV infection.

Between 15–45% of people with acute HCV infection will spontaneously clear the virus.

True or false?
All adults age ≥18 years should be encouraged to be tested for hepatitis C.

Women who are pregnant should be encouraged to be HCV tested with each pregnancy.

Adults born from 1945 through 1965 have a relative low rate of HCV.

Newly Reported Chronic HCV By the Ages

- Millennials
  - Birth years=1981–1996
    - 36.5% of newly reported chronic hepatitis C infections
- Generation X
  - Birth years=1966–1976
    - 23.1% of newly reported chronic hepatitis C infections

- Baby boomers
  - Birth years=1946–1965
    - 36.3% of newly reported chronic hepatitis C infections

Source: https://www.cdc.gov/hepatitis/hcv/cfaq.htm#B1
Mariana
68-yo Woman New to Your Practice

• Med Hx
  – T2DM, dyslipidemia, HTN, depression, inactivity
• Current medications
  – HD HCTZ (≥25 mg/d), SU, ASA
  – Told she could not take a statin due to “liver problems”

• Habits
  – “Never” drinks alcohol, denies tobacco or other substances, now or past, “not allowed in my church”
  – No regular physical activity

• BP=158/98 mm Hg
• Random glucose=240 mg/dL (13.3 mmol/L)
• BMI=36 kg/m²
• Waist=35” (88.9 cm)
• Acanthosis nigricans

• ALT=93 units/L (0–40)
  – Most hepatic specific
• AST=55 units/L (0–40)
  – Liver, myocardium, skeletal muscle
• ALT:AST ratio >1

• GGT=32 units/L (0–45)
  – Rise parallels ALP
• ALP=185 units/L (0–125)
  – Marker of cholestasis (impaired bile flow) with many false positives
  • Also found in intestine, bone, placenta

• Neg testing for other sources of acute or chronic hepatitis
• UA=30 mg/dL (1+) protein (10.7 mmol/L)
  – Microalbuminuria for 5–10 y prior to macroproteinuria
Mariana (continued)

- HgA1C=8.8% (0.088 proportion)
  - 90–120 d, best for last 4–6 wks
- Cr=1.0 mg/dL (88.4 µmol/L)
  - If African ancestry=Stage 2 CKD,
    eGFR=67 mL/min/1.73 m²
  - If "other" ancestry=Stage 3A CKD,
    eGFR=58 mL/min/1.73 m²

Mariana (continued)

- TC=220 mg/dL (5.7 mmol/L)
- HDL=33 mg/dL (0.85 mmol/L)
- LDL=178 mg/dL (4.6 mmol/L)
  - Candidate for moderate-to-high intensity statin therapy with LDL reduction ≥33–50%
- TG=295 mg/dL (3.3 mmol/L)
  - Goal ≤150 mg/dL (1.7 mmol/L)

Steatohepatitis
Fatty Deposition within the Hepatocyte

- Nonalcoholic steatohepatitis (NASH)
  - Hepatocellular enzymes elevated
- Other reasons for elevation ruled out
  - Infectious hepatitis (A, B, C, etc.)
  - Autoimmune
  - Alcohol- or drug-induced

NASH – Established Risk Factors

- Obesity
- Type 2 DM
- Dyslipidemia
- Metabolic syndrome
  - Source: https://www.gastrojournal.org/article/S0016-5085(12)00160-6/pdf

NASH Risk Factors – Hepatic Part of Metabolic Syndrome

- PCOS
- Obstructive apnea
- Hypothyroidism
- Hypopituitarism
- Hypogonadism

True or false?
NASH ranks as the second most common reason for liver transplant in the United States and will likely surpass hepatitis C in the coming years as the most common.
Nonalcoholic Steatohepatitis
Alcohol Abuse Excluded

- Initial findings
  - Elevated aminotransferase
  - Exclusion of viral, metabolic, other causes
- Histologic diagnosis
  - Liver biopsy findings similar to alcoholic liver disease including Mallory bodies, ballooning hepatocyte degeneration

NAFLD Lab Findings

- AST, ALT
  - Seldom > 3 × ULN
- ALT:AST ratio
  - Usually > 1
- ALP, GGT
  - Up to 2–3 × ULN in less than ½

What is the difference?

- ALT=78 units/L
- AST=40 units/L
- GGT=32 units/L
- ALP=155 units/L
- MCV=82 fL
- ALT=50 units/L
- AST=90 units/L
- GGT=103 units/L
- ALP=225 units/L
- MCV=104 fL

Differentiating Between NAFLD and NASH

- NAFLD fibrosis score for Mariana
  - Age=68 y
  - BMI=36 kg/m²
  - Hyperglycemia=Yes
  - Platelet count=140,000 mm³
  - Albumin=3.6 g/dL (36 g/L)
  - AST=55 mg/dL
  - ALT=98 mg/dL
NAFLD Score

- [http://nafldscore.com](http://nafldscore.com)
  - Score <-1.455: 90% sensitivity and 60% specificity to exclude advanced fibrosis
  - Marianna=-1,814.297=Indeterminate score
  - Score >0.676: 67% sensitivity and 97% specificity to predict advanced fibrosis

Which of the following is most consistent with the hepatic enzyme profile of a person with nonalcoholic fatty liver disease?

- A. AST=678 units/L, ALT=990 units/L
- B. AST=98 units/L, ALT=210 units/L
- C. AST=45 units/L, ALT=88 units/L
- D. AST=1208 units/L, ALT=560 units/L

Conclusion

References

References (continued)


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The Liver

- Largest solid internal organ
- Critical to drug metabolism

Multiple Roles
Synthesis of Plasma Proteins (continued)

- Prothrombin
  - Glycoprotein (carbohydrate-protein compound) that is an essential component of blood-clotting mechanism
  - Transformed into thrombin by clotting factor X
### Child-Pugh Scoring System

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### Hepatitis A Serology

![Hepatitis A Serology Diagram](Image)
Serologic Markers in Acute Hepatitis B


Serologic Pattern of Acute HCV Infection with Progression to Chronic Infection