Challenging Case Studies in Laboratory Diagnosis: A Focus on WBC and Hepatic Testing

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Objectives

• Identify the appropriate use of laboratory testing as part of the clinical evaluation process.
• Discuss the clinical utility of commonly ordered WBC and hepatic laboratory parameters.

Objectives (continued)

• Identify the appropriate use of laboratory testing as part of the evaluation process of the person with a variety of health problems, especially clinically significant infection and hepatic dysfunction.

References


Leukocytes

• Heterogeneous group of cells
  – Arise from single stem cell
  • Differentiation occurs during stem cell maturation
Primary Action

- Phagocytosis
  - By the granulocytes and monocytes
- Formation of antibodies
  - By the B-cell lymphocytes
- Delaying hypersensitivity response
  - By the T-cell lymphocytes

WBC Cell Line

<table>
<thead>
<tr>
<th>WBC</th>
<th>Point of action</th>
<th>In health, % of differential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil</td>
<td>Bacteria, fungi</td>
<td>~60%</td>
</tr>
<tr>
<td>Lymphocyte</td>
<td>Virus</td>
<td>~30%</td>
</tr>
<tr>
<td>Monocyte</td>
<td>Debris</td>
<td>~6%</td>
</tr>
<tr>
<td>Eosinophil</td>
<td>Allergens, parasites</td>
<td>~3%</td>
</tr>
<tr>
<td>Basophils</td>
<td>Unknown, likely immunologic</td>
<td>1%</td>
</tr>
</tbody>
</table>

Leukocytosis

- Leukocytosis refers to an increase in the total number of WBCs from any cause

Leukocytosis: Defining the Reason

- Increase in certain cell or combination
  - Neutrophil count (neutrophilia)
    - Most common reason for leukocytosis
  - Lymphocyte count (lymphocytosis)
  - Monocyte count (monocytosis)
  - Eosinophilic count (eosinophilia)
  - Basophilic count (basophilia)
  - Immature cells (blasts)

Leukocyte Forms

- Granulocytes
  - All with granules in cytoplasm
    - Neutrophils
      - AKA polys, segs
    - Eosinophils
    - Basophils
Neutrophils (AKA polys, segs)

- Life span
  - 10-hours in circulation
  - 4-5 days in tissue
- Bacterial infection
- Highly motile

Neutrophils, Bands

Neutrophil Forms That Do Not Belong in Circulation

Young forms that belong in the granulocyte pool and are only called up when the normal responses are exhausted.

- Myelocytes
- Metamyelocytes

Lymphocyte

- 2nd most numerous WBC
- Mature into T and B cells in lymphoid tissue
- First cell to act against virally infected tissue
- 20-40% of total WBC
- Lymphocytosis
  - ALC >4000 mm3 in adult
  - ALC >7200 mm3 in child

Leon

- 62 year-old man w/intermittent fever, congested cough, and an ache in the side of his chest
  - PE-T=101.8°F (38.8°C), AP=110, RR=24
  - Dullness to percussion at ® base, crackles, tubular breath sounds

Leon’s CBC with WBC Differential Results

- H & H=15 g/50%
- WBC=13,550 mm3
- Neutrophils=80%
  - ANC=10,840
- Bands=4%
  - ABC=542
- Lymphs=11%
  - ALC=1489
Samantha
• 16 year-old with 3-d history lower abdominal pain accompanied by purulent vaginal discharge
• + cervical motion tenderness

Samantha’s CBC w/WBC with Differential Results
• H & H=12.5 g/38%
• WBC=13,550 mm3 (6,000-10,000 mm3)
• Neutrophils=75% (50-70%)
  –ANC=10,012, toxic granulation
• Bands=7% (0-4%)
  –ABC=934
• Lymphs=11% (30-40%)
  –ALC=1485

Neutrophil Morphology
• Seen in inflammation, infection
  –Toxic granulation
  • Coarse black or purple granules
  –Dohle bodies
  • Small blue cytoplasmic inclusions

Degenerative Left Shift
What if Samantha Did Not Come in for a Visit?
• H & H=11g/37%
• WBC=5,800 mm3
• Neuts=22% (AMNC=1232)
• Bands=42% (ABC= 2436)
• Lymphs=34% (ALC=2204)
• Monos=2% (AMC=116)
• Platelets=600,000 mm3

Thomas
• 15 year-old man
  –CC: headache and intermittent fever X 3 days
• Physical exam
  –Photo/phonophobia
  –Nuchal rigidity

Thomas (continued)
• WBC=5,300 mm3 (4.0-10.8)
• Neuts=25% (40-70%)
  –ANC=1300
• Bands=7% (2-6%)
  –ANC=364
• Lymphs=64% (20-42%)
  –ALC=3396
Atypical (Reactive) Lymph...

- Atypical/reactive lymphs=14%
  - Cells become enlarged as a result of antigen stimulation
  - Most often noted in viral infection, less often in drug reactions

22 Year-old Well Woman on Anticonvulsant

- Hg=9.1 g (91 g/L)
- Hct=28% (.28 proportion)
- RBC=2.8 million (4.2-5.4)
- Platelets=75 K (130-400K)

22 Year-old Well Woman on Anticonvulsant (continued)

- MCHC=34.8 G/dL (31-37) (348 g/L {310-370})
  - NL size
- MCV=81 fl (81-99)
  - NL size
- RDW=12.1% (11.5-15%) (.121 proportion {115-.15})
  - New cells similar size to old cells
- Retics=1.8% (.018 proportion)

Select Anticonvulsant Therapy: Recommended Monitoring

- CBC with WBC and platelets
  - With carbamazepine use, due to bone marrow suppression potential
    - Baseline, monthly for 2 or 3 months, then at least every two years

Neutropenia: Etiology

- Drug effects
  - PTU
  - Phenytoin
  - Carbamazepine
  - Cancer chemotherapeutic agents
  - Immunosuppressive agents
Neutropenia: Etiology (continued)

- Nutritional deficiencies
  - Vitamin B12
  - Folate
  - Copper deficiency
- Hormonal disorders
  - Thyrotoxicosis
  - Addison disease
  - Acromegaly

Agranulocytosis

- Increased susceptibility to serious bacterial infection
  - Klebsiella pneumoniae
  - Escherichia coli
  - Pseudomonas aeruginosa
  - Staphylococcus aureus

Hepatic testing for what? Do LFTs exist?

- Is there hepatocellular damage?
  - Alanine aminotransferase (ALT, formerly known as SGPT), aspartate aminotransferase (AST, formerly known as SGOT)
- How severe is the injury?

- Is there cholestasis?
  - \( \gamma \)-Glutamyltransferase (GGT)
  - Alkaline phosphatase (ALP)

Hepatic testing for what? Do LFTs exist? (continued)

- How is the liver’s excretion function?
  - Bilirubin
    - Indirect bilirubin (unconjugated)
      - Not water soluble, not found in urine
    - Direct bilirubin (conjugated)
      - Water soluble, is found in urine

- Can the liver synthesize plasma protein?
  - Albumin (longer T½, 19-21 days)
  - Prothrombin (shorter T½, 24-60 h)
- Perhaps best test of how liver actually functions
What is the difference?
Alcohol Abuse vs. Non Alcoholic Steatohepatitis (NASH) Patient A

- ALT = 78 U/L  
  -(0-40)  
- AST = 40 U/L  
  -(0-40)  
- ALT > AST

- GGT = 32 U/L  
  -(0-45)  
- ALP = 155 U/L  
  -(0-125)  
- MCV = 82 fl  
  -(80-96)

What is the difference?
Alcohol abuse vs. Non Alcoholic Steatohepatitis (NASH) Patient B

- ALT = 50 U/L  
- AST = 90 U/L  
  - AST > ALT

- GGT = 103 U/L  
- ALP = 225 U/L  
- MCV = 104 fl  
  -(80-125)

References

  - Available at store.fhea.com

Drug-induced Hepatic Injury

- Most frequent reason for drug to be withdrawn from market  
- Accounts for >50% cases of acute liver failure in US  
  - >75% of cases of idiosyncratic drug reactions result in liver transplantation or death

- Gender issues  
  - In one study, women accounted for 79% of reactions due to acetaminophen, 73% of idiosyncratic drug reactions  
- Elders at particular risk of death from drug-induced hepatic injury
Hepatotoxic Drug Reactions

• Usual response with moderate-to-severe injury
  – Resembles viral hepatitis
• Rapid onset malaise, jaundice
  – Elevated aminotransferase levels (= >5 X ULN)


Mr. S. is a 44 Year-old Man

• Presents for a sick visit
• Recent URI, given antibiotic for acute sinusitis 5 days ago
• Now presents with a CC: “Funny colored urine,” fatigue, “yellow eyes”

Mr. S. (continued)

• Alanine aminotransferase (ALT)= 876 U/L (reference range= 0 to 40 U/L)
  – How many times ULN?
• Aspartate aminotransferase (AST)= 200 U/L (reference range= 0 to 40 U/L)
  – How many times ULN?
• Ratio?

Mr. S. (continued)

• Alkaline phosphatase (ALP)= 291 U/L (reference range= 0 to 40 U/L)
  – Marker of cholestasis
• Total bilirubin= 3.2 mg/dL (54.7 µmol/L) (reference range= 0.3-1.2 mg/dL {5.13-20.5 µmol/L})

Mr. S. (continued)

• Direct bilirubin= 1.99 mg/dL (34.03 µmol/L) (0.0-0.3 mg/dL {0.0-5.13 µmol/L})
  – Excretion function, rises when capacity exceeded
  – Direct= conjugated= water soluble, found in the urine
  – Indirect= non conjugated, not water soluble, not found in urine

Mr. S. (continued)

• Albumin= 48 g/L (reference range= 35 to 55 g/L)
  – Long T ½, 19-21 days
• International normalized ratio= 1.3
  – Short T ½, 24-60 h, reflective of prothrombin synthesis
• Serologic evaluation for acute and chronic viral hepatitis= Negative
51 Year-old Woman

"Yellow eyes" that developed 1 week post termination of a 5-d course of antimicrobial therapy

- AST = 930 U/L (0 to 40 U/L)
- ALT = 730 U/L (0 to 40 U/L)
- GGT = 250 U/L (0 to 60 U/L)
- ALP = 188 U/L (25 to 150 U/L)

References (continued)


References (continued)


End of Presentation!

Thank you for your time and attention.

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