ANEMIA: INTERPRETING THE LABS & MAKING THE DIAGNOSIS

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PRESENTATION OBJECTIVES

1. Properly interpret laboratory tests to determine the cause of a patient’s anemia.

2. Discuss the common etiologies of anemia.

3. Understand the appropriate treatment for each type of anemia, including when a patient should be referred to a specialist for further evaluation and treatment.
Presentation Outline

- Overview
- Review of Labs
- Causes of Anemia
  - Microcytic Anemia
  - Normocytic Anemia
  - Macrocytic Anemia
- Case Studies
ANEMIA: OVERVIEW

Definition:
- A decrease in the red blood cell (RBC) mass
  - Adult males: Hct <41%, Hgb <13.5 g/dL
  - Adult females: Hct <37%, Hgb <12 g/dL

Etiologies
- Decreased production of RBCs
- Blood loss
- Increased RBC destruction – Hemolysis

Epidemiology: 8% of women, 4% of men
ANEMIA: OVERVIEW

Complications

- Arise from tissue hypoxia
- Include shock, hypotension, coronary insufficiency, pulmonary insufficiency
- Skull and skeletal deformities in children
- Poor quality of life
**Review of Labs**

- **CBC**
  - RBC – total number of erythrocytes in a uL of blood
  - Hgb – vehicle in RBCs that transports O2 and CO2
  - Hct – the percentage by volume of packed RBCs in whole blood; indirect measurement of RBC mass

- **RBC Indicies** – used to differentiate anemia
  - MCV – individual cell size
  - MCH – average weight of Hgb per RBC
  - MCHC – avg. concentration of Hgb in RBCs
  - RDW – indication of degree of anisocytosis
REVIEW OF LABS

- Erythropoetin (EPO)

- Retic Count

- Iron Studies
  - Iron – amount of circulating iron in blood
  - Ferritin – total iron stores

- Vitamin B12 level

- Folic Acid/Folate level
Anemia: Differential Diagnosis

Microcytic
- Iron Def.
- Thalassemia
- Chronic Dz.
- Lead Toxicity

Normocytic
- Hemolysis
- Aplasia
- Myelofibrosis
- Chronic Dz.
- Hypothyroid

Macrocytic
- B12 Def.
- Folate Def.
- Hypothyroid
Microcytic Anemia
IRON DEFICIENCY

Overview
- Most common cause of anemia worldwide

Causes
- Increased loss of iron
- Decreased intake/absorption
- Increased utilization

Laboratory Evaluation
- Low ferritin, iron
- +/- High platelets
IRON DEFICIENCY

Treatment: Oral iron
- Ferrous sulfate / ferrous gluconate
- 200 mg elemental iron = 0.25 g/dL Hgb
- Side effects: nausea, constipation, dark stool
- ? Take with food
  - ? Take with Vitamin C
  - ? Slow-release formulation

Treatment: lean meat intake

Treatment: IV iron
- Cannot tolerate iron or severe/recurrent hemorrhage
- DexFerrum, Ferrlecit, Venofer
IRON DEFICIENCY

Medications that reduce iron absorption:
- Antacids (H2-blockers, PPIs)
- Tetracycline antibiotics
- Pancreatic enzyme supplements
- Bisphosphonates
- Cholestyramine
- Calcium supplements
- Tea
- Dairy products
- Phosphonates (vegetables)
IRON DEFICIENCY

Medications malabsorbed because of iron:

- Quinolone antibiotics
- Biphosphonates
- Cefdinir
- Levodopa, carbidopa, methyldopa
- Thyroxine
- Penicillamine
- Mycophenolate mofetil
- Zinc or copper salts
**Thalassemia**

- Hereditary disorders characterized by reduction in the synthesis of alpha or beta globulin chains
  - Normal hgb: 2 alpha & 2 beta chains
  - Thalassemia: imbalance/accumulation of chain

- Characterization:
  - Trait: lab features, but no significant clinical impact
  - Intermedia: RBC transfusion requirement or other moderate clinical impact
  - Major: disorder is life-threatening
THALASSEMIA

- **Laboratory Evaluation**
  - Microcytic, hypochromic anemia
  - Normal to elevated reticulocyte count

- **Diagnosis**
  - Made by hemoglobin electrophoresis

- **Treatment**
  - Mild thalassemia – no treatment
  - Splenectomy if hypersplenism is present
  - Beta-thalassemia major – allogeneic BMT is preferred
ANEMIA OF CHRONIC DISEASE

Overview
- Due to infection, inflammation, trauma, malignancy
- Caused by decreased RBC production

Laboratory Findings
- Microcytic or normocytic & normochromic anemia
- Low iron, low TIBC, normal or elevated ferritin
- Low or normal erythropoietin (EPO)
- Low reticulocyte count

Treatment
- Directed toward the underlying cause
- Transfusions
- Administration of erythropoietin
Lead Toxicity

- Results from chronic, repeated exposure
- Found in batteries, solders, paints, pottery, plumbing, gasoline, bullets, traditional ethnic medications

Symptoms:
- Colicky abdominal pain
- Constipation
- Headache
- Irritability
- Severe poisoning: convulsions & coma
- Learning disorders in children
- Motor neuropathies
LEAD TOXICITY

Laboratory Evaluation
- Microcytic anemia
- Basophilic stippling

Diagnosis: Blood lead level
- < 10 mcg/dL: nontoxic
- 10 – 70 mcg/dL: noticeable symptoms
- >70 mcg/dL: severe poisoning

Treatment
- Determine source of exposure
- Whole bowel irrigation
- Iron chelation therapy
Normocytic Anemia
Hemolysis

Overview
- Decreased levels of RBCs because of accelerated destruction, either continuously or episodically
- Account for about 5% of anemia

Laboratory Findings
- Microcytic or Normocytic anemia
- Increased reticulocyte count
- Decreased haptoglobin level
- Increased LDH level
- Increased indirect bilirubin level
Hemolysis

- Thalassemia
- G6PD deficiency
- Sickle Cell Anemia
- Autoimmune hemolytic anemia
- Hereditary spherocytosis
- Prosthetic cardiac valves
- Thrombotic Thrombocytopenic Purpura (TTP)
- Disseminated Intravascular Coagulation (DIC)
- ABO incompatible blood transfusion
- Paroxysmal Nocturnal Hemoglobinuria (PNH)
- Hemolytic Uremic Syndrome (HUS)
- Many more!
Hemolysis: G6PD Deficiency Anemia

Overview
- An X-linked recessive disorder
- Affects people from Med. region, Africa, China

Signs and Symptoms
- Patients are usually healthy
- Hemolysis with infection or medications
  - Antimalarials (quinine, hydroxychloroquine)
  - Sulfa
  - Nitrofurantoin

Laboratory Findings during an episode
- Heinz bodies are present

Treatment
- None, except to avoid known oxidants
- Consider blood transfusion and splenectomy
HEMOLYSIS: SICKLE CELL ANEMIA

Overview
- Autosomal recessive disorder
- Acute, painful episodes may be spontaneous or be provoked by infection, dehydration, hypoxia, or cold temps
- Clusters of sickled cells occlude microvasculature
- Episodes last hours to days and produce pain and low-grade fever

Laboratory Findings
- Increased reticulocyte count
- Nucleated RBCs, Howell-Jolly bodies, Target cells

Diagnostic Test
- Hemoglobin electrophoresis
  - Hemoglobin S comprises >85% of hemoglobin
Hemolysis: Sickle Cell Anemia

- **Treatment**
  - Hydroxyurea (Hydrea)
  - Folic acid supplementation
  - Pnuemococcal vaccination
  - Consider allogenic BMT for young patients

- **Treatment during crisis**
  - Treat infection or precipitating factor
  - Hydration, Oxygen, Blood Transfusion, Pain Control

- **Prognosis**
  - Life expectancy is between 40 – 50 yo
  - Repeated episodes of vascular occlusion can lead to organ damage and failure
Aplastic Anemia

Overview
- Condition of bone marrow failure
- Bone marrow becomes hypoplastic and pancytopenia develops

Causes
- Autoimmune
- Stem cell injury from chemotherapy, radiation, toxins, or certain medications

Laboratory Findings
- Pancytopenia
- Decreased reticulocytosis
Aplastic Anemia

- **Diagnostic Test**
  - Bone marrow aspiration and biopsy: hypocellular marrow (“empty” marrow), few hematopoietic stem cells, no abnormal cells

- **Treatment**
  - Supportive care with transfusions and antibiotics
  - Immunosuppression
  - Allogeneic BMT

- **Prognosis**
  - No treatment: median survival is 3 months
  - Treatment: 5-year survival rate is 75%
Myelofibrosis

- Scarring of the bone marrow + splenomegaly

- Signs & Symptoms
  - Fatigue
  - Abdominal fullness

- Laboratory Findings
  - Anemia
  - Teardrop RBCs
  - Variable WBC and Plt counts

- Diagnostic Test
  - Bone Marrow – dry tap; collagen replaces hematopoietic cells
Macrocytic Anemia
B12 DEFICIENCY

- Develops after chronic malabsorption

- Signs and Symptoms
  - Peripheral neuropathy
  - Spinal cord degeneration
  - Memory loss, disorientation, depression
  - Malabsorption (weight loss, diarrhea, abd pain)
  - Glossitis
  - Infertility, fetal loss
B12 DEFICIENCY

- Laboratory Findings
  - Macrocytic anemia
  - Low to low-normal B12 level
  - Increased EPO
  - Decreased reticulocyte count
  - Increased LDH

- Treatment
  - Lifelong with PO or IM B12
**B12 Deficiency: Pernicious Anemia**

- Parietal cells in the fundus of the stomach secrete acid and intrinsic factor
- Intrinsic factor – protein that transfers cobalamin to the duodenum
- More common >60-70 yo
- If dx in <50 yo, need to r/o gastric CA
- Causes
  - Autoimmune atrophic gastritis – most common
  - Any process that affects parietal cells
- Labs
  - Anti-intrinsic factor antibodies
  - Antiparietal cell antibodies
  - Serum gastrin – diagnostic for atrophic gastritis
- Treatment
  - B12 IM or PO
Folate Deficiency

- Caused by inadequate dietary folate intake
- All grains are fortified – 1996 FDA Mandate

Laboratory Findings
- Macrocytic anemia
- Decreased folic acid level
- Increased EPO
- Decreased reticulocyte count
- Elevated LDH

Treatment
- PO Folic acid supplementation
When To Refer...

- Severe anemia
- Anemia that is not responding to treatment
- Anemia + other CBC abnormalities
- Fe deficiency anemia + male/post-menopausal female
- Anemia that’s “not making sense”
- Hereditary/genetic cause of anemia
Case Studies
CASE STUDY #1

A 62 yo male presents to your clinic for his annual preventative exam. He has a history of HTN, controlled with lisinopril. He also takes a daily aspirin 81mg and fish oil. He has no complaints and his exam is negative. Routine blood work is performed including a CBC, CMP, PSA, lipid panel, and HgbA1C. Results of CBC are as follows:

- WBC: 6.6 (5-10)
- Hgb: 10.8 (12-17 g/dL)
- Hct: 31 (35-50%)
- MCV: 70 (80-100)
- Plt: 210 (150-450)

What type of anemia does he have?
CASE STUDY #1

Retic: 0.5% (0.5 - 1.5%)
EPO: 40 (5 - 36)
Ferritin: 25 (20-250)
B12 level: 544 (>200)
Folic Acid: 45 (2-20)

What is the diagnosis?

What is the appropriate treatment?
CASE STUDY #2

A 45 yo female presents to your primary care office with complaint of fatigue x 3 months. She has a history of Type 2 diabetes, controlled with metformin and victoza, and rheumatoid arthritis, controlled with Humira and mobic. Her exam is negative. You perform a laboratory evaluation.

WBC: 8.4  (5-10)
Hgb: 11.3  (12-17 g/dL)
Hct: 34%   (35-50%)
MCV: 85   (80-100)
Plt: 290  (150-450)

What type of anemia does she have?
## Case Study #2

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<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
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<td>(0.5 - 1.5%)</td>
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<td>EPO</td>
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<td>(5 - 36)</td>
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<td>Iron</td>
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<td>(50 - 175)</td>
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<td>Ferritin</td>
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<td>(20 - 250)</td>
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<td>B12</td>
<td>674</td>
<td>(&gt;200)</td>
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<tr>
<td>Folic acid</td>
<td>18</td>
<td>(2 - 20)</td>
</tr>
<tr>
<td>TSH</td>
<td>1.9</td>
<td>(0.4 - 4.2)</td>
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What is the diagnosis?

What is the treatment?
CASE STUDY #3

An 89 yo female with h/o osteoarthritis and osteopenia presents to your primary care office for a routine preventative visit. She currently takes Tylenol arthritis and Boniva. She has no complaints and her exam is neg. Routine blood work is performed.

WBC: 7.6 (5-10)
Hgb: 11.6 (12-17)
Hct: 33% (35-50%)
MCV: 112 (80-100)
Plt: 248 (150-450)

What type of anemia does she have?
CASE STUDY #3

- Retic: 0.5% (0.5 - 1.5%)
- EPO: 45 (5 - 36)
- Ferritin: 129 (20 - 250)
- B12 level: 219 (>200)
- Folic Acid: 28 (2 - 20)
- TSH: 2.2 (0.4 - 4.2)

What is the diagnosis?

What is the treatment?
A 72 yo M presents to your primary care office c/o recent onset of extreme fatigue. PMH includes Stage I colon cancer s/p resection, NED; HTN & dyslipidemia, controlled with metoprolol & lipitor. He has recently noticed that he has been bruising easily. On exam, his pulse is 118 and he looks pale and acutely ill. Bruises and petechiae are noticed on his skin. CBC reveals:

WBC: 6.6 (5-10)
Hgb: 8.9 (12-17)
Hct: 27% (35-50%)
MCV: 90 (80-100)
Plt: 32 (150-450)
**Case Study #4**

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<td>EPO</td>
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<td>Ferritin</td>
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<td>(20-250)</td>
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<tr>
<td>B12 level</td>
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<td>(&gt;200)</td>
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<tr>
<td>Folic Acid</td>
<td>18</td>
<td>(2-20)</td>
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</table>

What is the diagnosis?

What is the treatment?
CASE STUDY #5

A 20 yo male presents to the ER c/o fever & severe bone pains x 2 days. He has travelled here from Greece with his school friends for a short vacation. He understands conversational English, but not medical terms. He states that he has a blood problem & these symptoms occur every few years & he is treated with strong medications for the pain. CBC reveals:

- WBC: 12.1 (5-10)
- Hgb: 10.8 (12-17)
- Hct: 30% (35-50%)
- MCV: 88 (80-100)
- Plt: 292 (150-450)

Peripheral smear shows nucleated RBCs.
CASE STUDY #5

Retic: 2.1%  (0.5-1.5%)
EPO: 45     (5-36)
Ferritin: 280 (20-250)
Haptoglobin: 32 (40-200)
Bilirubin: 2.1 (0.3-1.0)

What is the diagnosis?

What is the treatment?
A 38 yo female with no PMH presents to her ob/gyn c/o menorrhagia x 6 months. Evaluation reveals the etiology to be uterine fibroids and you suggest a hysterectomy to treat her condition. During pre-op evaluation, CBC reveals the following:

- WBC: 8.8 (5-10)
- Hgb: 10.8 (12-17)
- Hct: 31% (35-50%)
- MCV: 67 (80-100)
- Plt: 481 (150-450)

What type of anemia is this?
Case Study #6

Retic: 0.6% (0.5-1.5%)
EPO: 40 (5-36)
Ferritin: 8 (20-250)
B12: 423 (>200)
Folic acid: 18 (2-20)

What is the diagnosis?

What is the treatment?
REFERENCES