ALL ABOUT ANEMIA

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Objectives

Upon completion of the discussion the participant will be able to:

- Discuss the presentation and pathophysiology of anemia
- Identify the diagnostic criteria for a variety of anemias
- Discuss the treatment modalities for anemia
- Utilize a case-based application of clinical concepts
Definitions

- Anemia - Values of hemoglobin, hematocrit or RBC counts which are more than 2 standard deviations below the mean
  - HGB < 13.5 g/dL (men) < 12 (women)
  - HCT < 41% (men) < 36 (women)
Etiology

- Depends on the underlying problem or disease that is causing the anemia
  - Nutritional deficiencies
    - Malabsorption syndromes
  - Blood loss
  - Iatrogenic
  - Chronic disease
  - Inherited diseases
  - Infections
  - Neoplasms
Erythropoiesis

Red Blood Cells

Bone Marrow

Increase in Red Blood Cell Production

Increase in Response to Erythropoietin

Lack of Oxygen (Hypoxia)

Increase in Erythropoietin Production

Kidney

Erythropoietin
RBC development

- Pluripotent Stem Cell
- Burst-Forming Unit-Erythroid Cells (BFU-E)
- Colony-Forming Unit-Erythroid Cells (CFU-E)
- Proerythroblasts
- Erythroblasts
- Reticulocytes
- RBCs

Bone Marrow

Erythropoietin

10 Days

1-2 Days
Normal Iron Cycle

Iron absorption and losses
Iron absorption 1–2 mg/day
Iron loss 1–2 mg/day

Energy
Muscle 300 mg

Iron transport
Transferrin 3–4 mg

Iron storage
Iron storage 1000 mg

RBC formation
RBCs 2000 mg
Anemia Prevalence

The bar chart shows the percentage of people with anemia by age group and gender.

- **1-16 years**
  - Male: 6.0%
  - Female: 1.5%

- **17-49 years**
  - Male: 8.7%
  - Female: 12.2%

- **50-64 years**
  - Male: 4.4%
  - Female: 6.8%

- **65-74 years**
  - Male: 7.8%
  - Female: 8.5%

- **75-84 years**
  - Male: 15.7%
  - Female: 26.1%

- **85+ years**
  - Male: 10.3%
  - Female: 20.1%
Causes of Anemia in the Elderly

- Nutritional Deficiency or Blood Loss
- Chronic Disease
- Unexplained

Morbidity and Mortality Related to Geriatric Anemia

- Increased mortality
- Increased hospitalization
- Cardiovascular disease
- Falls
- Functional impairment
- Cognitive impairment and mood dysfunction
Presentation of Anemia

- Dependent on degree of severity
  - Individuals with heart disease/elderly more symptomatic (i.e. angina, syncope, SOB)

- Dependent on how quickly anemia occurs
  - May be asymptomatic until hgb < 10 g/dl

- Symptoms related to low oxygen states
History is key

- Family history
- Past medical history
- Current health state
  - Medications
  - Hobbies
  - Occupation
  - Dietary history
  - Menstrual history
  - GI/GU
Review of Symptoms

- Decreased oxygen delivery to tissues
  - Exertional dyspnea
  - Dyspnea at rest
  - Fatigue
  - Signs and symptoms of hyper-dynamic state
    - Bounding pulses
    - Palpitations
  - Life threatening: heart failure, angina, myocardial infarction

- Hypovolemia
  - Fatigue, postural dizziness, lethargy, hypotension, shock and death
Physical exam – Evaluation of the Patient

- Dermatologic manifestations
  - Nail defects
  - Hair changes
  - Skin changes
    - Pale conjunctiva (usually <8 g/dl)

- Cardiovascular
  - Palpitations, tachycardia, syncope
  - Murmur (early systolic/increase blood flow)

- Neurological manifestations
  - Paresthesia, stocking glove neuropathy (B12)

- Gastrointestinal

- Female reproductive system
Laboratory testing

- **CBC:**
  - RBC count: 4.5-5.5 in men, 4-5 in women
  - Hemoglobin: < 13.5g/dL in men, < 12g/dL in women
  - Hematocrit: < 41% in men, < 37% in women
  - MCV: 80-100
  - MCHC: 31-37 g/dL
  - RDW: 11.5-14.5
- Reticulocyte count: 0.5-1.5%
- Peripheral Smear
- Serum Ferritin: Men 15-200, Women 12-150ng/ml
- Total Iron Binding Capacity: 250-400
Classifying Anemias

**MCV < 80**
- **Microcytic Anemia**
  - Iron deficiency anemia
  - Lead poisoning
  - Chronic Disease
  - Thalessemias
  - Sideroblastic anemias

**MCV 80-100**
- **Normocytic Anemia**
  - Infections
  - Drugs
  - Renal Disease
  - Acute Blood loss
  - Aplastic anemia
  - Hemorrhage
  - G-6-PD deficiency
  - TTP
  - DIC
  - Artificial heart valve

**MCV > 100**
- **Macrocytic Anemia**
  - B12 deficiency
  - Folate deficiency
  - Medication induced
  - Artificial heart valve
Macrocytic Anemia

- Inhibition of DNA synthesis (cell multiplication)
- Vit. B₁ deficiency
- Folate deficiency
- A very few large hemoglobin-rich erythrocytes

Microcytic Anemia

- Inhibition of hemoglobin synthesis
- Iron deficiency
- A few small hemoglobin-poor erythrocytes
Reticulocytes

- Immature cells released into the bloodstream
- Best indicator of how anemia is affecting the bone marrow
- Lab reports: retics as % of total RBC count
- Calculate retic. production index (RPI)
  - < 2% = decreased marrow production
  - > 2% = red cell loss, increased erythropoietic response
Reticulocyte Production Index RPI

- Indicator of the degree of bone marrow response to anemia

\[ \text{RPI} = \frac{\% \text{ retic count} \times \text{hematocrit}}{0.45} \]

maturation time in peripheral blood
Classification of Anemia

Hgb < 12 g/dL

↓

CBC

Reticulocyte Index

Normocytic

<2

↓

Hypoproliferation

↓ production

Macrocystic or microcytic

<2

↓

Maturation disorder

(ineffective)

Normocytic

> 3-5

↓

Hemolytic

↑ destruction

Peripheral Blood Smear

- Smear reveals clues about the etiology of the anemia
- Abnormalities of RBC shape (i.e. Burr cells, Target cells)
- Basophilic stippling with thalassemia, sideroblastic, lead
Classifying Anemia

- RDW- # cells of widely different sizes.
- Anisocytosis- variation of cell size
- Poikilocyosis- variation of cell shape
Differentials for Microcytic

- Disorders of iron metabolism
  - Iron deficiency-blood loss
  - Chronic Infections
  - Neoplasms
- Disorders of heme synthesis
  - Sideroblastic
- Disorder of globin synthesis
  - Thalassemias
  - Lead poisoning
  - Aluminum toxicity
Iron-deficiency Anemia

- Microcytic, hypochromic
- Most common type of anemia worldwide
- Most frequent in children, pregnancy, any blood loss
- Fatigue, pallor, possible cardiovascular symptoms

Treatment:
- Ferrous Sulfate
- Vitamin C - enhances absorption
Microcytic Anemia - Sideroblastic Anemia

- Defective RBC (*hemoglobin*) production
- Hypochromic, microcytic RBC
- Ineffective erythropoiesis
- Inherited or acquired

- Hereditary sideroblastic anemia generally manifests during the first three decades of life especially during adolescence

- Acquired sideroblastic anemia is due to prolonged exposure to toxins like alcohol, lead, drugs or nutritional imbalances such as deficiency in folic acid, deficiency in copper or excess zinc.
Microcytic Anemia: Thalassemia

- Genetic, inherited abnormality
- Diminished production of alpha or beta globin chain
- Alpha Thalassemia Trait
- Beta Thalassemia Minor
- Beta Thalassemia Major
- Causes lowered hemoglobin A synthesis
Microcytic Anemia diagnosis

- Serum iron level
- TIBC
- Serum ferritin
- Serum Transferrin
- Peripheral smear
- Reticulocyte count
- Hemoglobin electrophoresis
# Lab findings – Microcytic Anemia

<table>
<thead>
<tr>
<th></th>
<th>Red cell Morphology</th>
<th>Serum Fe Level</th>
<th>TIBC</th>
<th>Serum Ferritin</th>
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<tbody>
<tr>
<td><strong>Iron Deficiency Anemia</strong></td>
<td>Microcytic Hypochromic</td>
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<td><strong>Anemia of Chronic Illness</strong></td>
<td>Normocytic microcytic</td>
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<td><strong>Sideroblastic</strong></td>
<td>Microcytic hypochromic</td>
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<td>Normal</td>
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<tr>
<td><strong>Thalassemia</strong></td>
<td>Microcytic</td>
<td>Normal or ↑</td>
<td>Normal</td>
<td>Normal or ↑</td>
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Treatment

- Depends upon the cause
  - Blood loss
  - Chronic disease – treat the illness
- Iron replacement
  - Ferrous Sulfate
  - Vitamin C enhances absorption
45-year-old Caucasian female presents with a chief complaint of "I'm always tired. There must be something wrong with me" Progressive fatigue to 2 months; Has a history of obesity, reflux, depression asthma and arthritis. Only GI symptoms are poor appetite and usual reflux; has no vomiting, melena or rectal bleeding. Regular menses that are occasionally heavy

**Objective:** T -98, P-92, R-18, B/P-134/84.

PE: reveals a 45 year old female in no apparent distress; oriented x 3; appropriate response to questions. Ht. 5'4"; Wt. 210#

Skin: tanned without bruising, ecchymosis or other lesions; nail beds sl. pale; refill < 3sec.

HEENT: sclera clear/white; gums pale, teeth in good repair; no adenopathy.

Lungs: clear; vesicular breath sounds thru out.

Heart: physiologic split of S2; no S3 or S4; RRR

Abd: round, no organomegaly, masses or tenderness

Pelvic: deferred

Ext: bil. symmetric; no deformities; gait nl.

Neuro: unremarkable

**Laboratory Data:** WBC: 5.2/cm; RBC: 3.9/cm; HGB: 8.9m/dl; HCT: 30%; MCV:76; MCHC: 30g/dL, RDW is increased.
Normocytic differentials

- Aplastic anemia
- Intravascular hemolysis
- Extravascular hemolysis
- Chronic inflammatory disorders
- Chronic infections
- Neoplasms
- Hereditary disorders
- Acquired or extrinsic disorders
- Trauma
Normocytic anemia diagnosis

- Serum Iron
- TIBC
- Ferritin
- Peripheral smear
- Reticulocyte count
- LDH
- Serum Haptoglobin
- Hemoglobin Electrophoresis
Anemia of Renal Failure

- Common with Chronic Renal Failure
- Due to decreased erythropoietin
- Usually normocytic, normochromic
- Tends to correlate with the degree of Renal Failure
Normocytic Anemia - Hemolysis

Premature destruction of RBCs; Typically you will see increased reticulocytes

**CAUSES:**
- Hemoglobinopathies (i.e. sickle cell)
- Enzyme deficiency (pyruvate-kinase, pyrimidine-5-nucleotidase, G6PD)
- Medications (sulfa, IV PCN, quinine…)
- Autoimmune disorders
- Trauma to the red cells
Sickle Cell Anemia

- Hemoglobinopathy
- Abnormal form of hemoglobin (HbS)
- Underlying moderate-severe hemolysis (RPI up during hemolysis)
- Intermittent hemolytic crisis; often severe
- Hgb usually 6-10 range
- Diagnosis - Hgb electrophoresis
Treatment

- Treat the cause

- Epoetin and Darbopoetin
  - Procrit, Epogen and Aranesp
  - Current concerns (treat to $\leq 12$ Hgb max due to risk of cardiovascular/stroke risks)
Macrocytic differentials

- Megaloblastic anemia
  - Folic acid deficiency
  - Pernicious anemia – B12 deficiency
- Liver disease
- Alcoholism
- Drugs
- Myxedema
Macrocytic anemia diagnosis

- CBC - determines the macrocytosis
- Peripheral smear
- Reticulocyte count
- Vitamin B12
- Serum folate level
- Methylmalonic acid (MMA)
- Homocysteine levels
Treatment

- **Vitamin B12 deficiency**
  - Vitamin B12 cyanocobalamin 1000 mcg IM or oral daily for 1 week, then every week X 1 month then every month. 500 mcg in one nostril weekly for maintenance

- **Folate deficiency**
  - Folate 1 mg daily
Case Study

A 40-year old white female, presents with a chief complaint of "stomach problems". She has noticed lately that foods she used to enjoy seem to upset her digestion. She complains of increasing frequency of diarrhea, especially after eating. Foods seem to "go right through her". In addition, she has headaches and feels tired all the time. On occasion she has become unusually short of breath when running up stairs. She thinks these symptoms are a result of a recent urinary tract infection. She claims the medication she is taking for her bladder infection is making her tongue sore and her fingers tingle. Current medications include: occasional Tylenol for headaches; Bactrim DS i po bid.

Objective Assessment: T - 97°, P-100, R-24; Skin: pale Mouth: pale gums, red tongue, absent papillae; Lungs: clear to a & p; Heart: nl.S,S2 with tachycardia; Extremities: fingertips insensitive to temperature, decreased sensation to sharp objects bilaterally; Neurologic: loss of vibratory sensation

Laboratory data: Hemoglobin: 9gm/dl. MCV: 110 um3. WBC: 4000 per cubic millimeter. Platelets: 145,000 per cubic millimeter; many atypical cells.
Summary

- Once treatment has been initiated patient response should be evaluated on at least a monthly basis.
- Patient education is key for compliance with medications and diet.
- Diagnosis is a step by step process. Be sure to complete all necessary tests prior to treatment.
References


http://www.irondisorders.org/