Evaluation of Anemia

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Anemia - Definition

- Most common hematologic disorder
- Decrease from normal levels of Hgb, Hct, RBC:
  - Females – Mean Hgb = 14 g/dl; -2SD = 12 g/dl
  - Males – Mean Hgb = 15.5 g/dl; -2SD = 13.5 g/dl
- Caveat – Anemia is a syndrome, not a disease. An abnormal Hgb or Hct should ALWAYS be investigated if confirmed on repeat testing.
Anemia - Definition

- National Health and Nutrition Examination Survey (NHANES III) data:
  - 10-28% of patients over 65 years are anemic
  - One third of these are due to iron, folate, B12 deficiency alone or in combination
  - One third are due to renal disease, or other chronic inflammatory response
  - One third are due to various primary marrow disorders, malignancies or other disorders

Anemia Classification Schemes

- A simplified approach to anemia, emphasizing information already included in the CBC:
  - Mean Cellular Volume (MCV)
  - Red Cell Distribution Width (RDW)
  - Retic count
Anemia Classification Schemes

<table>
<thead>
<tr>
<th>Anemia Classification Schemes</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mean Cellular Volume (MCV)</td>
</tr>
<tr>
<td>• Decreased MCV (microcytic); &lt; 80 fL</td>
</tr>
<tr>
<td>• Normal MCV (normocytic); 80 – 99 fL</td>
</tr>
<tr>
<td>• Increased MCV (macrocytic); &gt; 100 fL</td>
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Anemia Classification Schemes

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<tr>
<td>• Red blood cell Distribution Width (RDW)</td>
</tr>
<tr>
<td>(actually the standard deviation of red blood cell volume divided by the mean volume)</td>
</tr>
<tr>
<td>✓ Normal; &lt; or = to app. 14</td>
</tr>
<tr>
<td>✓ Elevated; &gt; 14</td>
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</tbody>
</table>
### Anemia Classification Schemes

- **Red blood cell Distribution Width (RDW)**
  - A numerical expression of anisocytosis, or variation in RBC size

### Anemia Classification Schemes

- **Red blood cell Distribution Width (RDW)**
  - Normal RDW - representing a uniform population of RBCs with respect to size

![Bell-Shaped Curve](image)
## Anemia

### Classification Schemes

- Red blood cell Distribution Width (RDW)
  - Elevated RDW - representing RBCs with varying sizes

### Anemia MCV, RDW classification

- Microcytic indices (MCV < 80)
  - With normal RDW:
    - Anemia of chronic disease/inflammation
    - Thalassemia trait
**Anemia**

**MCV, RDW classification**

<table>
<thead>
<tr>
<th>Microcytic indices (MCV &lt; 80)</th>
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<tbody>
<tr>
<td>✓ With elevated RDW:</td>
</tr>
<tr>
<td>• Iron deficiency</td>
</tr>
<tr>
<td>• Sickle- Beta thalassemia</td>
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<tr>
<td>• Thalassemia major</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Normocytic indices (MCV 80-99)</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ With normal RDW:</td>
</tr>
<tr>
<td>• Acute blood loss</td>
</tr>
<tr>
<td>• Anemia of chronic disease/inflammation</td>
</tr>
<tr>
<td>• Anemia of chronic renal disease</td>
</tr>
</tbody>
</table>
### Anemia

**MCV, RDW classification**

#### Normocytic indices (MCV 80-99)
- ✓ With elevated RDW:
  - Early iron, folate, B12 deficiency
  - Combined deficiency states
  - Sickle cell anemia
  - Chronic liver disease

#### Macrocytic indices (MCV > 99)
- ✓ With elevated RDW:
  - Folate, B12 deficiency
  - Immune hemolytic anemia (also, other anemias with elevated Retic counts)
  - Myelodysplastic syndromes
Anemia
MCV, RDW classification

- Macrocytic indices (MCV > 99)
  - With normal RDW:
    - Alcohol
    - Myelodysplastic disorders
    - Aplastic anemia
    - Chemotherapy

Anemia
Laboratory Evaluation

- Reticulocytes
- Immature RBCs, released in response to decreased Hgb concentration. Increased numbers suggest ongoing RBC loss or destruction; reticulocytes show marrow compensation.
- Lab measures can include:
  - Reticulocyte Percentage
  - Absolute Reticulocyte count per flow cytometry
  - Reticulocyte Index (RI)
### Reticulocytes

- **Reticulocyte Percentage**
- Normally, RBCs live about 120 days, so a ‘normal’ retic count is about 0.8 - 1.0 %
- An elevated Retic percentage is suggestive of hyperproliferative anemia
- A normal or decreased Retic percentage is suggestive of hypoproliferative anemia

### Anemia Laboratory Evaluation

- **Reticulocyte Index**
- Reticulocyte Index < 2.0 suggests a hypoproliferative anemia
- Reticulocyte Index > 2.0 suggests a hyperproliferative anemia
Reticulocytes

- Absolute Reticulocyte counts: normally 25-75,000/uL
- < 75,000 / uL – c/w hypoproliferative anemias
- 75,000 – 100,000 / uL – indeterminate
- > 100,000 /uL – c/w hyperproliferative anemias

Anemia Evaluation

- Useful laboratory adjuncts: the smear
Anemia Evaluation

- Useful laboratory adjuncts:
  Technician comments: microcytosis, hypochromia

Anemia Evaluation

- Useful laboratory adjuncts:
  Technician comments: macrocytosis, aniso and poikilocytosis
Anemia Evaluation

• Useful laboratory adjuncts:
  Technician comments: elliptocytosis, anisocytosis

Anemia Evaluation

• Useful laboratory adjuncts:
  Technician comments: burr cells, acanthocytosis
Anemia Evaluation

• Useful laboratory adjuncts:
  Technician comments: sickle cells, aniso- and poikilocytosis

Anemia Evaluation

• Useful laboratory adjuncts:
  Technician comments: spherocytosis
## Combining MCV, RDW, Retic ct

<table>
<thead>
<tr>
<th>MCV, RDW</th>
<th>Retic count &lt; 75,000</th>
<th>Retic count &gt;100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low, Normal</td>
<td>Anemia of chronic disease</td>
<td></td>
</tr>
<tr>
<td>Low, High</td>
<td>Fe deficiency</td>
<td>Sickle cell, B-thalassemia</td>
</tr>
<tr>
<td>Normal, Normal</td>
<td>Anemia of chronic disease</td>
<td></td>
</tr>
<tr>
<td>Normal, High</td>
<td>Early Fe, Folate, B12 deficiency, Myelodysplasia</td>
<td>Sickle cell anemia</td>
</tr>
<tr>
<td>High, Normal</td>
<td>ChemoRx, antivirals, Etoh Aplastic Anemia</td>
<td>Chronic liver disease</td>
</tr>
<tr>
<td>High, High</td>
<td>Folate, B12 deficiency Myelodysplasia</td>
<td>Immune Hemolytic Anemia</td>
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</table>


## Anemia Evaluation

- Combine CBC findings (MCV, RDW, morphology) with Retic ct to further define
- Example: Macrocytic anemia with increased RDW, anisocytosis, increased RI or absolute Retic ct suggests immune hemolytic anemia.
Anemia Evaluation

- Once initial classification established, further lab studies can be used to confirm diagnosis
- Example, if hemolysis is suspected:
  - Consider LDH, T and D Bilirubin, haptoglobin, Coomb’s

In Summary
The End!

- Anemia is the most common hematologic lab abnormality
- Appropriate evaluation usually demonstrates a treatable cause
- Initial evaluation can be as simple as examination of CBC diff and plt ct.
- Use Retic count, adjunct tests to confirm initial impression
### Case 1

- 34 year old Indian female with history of heavy periods and recent pregnancy one year ago referred for anemia
- Admits to chewing ice daily
- No other significant personal or family history of medical problems

### Case 1

- Physical exam negative for varicosities or telengectasia
- No evidence of organomegaly or adenopathy
Case 1

- Lab
  - Hgb 8.0 g/dL, hct 28%, MCV 75 fL, RPI of 1, RDW of 15

- What is the morphologic and pathophysiologic type of anemia?
- What are the causes of this?
- What lab studies should be done?

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Case 1

- Microcytic Hypochromic Anemia
  a) Iron Deficiency
  b) Chronic Inflammation
  c) Thalassemia
  d) Lead Poisoning
  e) Sideroblastic Anemia

- Iron 10, TIBC 450, Ferritin 3
- Guaiac negative
## Case 1

- Iron deficiency in young menstruating female recently pregnant
- No reason for GI workup unless guaiac positive
- Evaluate also for celiac disease if no response to oral iron
- Ice craving good clinical sign
- Response to oral iron follow count and ferritin

## Case 2

- A 44 year old white female with history of rheumatoid arthritis sees you for anemia
- Disease activity is moderate and patient is on intermittent steroids and has received an inhibitor to TNF.
- No other medical problems are present
- Physical exam unremarkable except for joint deformity
Case 2

- Lab studies include hgb of 8.2 g/dL, hct of 25%, MCV of 75fL, RPI of 1, RDW of 12
- Characterize the anemia according to prior criteria and decide on appropriate labs

Case 2

- The anemia is microcytic with hypoproliferative state
- Patient had a sed rate drawn of > 140, iron of 20, TIBC of 140, saturation of 14%, ferritin of 100, and Erythropoietin level of 30 (nl 0-19)
### Case 2

- Anemia of Chronic Inflammation
- Due to inability to release iron from macrophages (relative iron deficiency)
- Treatment of underlying disease
- Erythropoietin approved for certain inflammatory states

### Case 3

- A 33 year old Mexican worker comes in with a week history of dyspnea and fatigue
- No prior history of significant medical problems or family history
- Physical exam is positive for tachycardia and scleral icterus
Case 3

- Lab studies drawn show a Hgb of 6.0 g/dL, Hct of 18.0%, MCV of 100 fL, RPI of 6.0, RDW of 20
- What steps are important next?

Case 3

- Evaluation of peripheral blood smear
- It shows spherocytes without fragments
- Lab studies for hemolytic anemia including coomb’s test, LDH, bilirubin, haptoglobin, urine hemosiderin
### Case 3

- Coomb’s test both direct and indirect are positive for IgG and C3
- LDH is slightly elevated to 250 (< 200), bilirubin in 4.0mg/dl with 3.0 indirect, haptoglobin is normal as is urine hemosiderin

### Case 3

- Patient has autoimmune hemolytic anemia and should be worked up for SLE, lymphoma, and CLL
- Initial treatment is steroids and be cautious about transfusing RBC’s
- Response may take 1-2 weeks and documented by increasing hemoglobin and clearance of positive coomb’s test
Case 4

• A 45 year old white female had gastric bypass surgery 5 years before. She notes marked fatigue and numbness in her hands and feet.

• The patient has no medical problems and is on no supplemental medications

Case 4

• Physical exam is unremarkable except for some gait unsteadiness

• Initial lab studies include a hgb of 9.0 g/dL, hct of 27%, WBC of 2.8, platelets of 100,000/ul, MCV of 110 fL, RPI of 1, and RDW of 18
Case 4

- What lab studies do you wish to get?
- Is this an expected problem?
- What therapy is appropriate?

• Peripheral blood smear
• Serum and RBC Folate
• Serum Homocysteine and Methylmalonic acid
• Serum B12
• Parietal cell Antibodies
• Intrinsic Factor Antibodies
• Schilling Test
Case 4

- Peripheral blood smear shows macrocytic red cells and hypersegmented neutrophils
- Red cell and serum folate normal
- Serum homocysteine and methylmelonic acid are elevated
- Serum B12 170 (nl> 250 ug/dl)
- Parietal and intrinsic factor antibodies normal

Case 4

- Schilling test not done
- Malabsorption of B12 common after gastric bypass and most patients should be on B12
## Case 5

- Patient is 52 year old male with diabetes and hypertension
- Patient noted to have mild fatigue and dyspnea
- Patient has required 2 units of packed RBC’s in the last two months
- Physical exam is unremarkable

## Case 5

- Patient’s hgb is 8.0 g/dL, hct 24%, MCV is 85 fL, RPI is 1, and RDW of 12
- The WBC and platelets are normal
- The peripheral blood smear is unremarkable
<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>What lab studies are appropriate?</strong></td>
</tr>
<tr>
<td><strong>What treatment should be considered?</strong></td>
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<tr>
<td><strong>The patient has a normocytic anemia with hypoproliferation</strong></td>
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<tr>
<td><strong>In a patient with diabetes and hypertension chronic renal disease is common</strong></td>
</tr>
<tr>
<td><strong>His creatinine is 2.5 mg/dl and erythropoietin level is 40</strong></td>
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<tr>
<td><strong>Patient may go on erythropoietin</strong></td>
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</table>
Case 6

- Patient is 65 year old white male with history of ischemic heart disease
- Patient has noted increasing angina and dyspnea
- He has no other medical problems and his blood counts were normal 2 years ago

Case 6

- He has blood work and his hgb is 7.5 g/dL, hct 20%, MCV 106 fL, RPI of 2, RDW of 22, WBC of 3.0 with an ANC of 1000, and platelets of 100,000.
- His differential also shows a monocyte count of 1500 and hypogranular neutrophils
Case 6

- What blood work do you order now?
- What procedures should be considered?

Case 6

- He has a macrocytic anemia but evidence of possible MDS
- His iron studies show an iron 200, TIBC of 350, iron saturation of 57%, and ferritin of 500
- He has normal folic acid and B12.
- A bone marrow aspirate and biopsy are done showing sideroblastic anemia and MDS