Evaluation of Anemia

Mark Wurster, M.D., F.A.C.P.
The Ohio State University

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

- **Mean Cellular Volume (MCV)**
- Decreased MCV (microcytic); < 80 fL
- Normal MCV (normocytic); 80 – 99 fL
- Increased MCV (macrocytic); > 100 fL

### 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)**
  - (actually the standard deviation of red blood cell volume divided by the mean volume)
  - Normal; < or = to app. 14
  - Elevated; > 14

---

![](Bell-Shaped-Curve.png)
• Red blood cell Distribution Width (RDW)
  ✓ Elevated RDW - representing RBCs with varying sizes

- Microcytic indices (MCV < 80)
  ✓ With elevated RDW:
    • Iron deficiency
    • Sickle- Beta thalassemia
    • Thalassemia major

- Normocytic indices (MCV 80-99)
  ✓ With normal RDW:
    • Acute blood loss
    • Anemia of chronic disease/inflammation
    • Anemia of chronic renal disease
<table>
<thead>
<tr>
<th>Anemia</th>
<th>Anemia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MCV, RDW classification</strong></td>
<td><strong>MCV, RDW classification</strong></td>
</tr>
<tr>
<td>Normocytic indices (MCV 80-99)</td>
<td>• Macrocytic indices (MCV &gt; 99)</td>
</tr>
<tr>
<td>✓ With elevated RDW:</td>
<td>✓ With normal RDW:</td>
</tr>
<tr>
<td>• Early iron, folate, B12 deficiency</td>
<td>• Alcohol</td>
</tr>
<tr>
<td>• Combined deficiency states</td>
<td>• Myelodysplastic disorders</td>
</tr>
<tr>
<td>• Sickle cell anemia</td>
<td>• Aplastic anemia</td>
</tr>
<tr>
<td>• Chronic liver disease</td>
<td>• Chemotherapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anemia</th>
<th>Laboratory Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MCV, RDW classification</strong></td>
<td>• Reticulocytes</td>
</tr>
<tr>
<td>• Macrocytic indices (MCV &gt; 99)</td>
<td></td>
</tr>
<tr>
<td>✓ With elevated RDW:</td>
<td>• Lab measures can include:</td>
</tr>
<tr>
<td>• Folate, B12 deficiency</td>
<td>• Reticulocyte Percentage</td>
</tr>
<tr>
<td>• Immune hemolytic anemia (also, other anemias with elevated Retic counts)</td>
<td>• Absolute Reticulocyte count per flow cytometry</td>
</tr>
<tr>
<td>• Myelodysplastic syndromes</td>
<td>• Reticulocyte Index (RI)</td>
</tr>
</tbody>
</table>
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

Reticulocytes

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

Anemia Laboratory Evaluation

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

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: macrocytosis, aniso and poikilocytosis

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 def Myelodysplasia</td>
<td>Sickle cell anemia</td>
</tr>
<tr>
<td>High, Normal</td>
<td>ChemoRx, antivirals, Etho 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>
</tr>
</tbody>
</table>


• 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

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

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

- Physical exam negative for varicosities or telangiectasia
- 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?

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 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 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

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lab studies include</strong></td>
<td><strong>Anemia of Chronic Inflammation</strong></td>
</tr>
<tr>
<td>hgb of 8.2 g/dL, hct of 25%, MCV of 75fL, RPl of 1, RDW of 12</td>
<td></td>
</tr>
<tr>
<td>Characterize the anemia according to prior criteria and decide on appropriate labs</td>
<td>Due to inability to release iron from macrophages (relative iron deficiency)</td>
</tr>
<tr>
<td></td>
<td>Treatment of underlying disease</td>
</tr>
<tr>
<td></td>
<td>Erythropoietin approved for certain inflammatory states</td>
</tr>
<tr>
<td>The anemia is microcytic with hypoproliferative state</td>
<td></td>
</tr>
<tr>
<td>Patient had a sed rate drawn of &gt; 140, iron of 20, TIBC of 140, saturation of 14%, ferritin of 100, and Erythropoietin level of 30 (nl 0-19)</td>
<td></td>
</tr>
</tbody>
</table>

Case 3

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A 33 year old Mexican worker comes in with a week history of dyspnea and fatigue</td>
<td>No prior history of significant medical problems or family history</td>
</tr>
<tr>
<td>Physical exam is positive for tachycardia and scleral icterus</td>
<td></td>
</tr>
</tbody>
</table>
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

- 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

- 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

- 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

- 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 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 4**

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

**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
### Case 5

- What lab studies are appropriate?
- What treatment should be considered?

<table>
<thead>
<tr>
<th>Case 5</th>
<th>Case 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>The patient has a normocytic anemia with hypoproliferation</td>
<td>Patient is 65 year old white male with history of ischemic heart disease</td>
</tr>
<tr>
<td>In a patient with diabetes and hypertension chronic renal disease is common</td>
<td>Patient has noted increasing angina and dyspnea</td>
</tr>
<tr>
<td>His creatinine is 2.5 mg/dl and erythropoietin level is 40</td>
<td>He has no other medical problems and his blood counts were normal 2 years ago</td>
</tr>
<tr>
<td>Patient may go on erythropoietin</td>
<td></td>
</tr>
</tbody>
</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

<table>
<thead>
<tr>
<th>Case 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
</tr>
<tr>
<td>His differential also shows a monocyte count of 1500 and hypogranular neutrophils</td>
</tr>
</tbody>
</table>
### 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