Evaluation of Anemia

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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 - 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
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

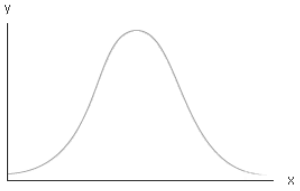
Anemia
Classification Schemes

- 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

Anemia
Classification Schemes

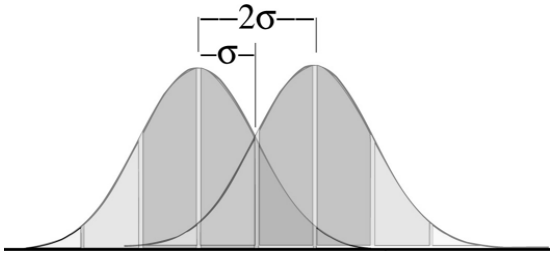
- Red blood cell Distribution Width (RDW)
  - ✓ Normal RDW - representing a uniform population of RBCs with respect to size



Bell-Shaped Curve

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 elevated RDW:
    - Iron deficiency
    - Sickle- Beta thalassemia
    - Thalassemia major

Anemia
MCV, RDW classification

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

Anemia
MCV, RDW classification

- Normocytic indices (MCV 80-99)
  - ✓ With normal RDW:
    - Acute blood loss
    - Anemia of chronic disease/inflammation
    - Anemia of chronic renal disease

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

Anemia
MCV, RDW classification

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

Anemia
MCV, RDW classification

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

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

Reticulocytes

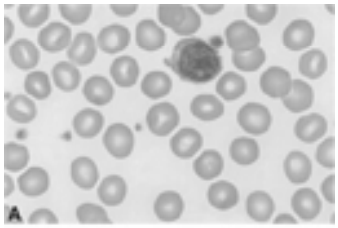
- Absolute Reticulocyte counts: normally 25-75,000/uL
- < 75,000 / uL– c/w hypoproliferative anemias
- 75,000 – 100,000 / uL – indeterminate
- > 100,000 /uL – c/w hyperproliferative anemias

Anemia
Laboratory Evaluation

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

Anemia Evaluation

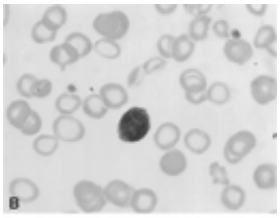
- Useful laboratory adjuncts: the smear



Anemia Evaluation

- **Useful laboratory adjuncts:**

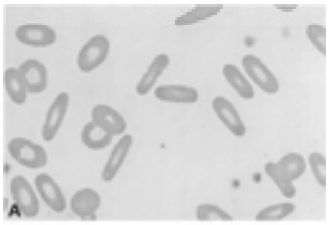
Technician comments: microcytosis, hypochromia



Anemia Evaluation

- **Useful laboratory adjuncts:**

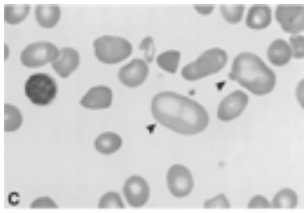
Technician comments: elliptocytosis, anisocytosis



Anemia Evaluation

- **Useful laboratory adjuncts:**

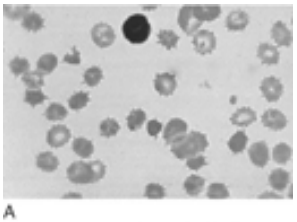
Technician comments: macrocytosis, aniso and poikilocytosis



Anemia Evaluation

- **Useful laboratory adjuncts:**

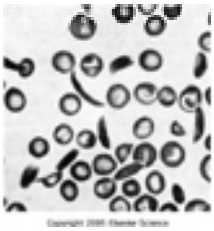
Technician comments: burr cells, acanthocytosis



Anemia Evaluation

- **Useful laboratory adjuncts:**

Technician comments: sickle cells, aniso- and poikilocytosis



Combining MCV, RDW, Retic ct

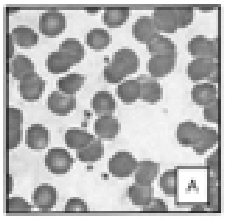
MCV, RDW	Retic count < 75,000	Retic count >100,000
Low, Normal	**Anemia of chronic disease**	
Low, High	**Fe deficiency**	**Sickle cell, B-thalassemia**
Normal, Normal	**Anemia of chronic disease**	
Normal, High	**Early Fe, Folate, B12 def Myelodysplasia**	**Sickle cell anemia**
High, Normal	**ChemoRx,antivirals,Etoh Aplastic Anemia**	**Chronic liver disease**
High, High	**Folate, B12 deficiency Myelodysplasia**	**Immune Hemolytic Anemia**

Hematology: Basic Principles and Practice. Hoffman R, et al.

Anemia Evaluation

- **Useful laboratory adjuncts:**

Technician comments: spherocytosis



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

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 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?**

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

- 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

- 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 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 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

- **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

Case 4

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

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

- 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?

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 5

- The patient has a normocytic anemia with hypoproliferation
- In a patient with diabetes and hypertension chronic renal disease is common
- His creatinine is 2.5 mg/dl and erythropoietin level is 40
- Patient may go on erythropoietin

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**