

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

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

Anemia

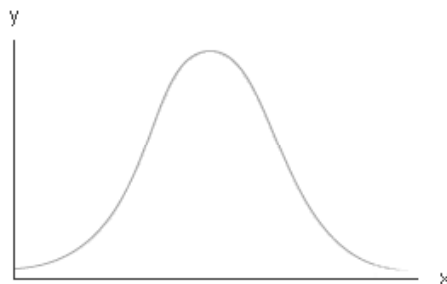
Classification Schemes

- Red blood cell Distribution Width (RDW)
 - ✓ 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

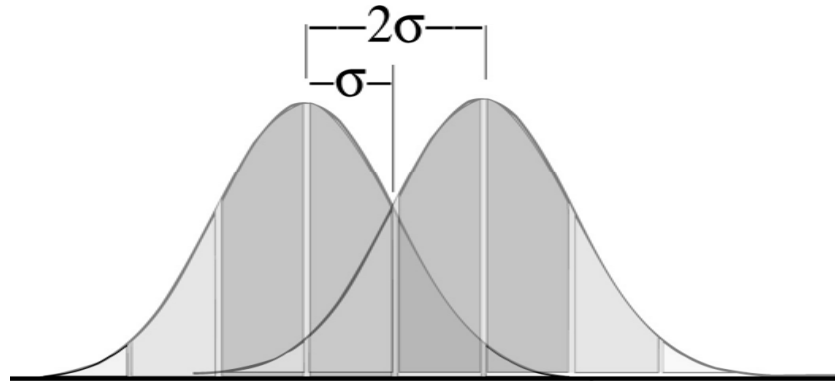


Bell-Shaped Curve

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

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

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 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

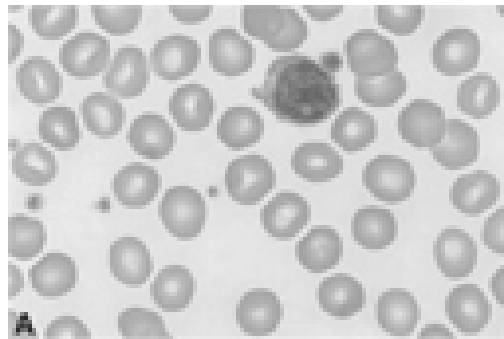
- Reticulocyte Index
- Reticulocyte Index < 2.0 suggests a hypoproliferative anemia
- Reticulocyte Index > 2.0 suggests a hyperproliferative anemia

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**

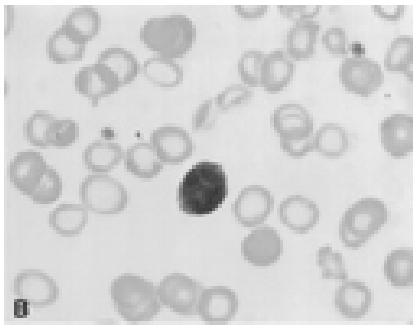


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Anemia Evaluation

- Useful laboratory adjuncts:

Technician comments: microcytosis, hypochromia

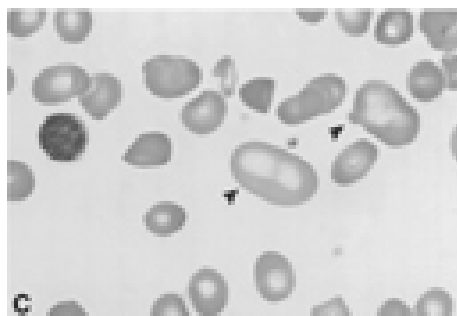


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Anemia Evaluation

- Useful laboratory adjuncts:

Technician comments: macrocytosis, aniso and poikilocytosis

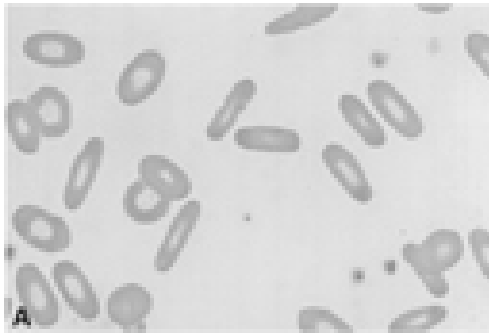


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Anemia Evaluation

- Useful laboratory adjuncts:

Technician comments: elliptocytosis, anisocytosis

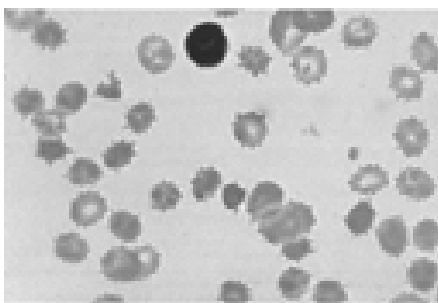


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Anemia Evaluation

- Useful laboratory adjuncts:

Technician comments: burr cells, acanthocytosis

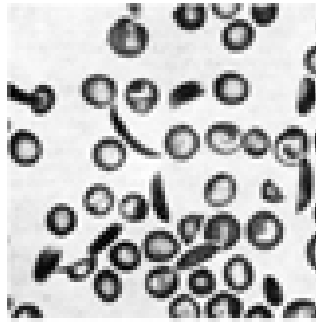


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Anemia Evaluation

- Useful laboratory adjuncts:

Technician comments: sickle cells, aniso- and poikilocytosis

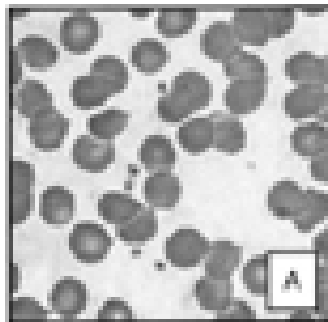


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Anemia Evaluation

- Useful laboratory adjuncts:

Technician comments: spherocytosis



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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

- 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?**

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**
- **Guaic 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?**

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 methylmalonic 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**

Case 5

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

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

- **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**