

# Anemia Dx and Rx

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## Diagnosis and Treatment of Anemia

### Goals

- Review the terminology used to discuss anemias.
- Address clues in the history and exam that can direct the evaluation.
- Describe one approach to using lab tests to make the diagnosis.
- Review some aspects of treatment of common anemias.

### I. Definitions

#### A. Anemia refers to a reduction in the number or volume of RBCs to less than a normal level. May occur due to:

- Acute/chronic blood loss
- Decreased production
- Breakdown of blood (hemolysis)

#### B. Strictly defined by decreased Hgb relating to a value 2SD below a mean

1. Normal values vary according to age and gender (and lab)

	Hgb(g/dl) (-2SD)	HCT% (-2SD)	MCV (-2SD)
1-3 days	18.0(14.0)	54(42)	108(95)
6 mo-2yr	12.0(10.5)	36(32)	78(70)
12-18 yr			
M	14.5(13.0)	43(38)	86(77)
F	14.0(12.0)	41(36)	88(78)
Adult			
M	15.5(13.5)	47(40)	88(78)
F	14.0(12.0)	41(36)	88(78)

Ref: PostGrad Med. 1991;89(6):162

2. Specific lab values must be interpreted in context of patient and illness; ie, are Hgb levels of 14.0 in a male smoker, or of 12.5 in a severely volume contracted woman, "normal?"

#### C. The clinical context and condition of the patient determine how urgently Dx and Rx must occur.

#### D. Indices

1. Hgb – most reliable value
2. Hct – reliable if spun; if automated it is an approximation.
3. MCV (mean corpuscular volume) – is a useful index for distinguishing anemias (if homogenous RBC population).
  - Normal MCV 82-97 fL
  - Macrocytosis > 97 fL

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- Microcytosis < 82 fL
- 4. MCHC (mean corpuscular Hgb concentration) – derived index
- 5. RDW (red blood cell distribution width) – calculated index (nml 11.5-14.5%); if elevated, indicates variability of RBC (anisocytosis) – unreliable value in diagnosis.

### **E. Remember the value and often the need, to actually examine the peripheral smear (a dying art among students, residents and nonpathologist physicians). At least order a manual exam.**

- Spherocytes/ovalocytes
- Sickle cells
- Schistocytes – traumatic hemolysis (prosthetic valve, DIC, TTP, hemolytic-uremic syndrome)
- “Teardrop” cells – bone marrow disease (fibrosis, tumor)
- Oval macrocytes, hypersegmented polys – megaloblastic anemia
- Immature (blast) cells – leukemia

## **II. Evaluation**

### **A. History**

1. Hx of chronic anemia or family Hx of anemia – may suggest inherited anemia.
  - Spherocytosis, ovalocytosis
  - Hemoglobinopathy
2. Medical Hx – many chronic illnesses can be associated with anemia.
  - Chronic infection
  - Diabetes, hypothyroid, renal, hypoadrenal, collagen vascular diseases are common causes.
  - Malignancy
3. Social Hx
  - Nutritional: strict vegan (B<sub>12</sub>); few fruits/veggies (folate)
  - Alcohol use (folate, marrow suppression, liver disease)
4. Surgical Hx: partial or total gastrectomy
5. Medications can cause
  - Bone marrow depression
  - Hemolysis (G-6-PD deficiency)
6. Review of systems
  - Pregnancy
  - Menses
  - Symptoms suggesting undiagnosed medical problem

### **B. Symptoms attributable to anemia alone**

1. Usually not present until Hgb level less than 7-8 g/dl
2. No correlation between level and signs/symptoms

### **C. Physical findings**

1. Pallor of oral mucosa/conjunctiva
2. Palmar crease pallor suggests Hgb < 7 g/dl.

3. Volume status: orthostasis, baseline tachycardia, widened pulse pressure, flow murmurs, flat neck veins, decreased urine output, decreased turgor
4. Skin: jaundice (hemolysis), petechiae/ecchymoses (bleeding disorders), lymphadenopathy (malignancy/infection)
5. Oral
  - Glossitis, macroglossia (pernicious anemia)
  - Angular cheilitis (Fe deficiency)
6. Neuro: paresthesias, dementia, ataxia, decreased proprioception/vibration (pernicious anemia)
7. Heme positive stool (GI loss)
8. Splenomegaly (hemolysis, sequestration, malignancy)

#### **D. Labs**

1. Approach varies greatly depending upon reference, anecdotal experience, circumstances, etc; regardless of approach, have a rationale for it.
  - Recognize the difference between patient in office vs in hospital (usually acutely ill).
  - Try not to “shotgun” (even though we all do it!)
2. One approach
  - a. CBC, peripheral smear
  - b. Check retic count
    - 1) Must calculate the corrected absolute retic count
      - Abs retic count = retic count x RBC
      - Abs retic count < 100,000 suggests defect in RBC production
      - Abs retic count > 100,000 suggests acute bleeding or hemolysis
    - 2) Corrected Abs retic count = Abs retic count/retic maturity time
      - Hct 45% Mat time 1 day
      - Hct 35%, 1.5 days
      - Hct 25%, 2.0 days
      - Hct 15%, 2.5 days
  - c. Use MCV and retic count to determine path for workup.
3. Specific pearls
  - a. Serum Fe: negative phase reactant – it decreases with any stress (fever, etc).
  - b. TIBC: only elevated in Fe def; however, it is also a negative acute phase reactant.
  - c. % Sat: decreases in both Fe def and ACD
  - d. Ferritin: proportional to body’s iron stores generally both increase with age.
    - Less than 16-35 ng/dl suggests depleted stores (if older than 65, less than 45 ng/dl).
    - Even though it is a positive acute phase reactant, must have Fe to elevate.

- Can have ferritin of 50-60 ng/mL and still have Fe-deficiency.
- e. Bone marrow iron stores: “gold standard”

### **III. Microcytic Anemia (MCV < 82 fL)**

#### **A. Algorithm (Fig. 1)**

1. Check ferritin level
  - a. Low value (generally < 30 ng/mL) suggests/confirms iron def.
  - b. Normal or high value – check serum iron.
    - 1) Low Fe – anemia of chronic disease (ACD)
    - 2) Normal or increased – check serum lead level.
      - High – lead toxicity
      - Normal – do Hgb electrophoresis: thalassemia

#### **B. Iron deficiency versus anemia of chronic disease (ACD or AOCD))**

		<b>Fe-Def</b>	<b>ACD</b>
Serum Fe (40-150 mcg/dl)		Low	Low
TIBC(Transferrin) (200-400 µg/dl)		High	NI or Low
% Sat (Fe/TIBC) (16-60%)		Low	Low
Ferritin	m: 16-200 ng/ml	Low	NI or High
	f: 4-160 ng/ml		

#### **C. Causes of iron-deficiency anemia**

1. Increased need
  - Pregnancy
  - Normal growth
2. Decreased intake or absorption
  - Childhood
  - Gastric surgery, achlorhydria
  - Celiac sprue
3. Increased blood loss
  - GERD, PUD, gastritis
  - IBD
  - Malignancy
  - Menstruation

#### **D. Fun Fe facts**

1. Prevalence:10-25% young women, 1% men, up to 10% elderly
2. Why worry?
  - a. Treatable
  - b. Clue to underlying diseases
    - 10-20% pts w/Fe def anemia have CA.
    - Up to 50% have GERD/PUD
3. Diet 10-15 mg/day – 10% absorbed
4. Daily loss 1 mg/d, plus 1 mg/d menstruation
5. FeSO4 20% elemental iron: 180 mg = 36 mg elemental Fe
6. Replace Fe at 6 mg/kg/day up to 200 mg/d elemental Fe
7. Consider Feosol elixir to minimize GI side effects common with FeSO4 tablets.

8. Vitamin C increases absorption of non-heme Fe; literature implies little clinical significance, but antioxidant Rx is becoming a hot topic.
9. Retic count up by 2 weeks
10. Anemia corrected by 6 weeks
11. 4-6 months to correct depleted Fe stores of 500 mg
12. In questionable cases, especially of distinguishing Fe-def vs ACD in an elderly ill patient, consider empiric trial of Fe replacement. Be sure to follow retic and Hgb; if no change, stop Fe

#### **IV. Normocytic Anemia (MCV 82-97 fL)**

##### **A. Algorithm (Fig. 2)**

1. Check corrected absolute reticulocyte count
  - a. Low or normal
    - 1) Any changes of marrow failure
      - a) Yes – do bone marrow biopsy
        - Myelodysplasia
        - Infiltrative disease
        - Aplastic anemia
      - b) No – Dx is ACD.
    - 2) Any splenomegaly?
      - a) Yes – check RBC morphology and Coombs’
        - Negative Coombs’ – hypersplenism, drug effect, infection, hemoglobinopathy
        - Positive Coombs’ – hemolytic disease
      - b) No – hemolytic disease
  - b. High
    - 1) Check LDH, haptoglobin
      - Normal – can be expected response to blood loss.
      - Abnormal – check Coombs’
    - 2) Any splenomegaly?
      - a) Yes – check RBC morphology and Coombs’
        - Negative Coombs’ – hypersplenism, drug effect, infection, hemoglobinopathy
        - Positive Coombs’ – hemolytic disease
      - b) No – hemolytic disease

##### **B. Causes**

1. Decreased RBC production
  - Bone marrow failure
  - Aplastic anemia
2. RBC destruction/loss
  - a. Acute blood loss (may be occult)
  - b. Hypersplenism
  - c. Hemolytic anemia
    - 1) Intrinsic RBC anomalies
      - Spherocytosis
      - G6PD defects
      - Hemoglobinopathies
    - 2) Extrinsic factors
      - Mechanical
      - Infectious (DIC)
      - Autoimmune antibodies

##### **C. Treatment**

- Directed at cause

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- If ACD, iron replacement doesn't help and may be detrimental.
- Consider erythropoietin

### V. Macrocytic Anemia (> 97 fL)

#### A. Algorithm (Fig. 3)

1. Evaluate peripheral smear for macrocytes, hypersegmented polys
  - a. Present – megaloblastic anemia
    - 1) Check B<sub>12</sub>, folate levels
      - One or both low – deficiency (replace): consider Schilling's test.
      - Normal – consider due to drug or idiopathic: referral for eval, bone marrow
    - b. Absent – nonmegaloblastic anemia
      - 1) Review Abs corrected retic count
        - a) Low or normal
          - Eval for liver disease, hypothyroidism
          - If absent, aplastic anemia
        - b) High
          - Hemolytic disease
          - Acute blood loss
          - Hypersplenism
  2. Many drugs can cause macrocytosis without megaloblasts.
    - Phenytoin, OCs, MTX, barbiturates, TMP-SMX, zidovudine
    - Alcohol is the most common cause of macrocytosis.

#### B. Treatment

1. Must be tailored to cause
2. Replacement
  - Folic acid: 1 mg/d
  - Vit B<sub>12</sub>: 1000 microgram/d IM for 5 days, then q week until Hct normal, then q month for life (some studies suggest p.o. replacement as effective)
3. Discontinue offending drugs/agents.
4. Transfusion
  - a. Avoid transfusion “triggers.”
  - b. Plan for autologous blood if possible.
  - c. Administer unit-by-unit based on reassessment.
  - d. Transfuse to relieve symptoms related to blood loss when other replacement has failed.
    - Syncope
    - Dyspnea
    - Shock
    - Angina/TIA

## References

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