

Microcytic Anemias

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Objectives

- Review of hemoglobin synthesis and function
- Definition of anemia and microcytosis
- Mechanisms, approach and workup of anemia
- Classification of anemias
- Causes of microcytic anemia

Terms

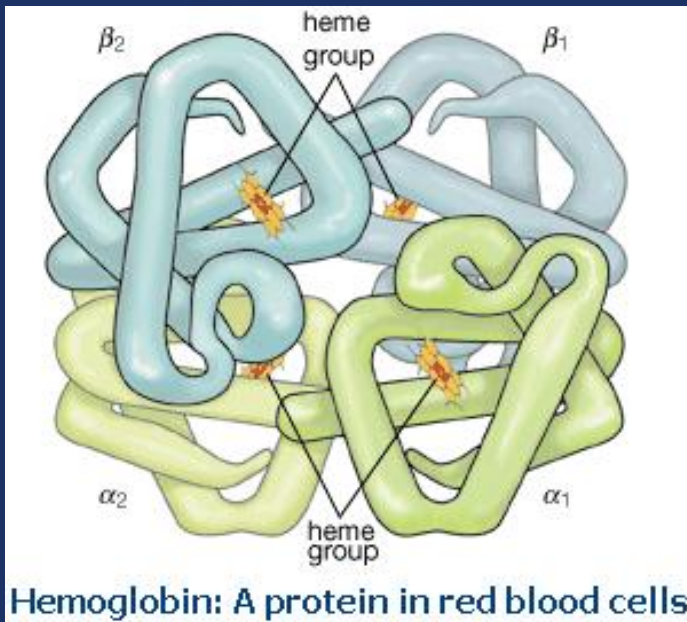
- RBC = red blood cells
- Hb= hemoglobin
- MCV = mean cell volume
- SD = standard deviation

Hemoglobin

- Tetramer of 4 globin chains (proteins)
- Each with a heme group containing iron
- Can be distinguished by electrophoresis

Chain types

Alpha– Beta – Gamma – Delta
(Zeta and epsilon)



Types of Hb in Older Children and Adults

Hemoglobin Type	Designation	Amount %	
		At birth	> 1 year
Fetal	HbF ($\alpha_2 \gamma_2$)	60 to 85	0 to 2
Adult (major)	HbA ($\alpha_2 \beta_2$)	15 to 40	96 to 98
Adult (minor)	HbA ₂ ($\alpha_2 \delta_2$)	1	1-3

Hemoglobin

- Oxygen carrier to tissues
- Major constituent of RBC
- Function of RBC dependent on
 - Membrane
 - Enzyme stability
 - Hemoglobin content

RBC

- Made in the bone marrow
- Lifespan about 120 days
- Cleared by the reticuloendothelial cells (mainly spleen)
- If there is a bone marrow production problem Hb will drop about 1 g/L per day
- If the rate of drop is faster than that then the anemia must be due to blood loss, sequestration, or hemolysis

Anemia

- Defined as Hb greater than 2 SD below the mean value for age
- Hemoglobin normal ranges vary by age
- Can also be defined physiologically by the Hb level below which oxygen delivery is impaired to tissues

Microcytosis

- Greater than 2 SD below the mean MCV for the patient's age

Age	Hb mean g/L (-2 SD)	MCV mean (fL) (-2 SD)
Birth	165 (135)	108 (98)
1 to 3 days	185 (145)	108 (95)
2 weeks	166 (134)	105 (88)
1 month	139 (107)	101 (91)
2 months	112 (94)	95 (84)
6 months	126 (111)	76 (68)
6 to 24 months	120 (105)	78 (70)
2 to 6 years	125 (115)	81 (75)
6 to 12 years	135 (115)	86 (77)
12 to 18 year male	145 (130)	88 (78)
12 to 18 year female	140 (120)	90 (78)
Adult male	155 (135)	90 (80)
Adult female	140 (120)	90 (80)

Mechanisms of Anemia

- Decreased bone marrow production
- Increased red cell destruction (hemolysis)
- Increased red cell loss (bleeding)

Workup of Anemia

- History
 - Blood loss
 - Family history
 - Recent illnesses
 - medications

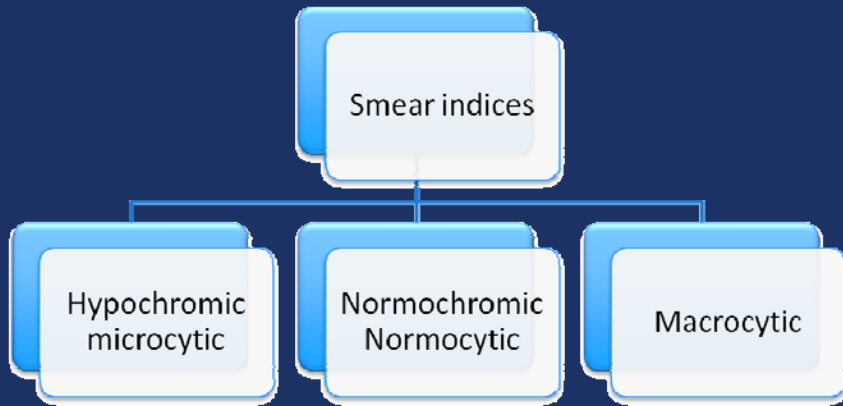
Workup of Anemia- cont'd

- Physical Exam
 - Pallor
 - Jaundice
 - Hepatosplenomegaly
 - Lymph nodes
 - Other signs of chronic illness

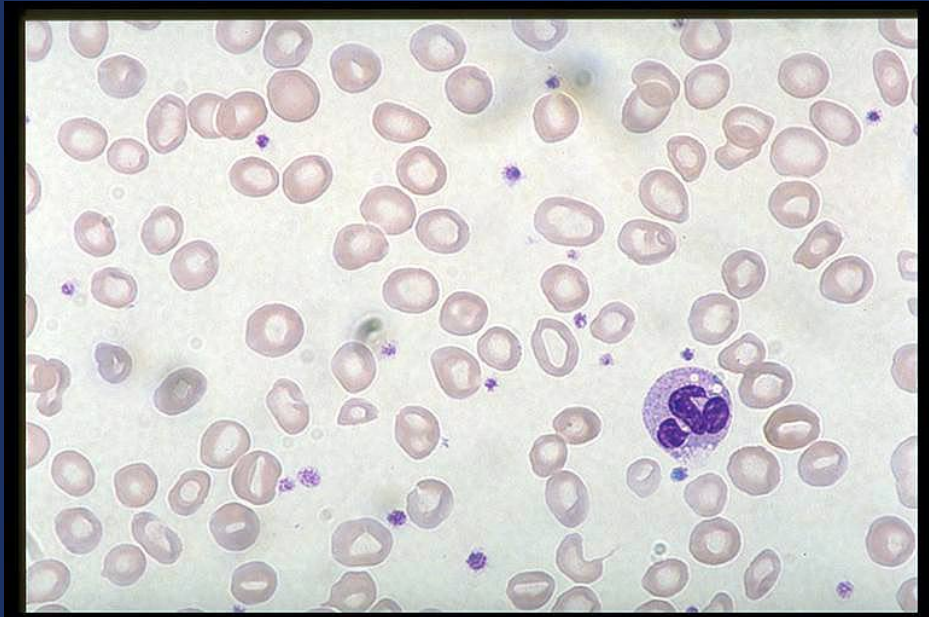
Workup of Anemia- cont'd

- Basic Labs
 - CBC with retic count
 - Evaluation of the blood film
 - Ferritin (especially if microcytic anemia is present)
- Other tests
 - Signs of hemolysis- bilirubin (total and direct), LDH, haptoglobin
 - Urinary hemosiderin
 - Hemoglobinopathy evaluation
 - Hemoglobin electrophoresis, A2 and F levels

Approach to Anemia



Hypochromic Microcytic Anemia



HypochromicMicrocytic Anemia

- Causes
 - Iron deficiency- most common and must be ruled out first
 - Thalassemia syndromes
 - Hemoglobinopathies
 - Hemoglobin E
 - Hemoglobin Lepore
 - Sideroblasticanemias
 - Congenital and acquired (lead)
 - Anemia of chronic disease

Thalassemia Syndromes

- Alpha thalassemia
 - Trait
 - Intermedia
- Beta thalassemia
 - Trait
 - Intermedia
 - major

Alpha Thalassemia Findings

Disorder	Genotype	MCV	Anemia
Silent carrier	$\alpha\alpha/\alpha-$	normal	none
trait	$\alpha\alpha/--$ $\alpha-/ \alpha-$	low	mild
Hb H	$\alpha-/--$	low	moderate
hydrops	$--/--$	low	fatal

Alpha Thalassemia

- Note that you can not make the diagnosis of alpha thalassemia trait on Hb electrophoresis
- Diagnosis is suspected on history and lab findings but must be confirmed by molecular PCR testing

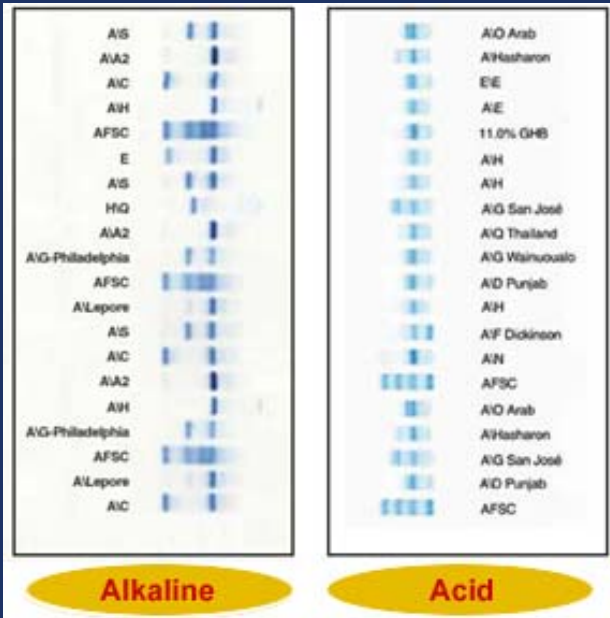
Beta Thalassemia Findings

Disorder	Genotype	MCV	Anemia
Silent carrier	β/β^+	low	mild
trait	β/β_0	low	mild
intermedia	β^+/β^+	low	moderate
major	β_0/β_0	low	severe

Beta Thalassemia

- Note that beta thalassemia trait can be diagnosed with hemoglobin electrophoresis
- Diagnosed by elevated hemoglobin A2 levels

Hemoglobin Electrophoresis



Hemoglobin E

- Glutamine to lysine mutation at position 26 of the beta globin gene
- Results in a thalassemia-trait type picture

Hemoglobin Lepore

- Uneven crossover between delta and beta globin genes
- Results in a thalassemia-trait type picture

Other causes of microcyticanemias

- Sideroblasticanemias
 - Defect in the heme synthesis pathway
 - Congenital
 - Lead poisoning
 - Acquired (toxin exposures)
- Anemia of chronic disease
 - Usually causes normocytic anemia but can sometimes cause microcytic anemia

Conclusion

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