How to anemia when it’s not iron deficiency

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Hematologist

What I will be discussing

- Hematologist's approach to anemia
- Low MCV anemia vs. high MCV anemia
- Autoimmune hemolytic anemia
- Coombs-neg hemolytic anemia
- Sickle cell disease as a cause of anemia

Hematologist's view of anemia

- Iron deficiency
  - Chronic bleeding
    - GYN
    - GI tract
    - GU tract

    (r/o malignancy)
  - Iron malabsorption
    - GI tract surgery
    - Autoimmune disease

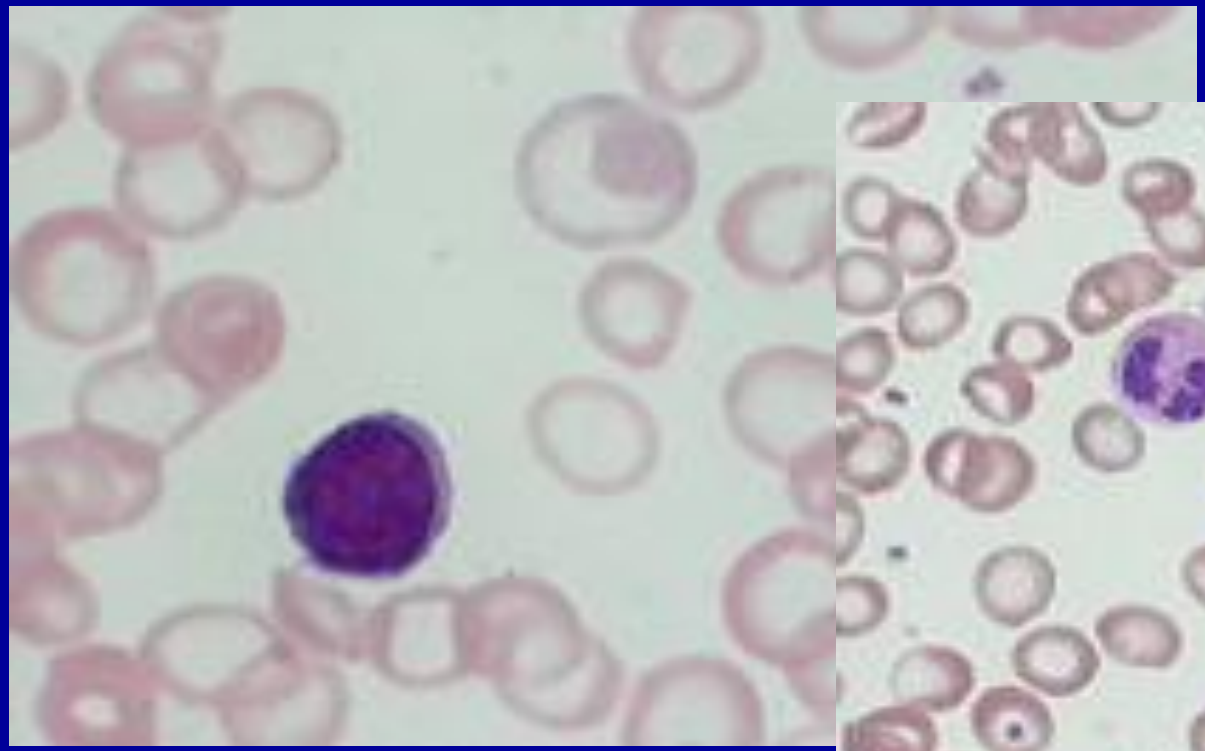
- Non-iron deficiency
  - Low MCV alpha thal
  - High MCV
    - B12/folate
    - Liver dysfunctiojn
    - Hypothyroidism
    - Meds-antibiotics
  - Production problem
    - Anemia of chronic dz
    - Epo deficiency CKD
  - Destruction problem
    - Autoimmune (AIHA)
    - Non-autoimmune
  - Heme malignancy
    - Myeloma, lymphoma, MDS, MPD, leukemia

Question 2: Low MCV vs. High MCV

MCV < 80	MCV > 100
Hgb synthesis problems --Iron-deficiency absolute iron deficiency functional iron deficiency "anemia of chronic disease" --"Thalassemia" alpha thalassemia beta thalassemia "thalassemia major"	DNA synthesis problems Drugs (cancer/HIV drugs) Vitamin B12 deficiency Folate deficiency malnutrition, malabsorption seizure meds alcohol dependence Hypothyroidism Liver disease, hypersplenism High retic counts

RBC size on a blood smear

"Microcytic"



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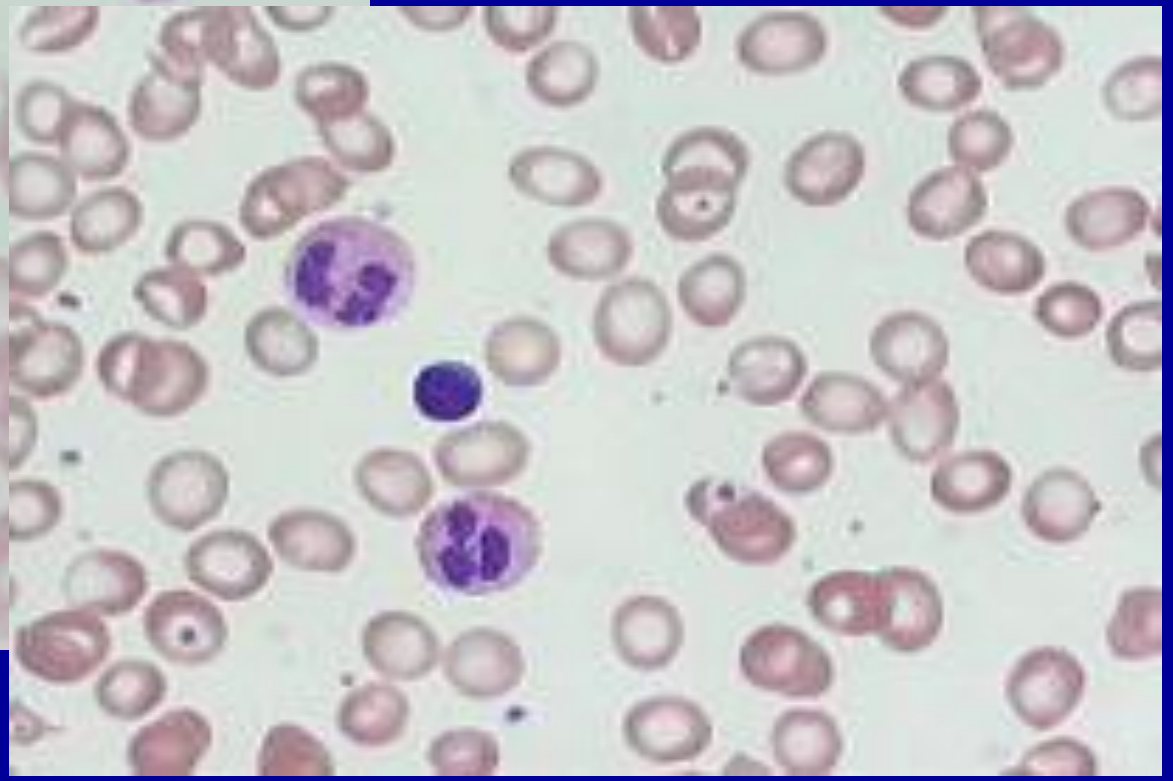
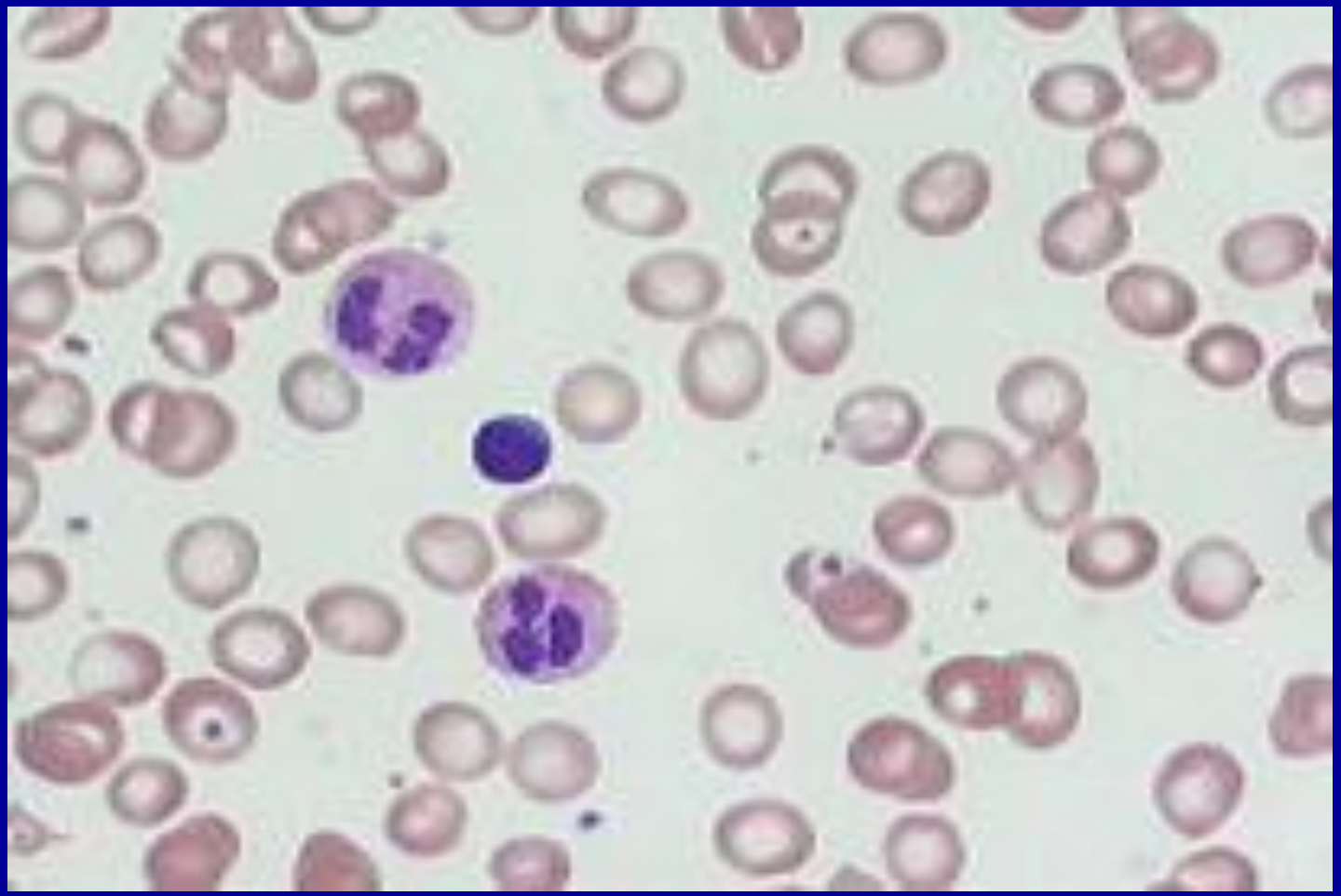


“Macrocytic” anemia



Question 2: What is the MCV?

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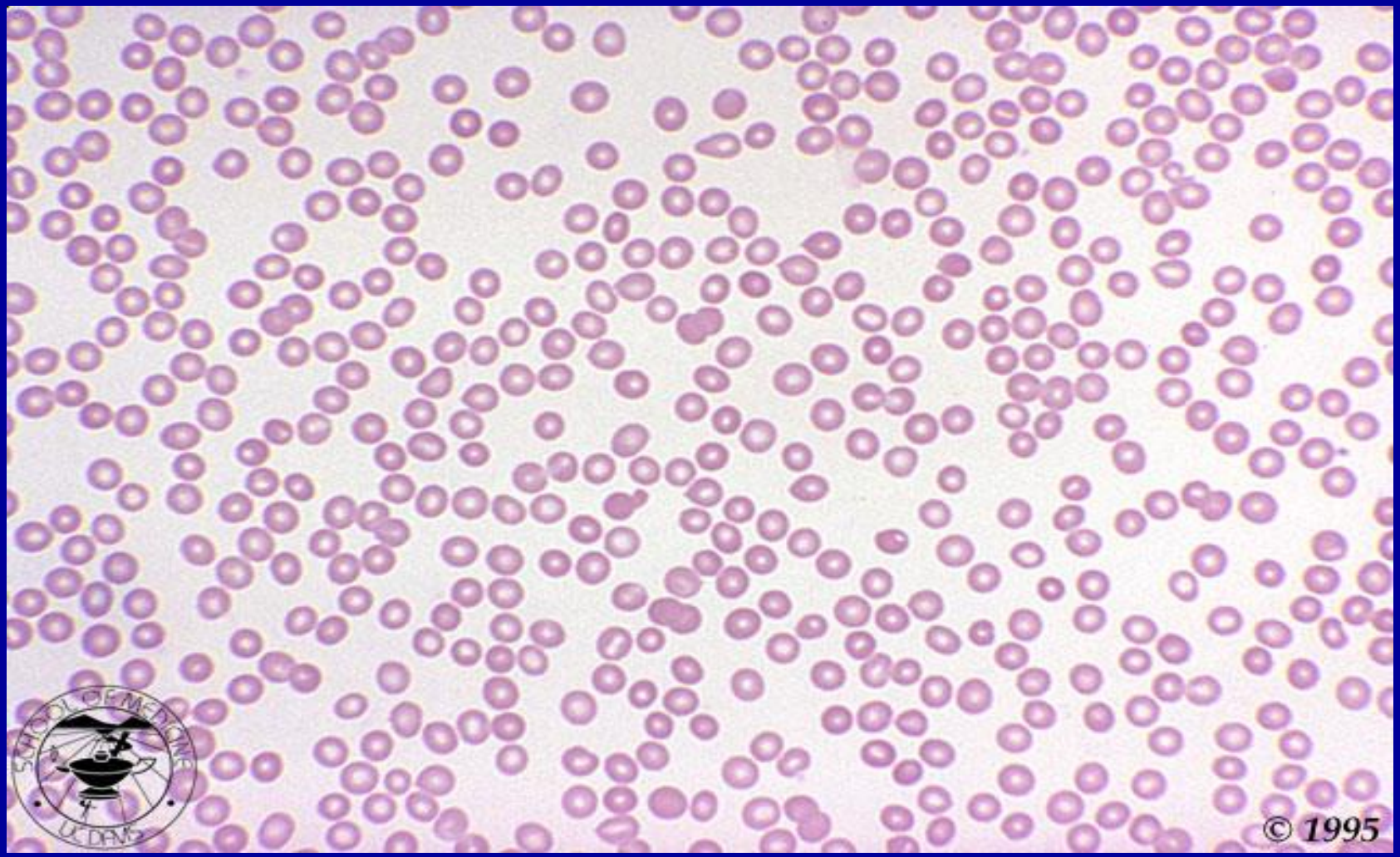
Question 3: RBC problem vs. RBC consumption/destruction?

- Low retic means production problem
- High retic means “destruction” problem
- High LDH and suggests hemolytic anemia
- Low hapto suggests “intravascular” hemolysis
- DAT=“Direct Coombs” suggests AIHA (autoimmune hemolytic anemia)

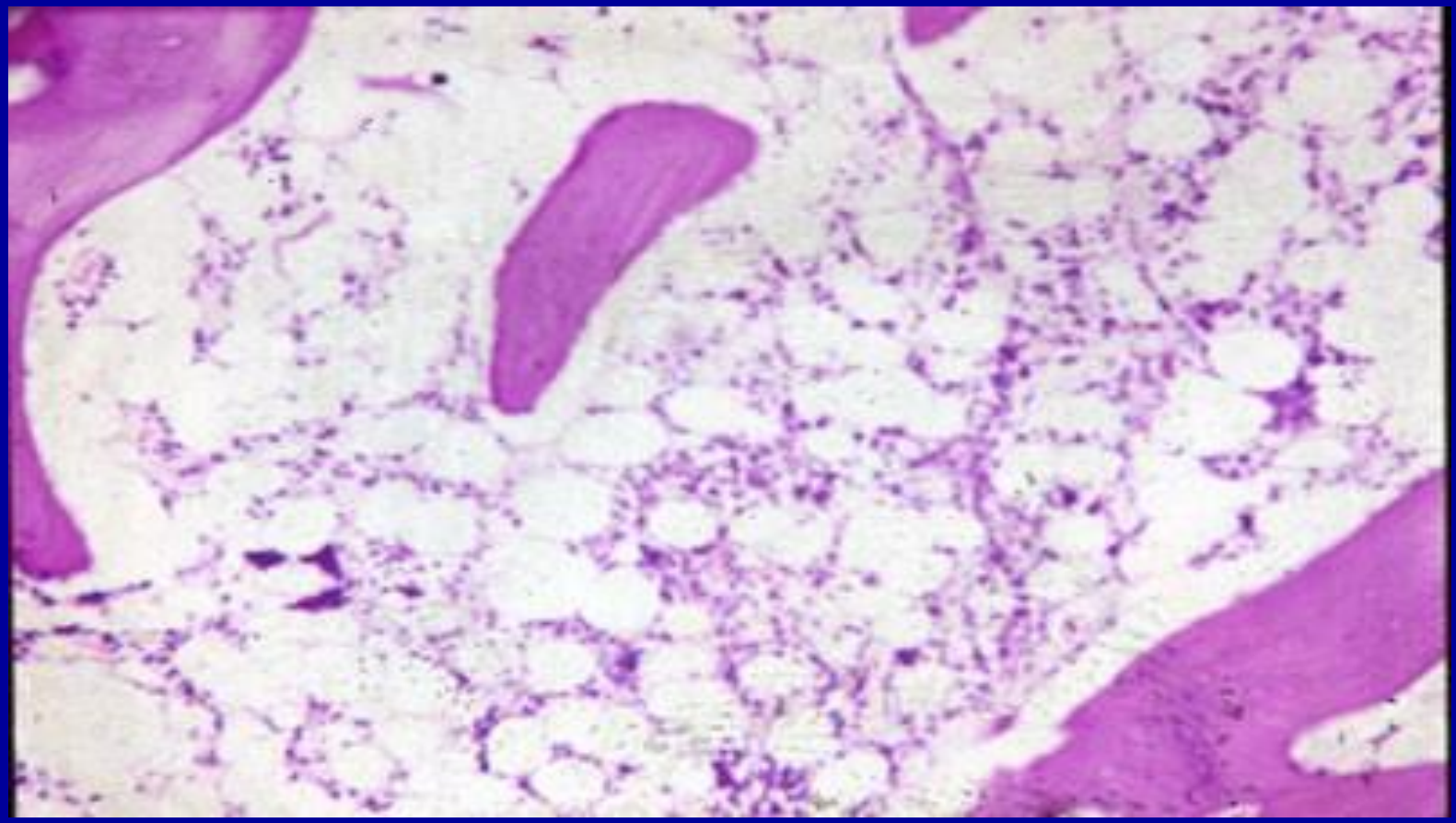
Production or destruction problem?

Production Bone marrow failure	Destruction Hemolytic anemia
Thalassemia Nutrient defic (iron, B12, folate) Drugs, chemotherapy Epo defic (CRI or ESRD) Anemia of chronic disease MDS, Aplastic anemia “Sideroblastic” anemia = MDS	Intravascular RBC membrane Sickle cell disease Microangiopathic: DIC, TTP, HUS Extravascular AIHA, Drug-induced

Aplastic anemia



Aplastic anemia



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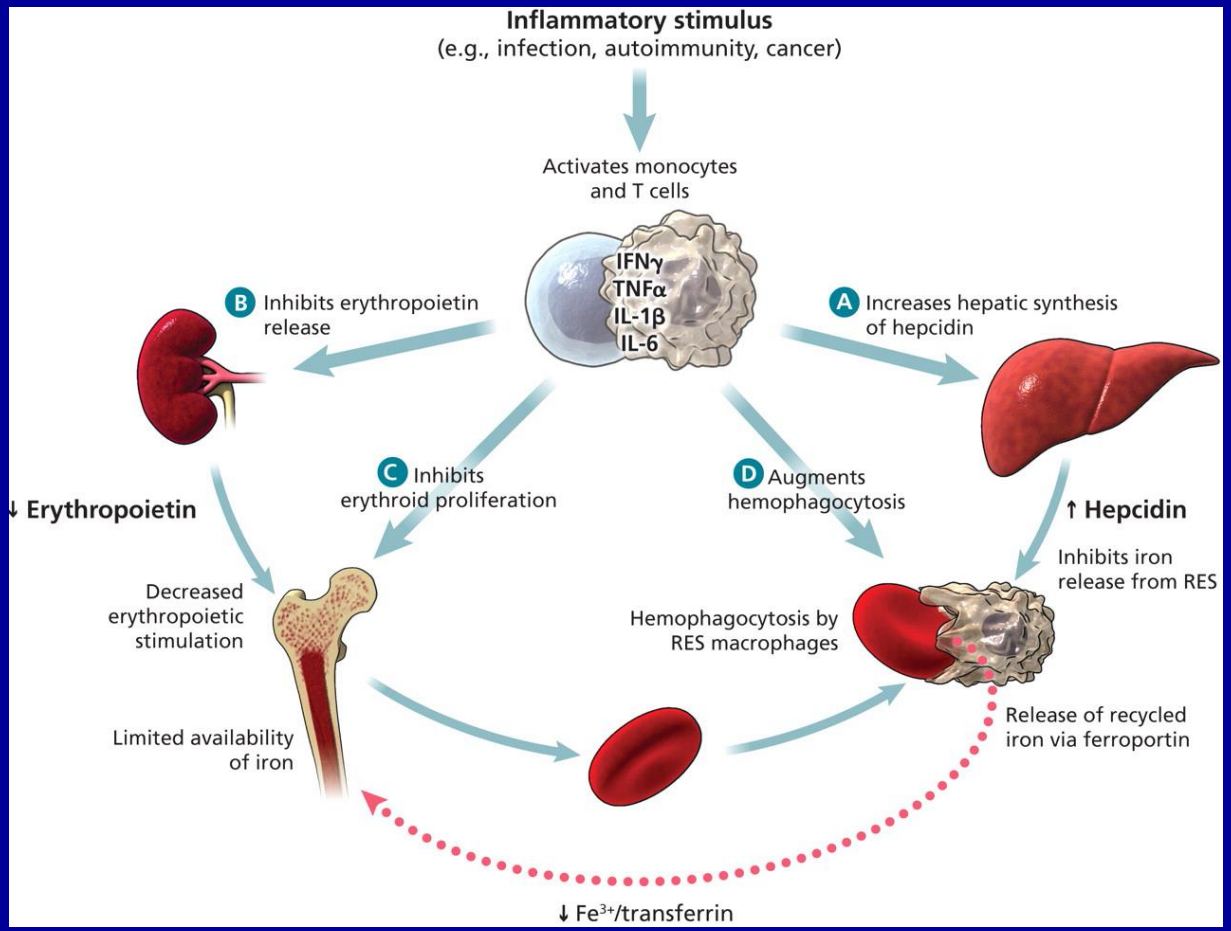
Anemia of chronic disease

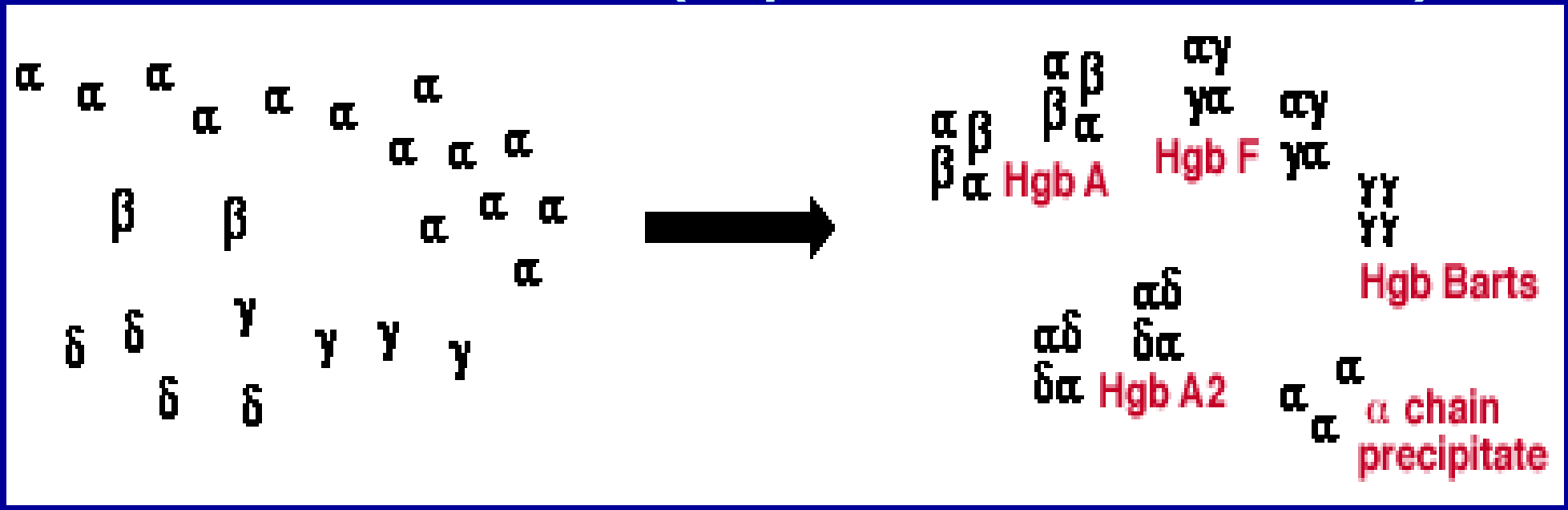
Anemia of chronic disease

	ACD	Fe Defic
Serum Fe	↓	↓
Transferrin	N ↓	↑
% Saturation	↓	↓
Ferritin	N ↑	↓
BM Fe Stores	↑	↓

Anemia of chronic disease

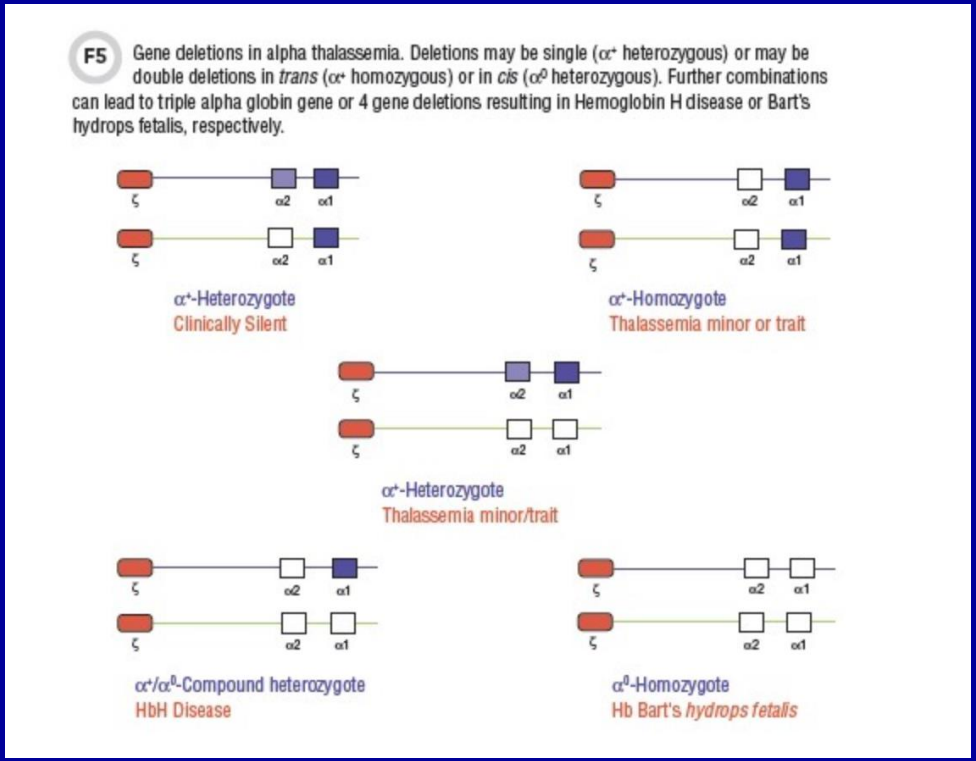


Thalassemia (alpha or beta thal)



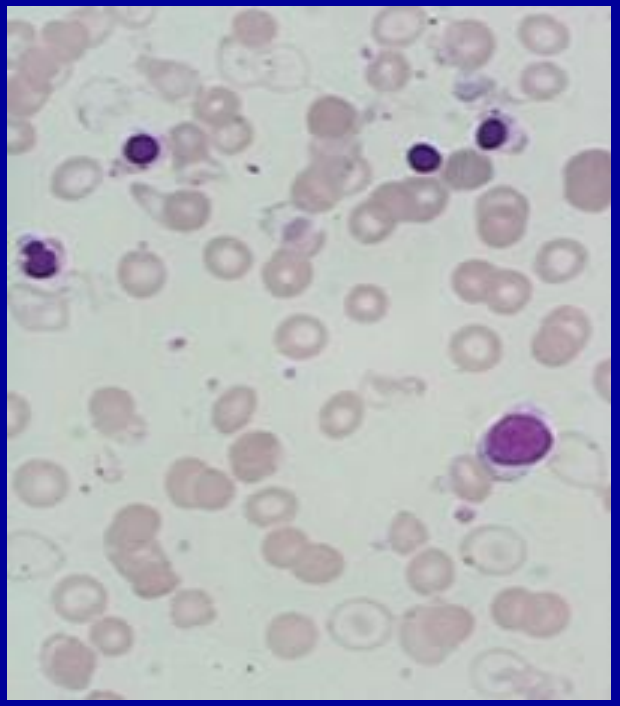
Alpha thalassemia

- Low MCV without iron deficiency
- Can be any ethnicity
- Can be inherited together with sickle or beta thalassemia
- This can be a guessed diagnosis (non-iron deficient low MCV)
- The only diagnostic test is gene sequence analysis
- NOT tested in Hemoglobin electrophoresis
- but sickle trait-alpha thal has a charateristic pattern on Hgb electro
- The main problem with alpha thal is the confusion with iron deficiency



Beta thalassemia

- Beta thal “minor”
  - No need for transfusions
- Beta thal “intermedia”
  - Occasional transfusion
- Beta thal “major”
  - Transfusion-dependent
- Iron overload/need for chelation
- Mediterranean descent
- Diagnosed by hemoglobin electrophoresis
- (alpha thal is different)



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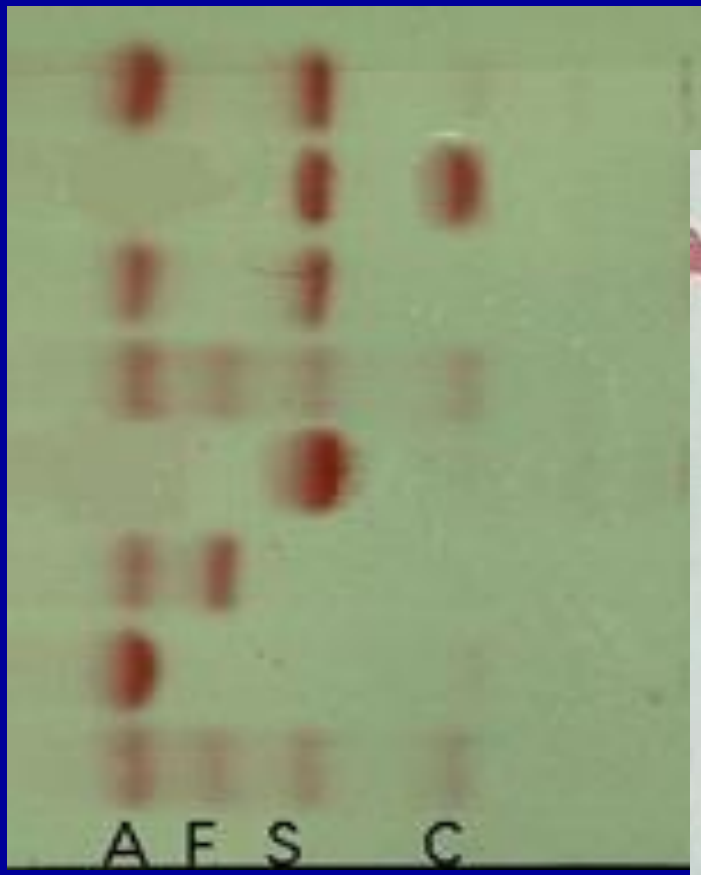
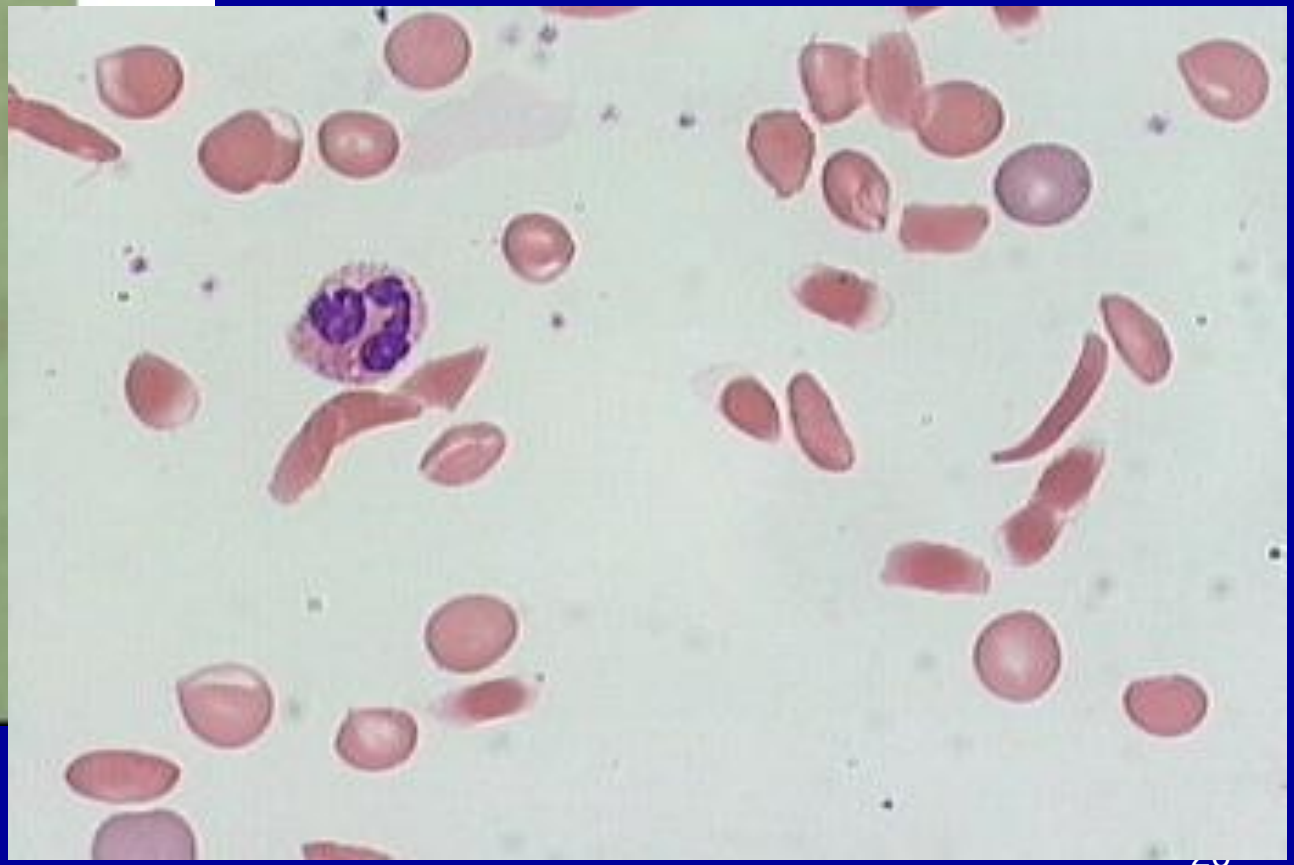
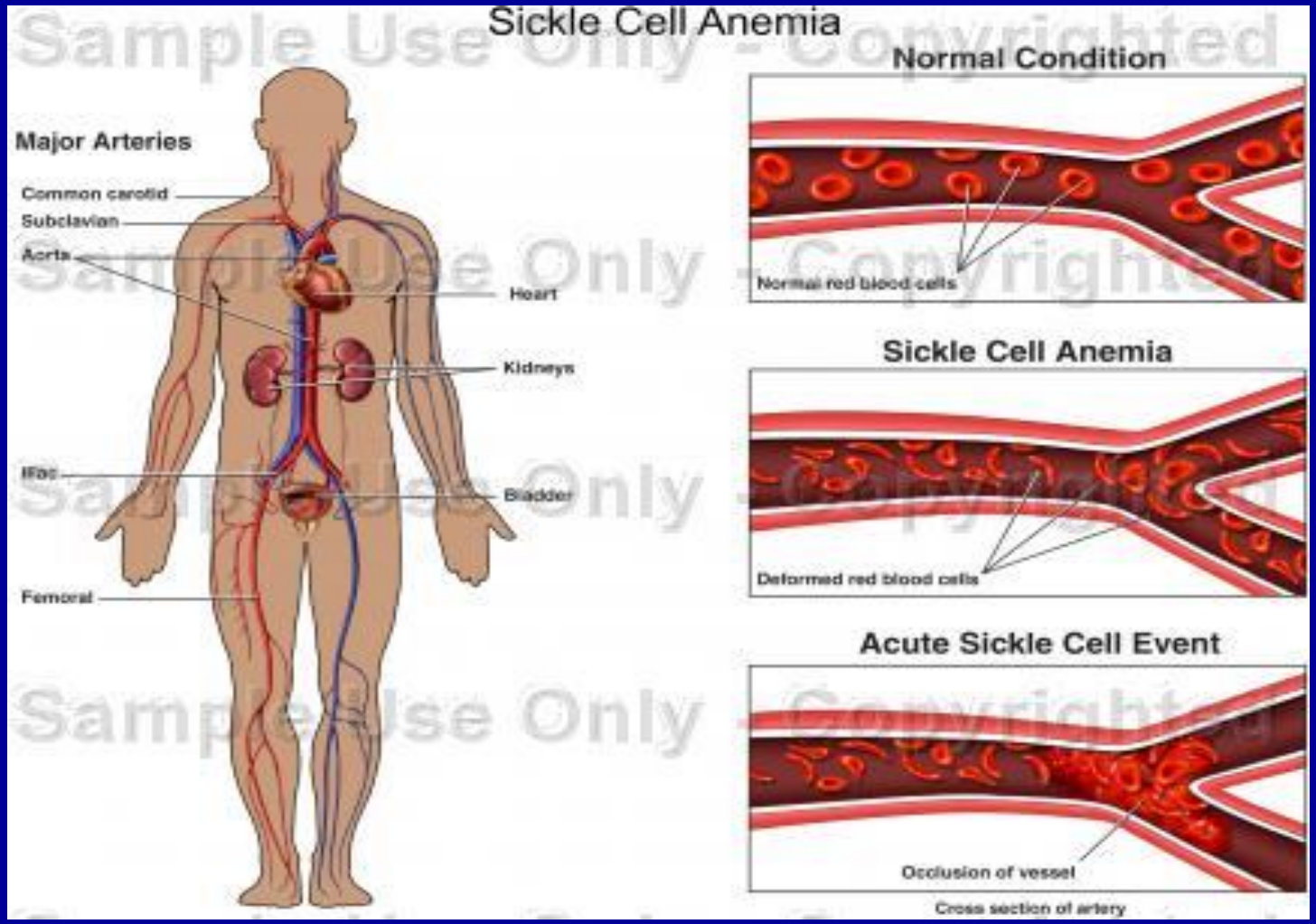
Sickle cell disease

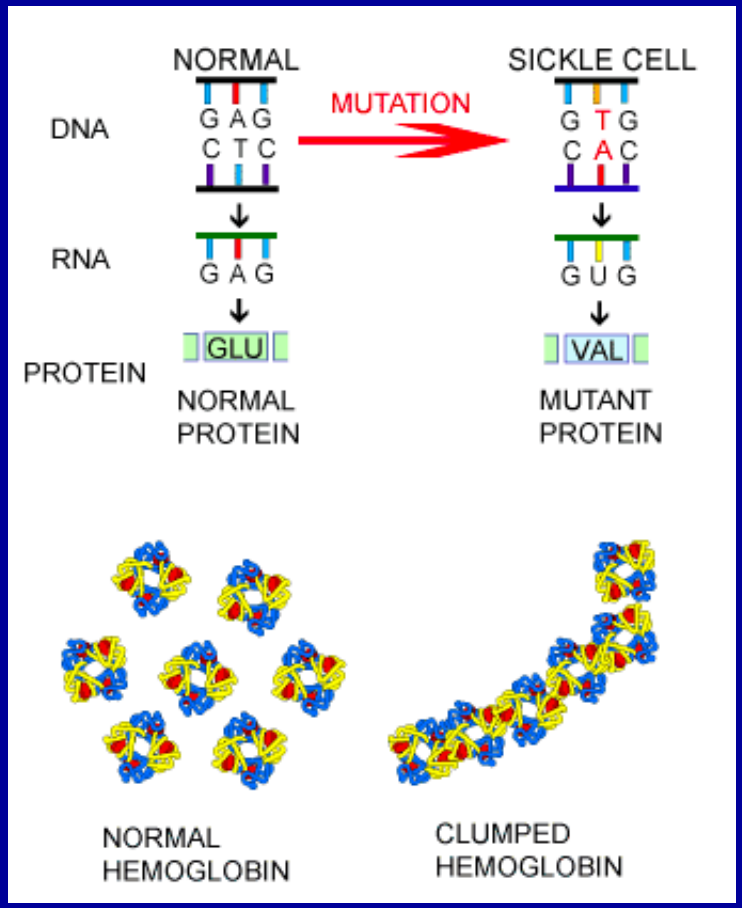


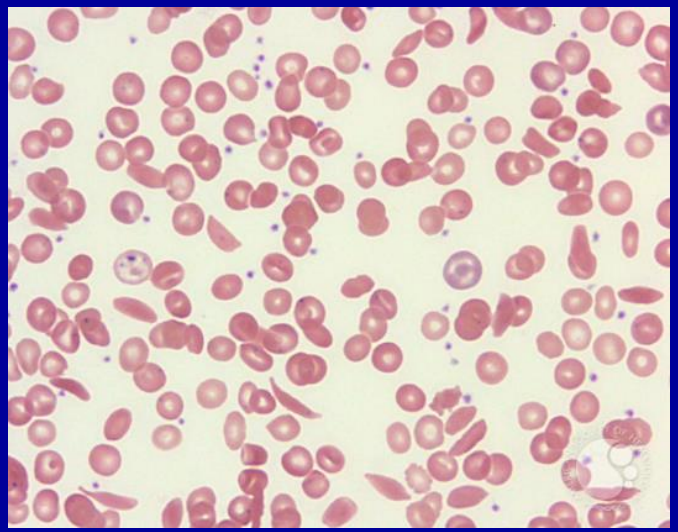


Sickle cell disease



How Sickle Cell Disease Occurs





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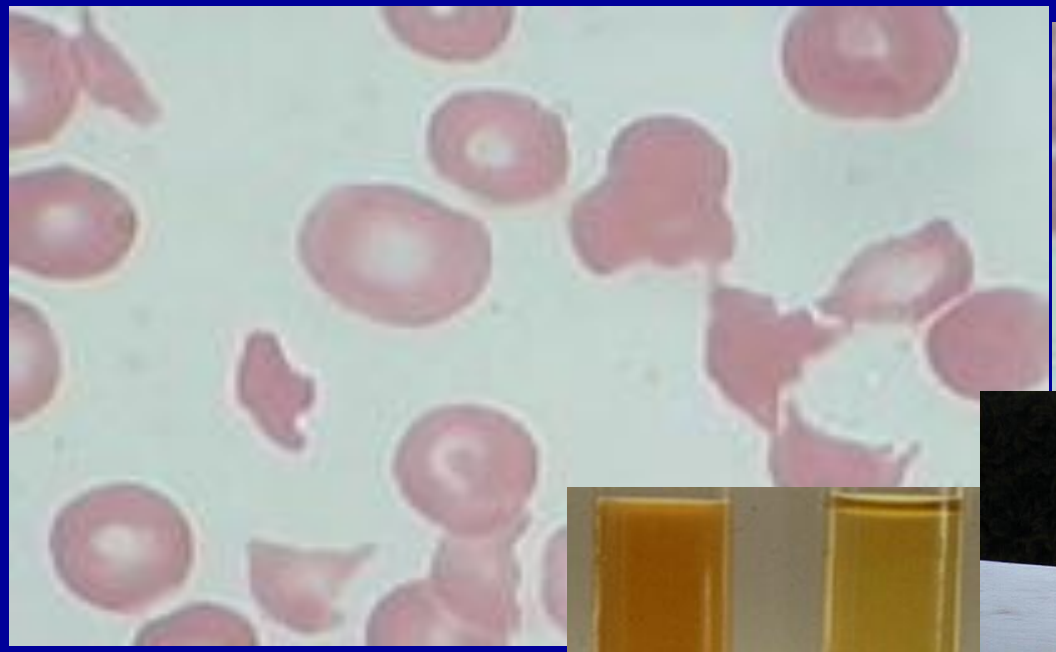
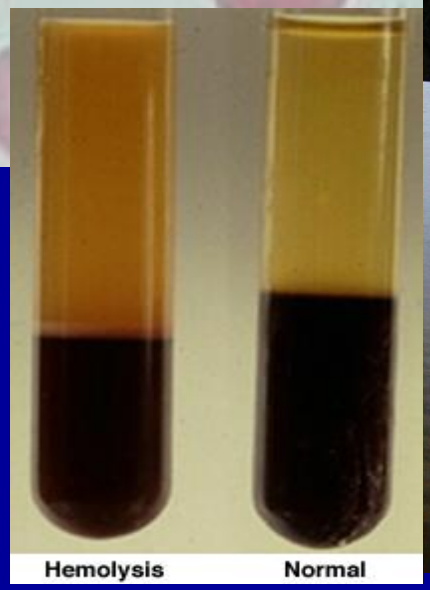
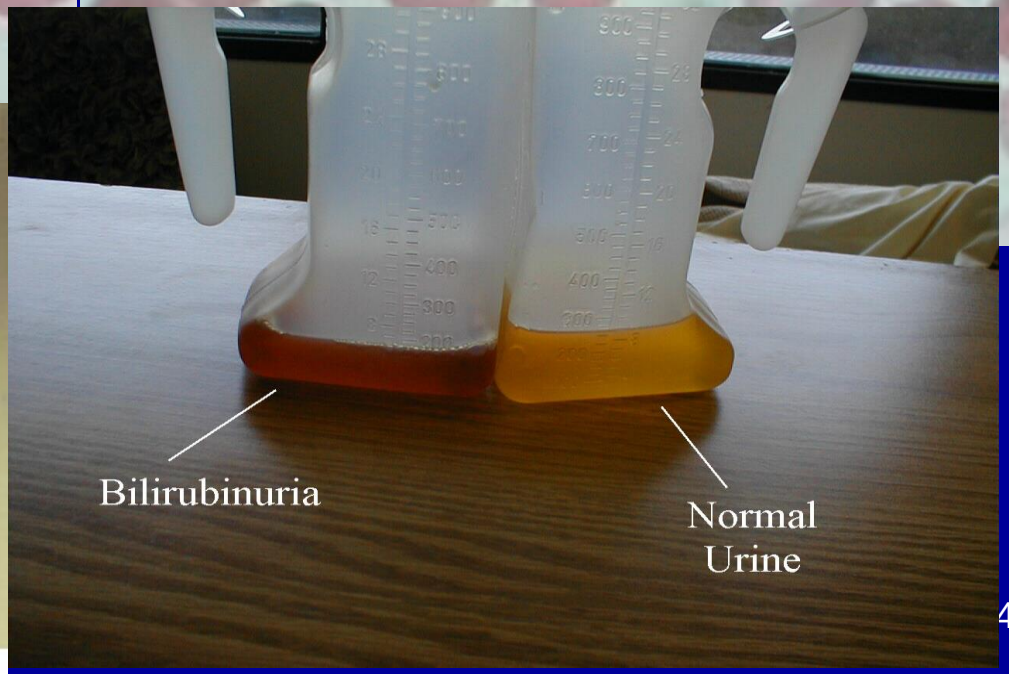
Hemolytic anemia

Intravascular





Extravascular (AIHA)



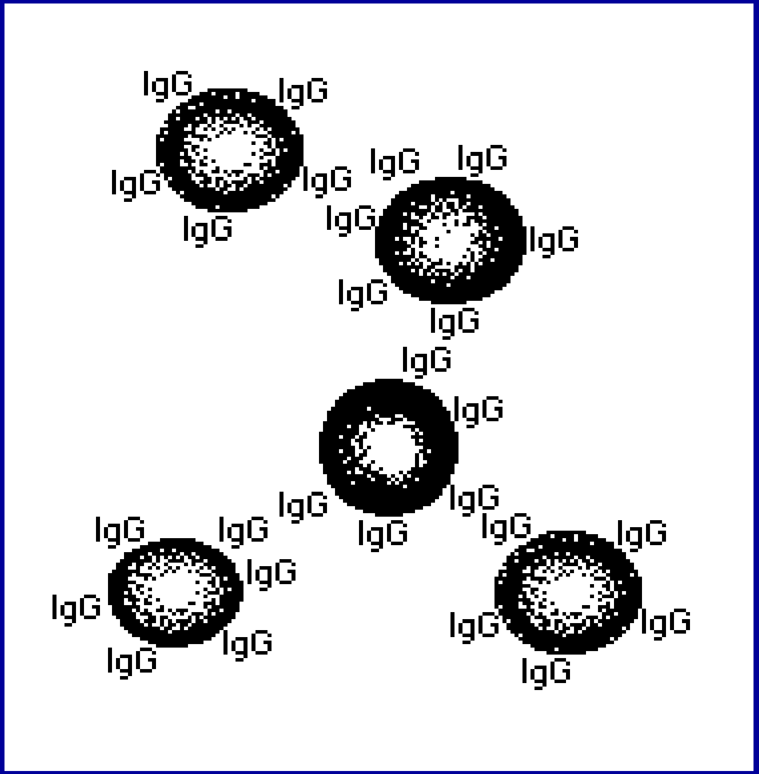
Hemolytic anemia

- **Intravascular**
- smear: schistocytes
- haptoglobin: low
- Urine heme: present
- DAT: negative
- LDH: high

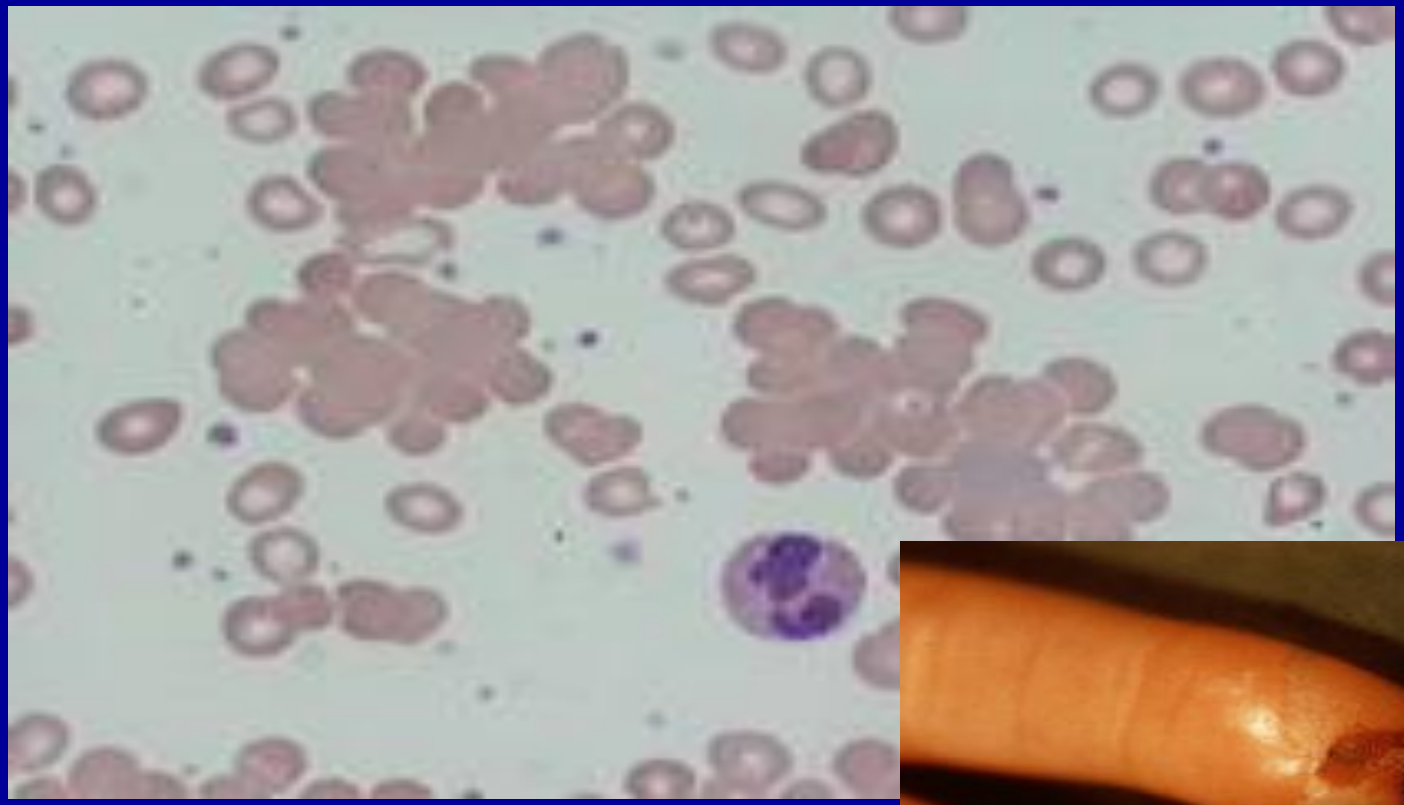
- **Extravascular** (AIHA)
- spherocytes
- Haptoglobin: nl
- Urine heme: absent
- DAT: positive
- LDH: high

Causes of AIHA

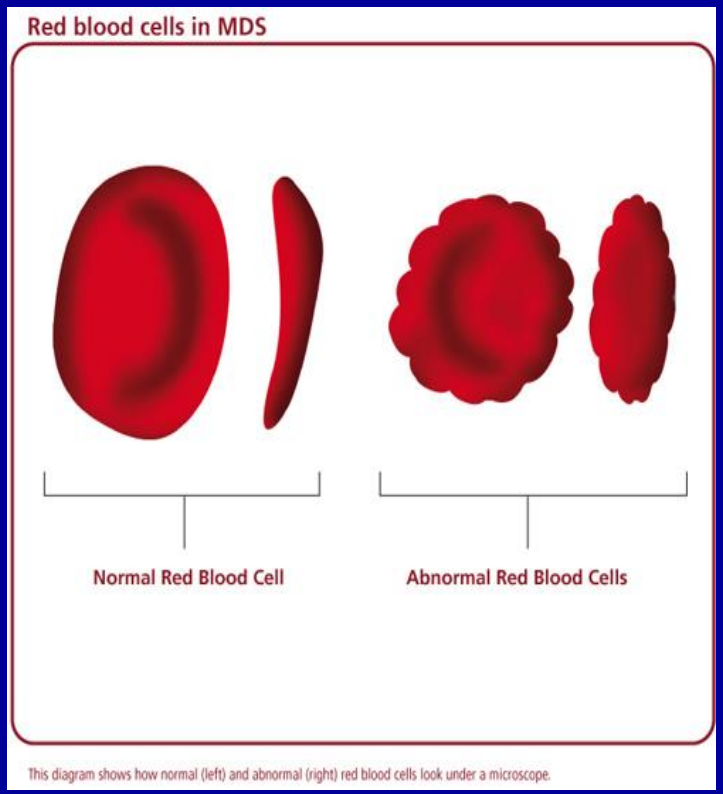
- Autoimmune disease (lupus, RA)
- Hematologic malignancies
  - CLL, Non-Hodgkins Lymphoma
- Drugs (methyldopa)
- Cold agglutinins (complement)
  - mycoplasma, EBV, NHL
- "Idiopathic"

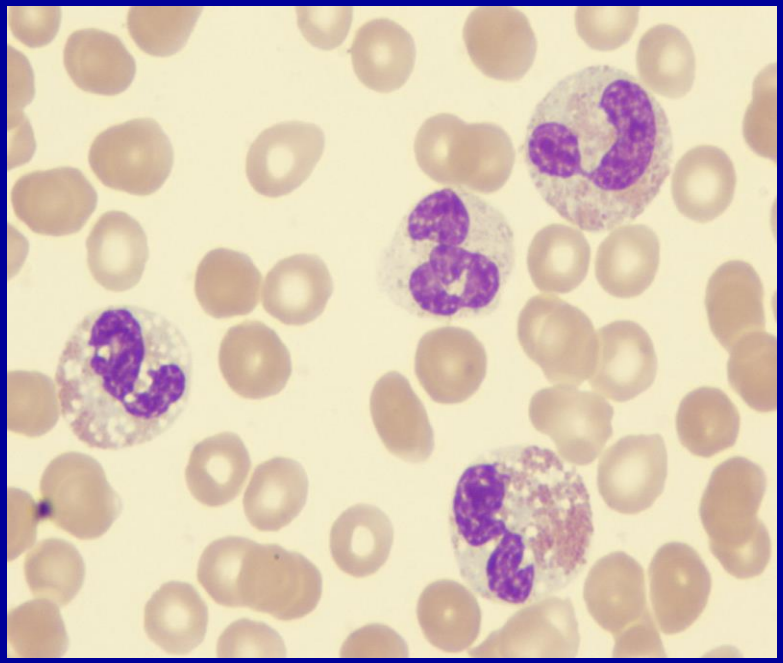


Cold Agglutinin Disease (cold-antibody AIHA)



Myelodysplastic syndrome (MDS): Anemia and RBC dysfunction





Case 1

- 72yo man with fatigue over several weeks
- Denies blood loss
- Soc: lives alone, cooks for himself
- Exam: P 90 SBP 110 not orthostatic
- Data: Hgb 5.3 HCT 15 MCV 122
  - WBC 4.1 Plt 125 Retic 1% TB 1.9 LDH 2750

- What is the most likely cause of anemia?
- Answer: ?

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- What is the most likely cause of anemia?
- Answer: Vitamin B12 deficiency

Case 2

- 64yo woman with progressive dyspnea for the past few weeks
- Soc: formerly alcohol dependent
- Data: HGB 5.1 HCT 15 MCV 112
  - WBC 4.6 Plt 109,000 RDW 21

- What is the most likely cause of anemia?
- Answer: ?

Case 2

- 64yo woman with progressive dyspnea for the past few weeks
- Soc: formerly alcohol dependent
- Data: HGB 5.1 HCT 15 MCV 112
  - WBC 4.6 Plt 109,000 RDW 21

- What is the most likely cause of anemia?
- Answer: Folate deficiency

Case 3

- 71yo man with dyspnea and cough 3 mos
- Blood on toilet paper attrib hemorrhoids
- PMH: TB treated during 1950's
- Exam: RUL crackles
- Data: Hgb 11 HCT 33 MCV 83
  - Ferr 188 Fe 18 TIBC 196 = 9% saturation

- What is the most likely cause of anemia?
- Answer: ?

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- What is the most likely cause of anemia?
- Answer: iron deficiency AND chronic disease

Case 4

- 47yo woman comes to clinic asking for her iron sulfate prescription to be rewritten
- Took iron for 20 years (since pregnancy)
- Menses “regular” with “moderate” flow
- Vegetarian but eats eggs and dairy
- FHx: mother took iron pills
- Data: Hgb 11 HCT 33 MCV 72
  - Ferr 166 Fe 84 TIBC 260 = 32% sat
- Answer: ?

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- Vegetarian but eats eggs and dairy
- FHx: mother took iron pills
- Data: Hgb 11 HCT 33 MCV 72
  - Ferr 166 Fe 84 TIBC 260 = 32% sat
- Answer: anemia caused by alpha thalassemia

Case 5

- 30yo AA man with no prior health problems now with post-op DVT & PE
- Exam: mild scleral icterus, splenomegaly
- Data: Hgb 10 HCT 30 MCV 75
  - TB 3 LDH 300
  - Target cells seen on blood smear
- What is the most likely diagnosis?

Case 5

- 30yo AA man with no prior health problems now with post-op DVT & PE
- Exam: mild scleral icterus, splenomegaly
- Data: Hgb 10 HCT 30 MCV 75
  - TB 3 LDH 300
  - Target cells seen on blood smear
- What is the most likely diagnosis?

  Answer: Sickle cell disease variant

Case 6

- 18yo man with no prior health problems now presenting with yellow eyes
- Exam: scleral icterus, spleen tip palpable
- Data: Hgb 14 HCT 38 MCV 84
  - Retic 2.2% TB 3.1 DB 0.4 AST 49 LDH 480

- What is the most likely cause of anemia?
- Answer: ?

Case 6

- 18yo man with no prior health problems now presenting with yellow eyes
- Exam: scleral icterus, spleen tip palpable
- Data: Hgb 14 HCT 38 MCV 84
  - Retic 2.2% TB 3.1 DB 0.4 AST 49 LDH 480

- What is the most likely cause of anemia?
- Answer: autoimmune hemolytic anemia

What we've discussed

- Organized anemia evaluation
  - Bleeding?
  - MCV?
  - Production/destruction?
- Hematologist's perspective of anemia
  - Iron deficiency anemia
  - Non-iron deficiency anemia

Reddy the Blood Drop Says...

GIVE BLOOD, GIVE LIFE !

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