Hematology

- Histology
- Biochemistry
- Pathology
- Pharmacology
- Physiology
- Microbiology

Dr. name : Dr. Tariq Aladily

lecture number :

RBC diseases

Done BY :

- Handout
- Sheet
- Slide 1

By: Amer Abu Shanab

Hematopathology Course

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- 3rd floor, Hematology Lab
- Office hours: Thursday 12-1
- Reference: Robbins Basic Pathology 9th ed

RBC DISORDERS

Anemia

Definition

- Reduction of total RBC MASS below normal amount
- Reduction of oxygen carrying capacity of the blood
- Leads to tissue hypoxia
- Practically, measure by Hemoglobin concentration (g/dL), and Hematocrit (ratio of packed RBCs to total blood volume)

Classification according to cause

Increased destruction

(hemolytic anemia)

Extrinsic factors (infection, antibody, mechanical)

Intrinsic RBC abnormalities:

1) Hereditary (membrane, enzyme, Hg abnormalities)
2) Acquired (Paroxysmal nocturnal hematuria)

Diminished Erythropoiesis

- Iron deficiency anemia
- Megaloblastic anemia
- Aplastic anemia
- Pure red cell aplasia
- Myelophthisic anemia
- Myelodysplastic syndrome

Blood loss

Classification according to morphology

1) **Hypochromic microcytic anemia**

Iron deficiency, thalassemia, anemia of chronic disease, sideroblastic anemia

2) **Normochromic normocytic anemia**

Anemia of chronic disease, some hemolytic anemias

3) **Macrocytic anemia**

Megaloblastic anemia, myelodysplastic syndrome, hypothyroidism

- **Shape:** anisopoikelocytosis, measured by RBCs distribution width (RDW)
- Hypochromic microcytic anemia usually reflects impaired Hg synthesis
- Macrocytic anemia reflects stem cell disease and maturation

A-LAB 0004

Lab. Request Form

مستشفى الجامعة الأردنية
Jordan University Hospital

Surname : .....
Forname : .....
Sex : ..... Date of Birth : .....
Hospital No. : .....
Ward / Clinic : .....
Consultant : .....
Address : .....

Lab. Ref. No. : .....
Rec. Date : .....
Rec. Hr. : .....
Charges J. D. Fils
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....

Nature of Specimen / s .....
Date .....
Hr .....
Dr. Sig. .....
.....

Code No.				Result	
C B C 103001	103005	❑	WBC × 12^{12}/L		4.0 - 10
	103004	❑	RBC × 10^9/L		M 5.5 ± 1.0 F 4.8 ± 1.0
	103003	❑	Hemoglobin g/dl		M 16 ± 2 F 14 ± 2
	103003	❑	HCT		M 0.46 ± 0.05 F 0.42 ± 0.05
		❑	MCV fl		80 - 100
		❑	MCH pg / cell		26 - 34
		❑	MCHC g / dl		31 - 36
103006		❑	Platelet × 10^9/L		140 - 440
103011		❑	ESR mm / hr		M 0 - 15 F 0 - 20
103010		❑	Retic. Count		0.005 - 0.015
103009		❑	Eosin. Count t × 10^9/L		0.05 - 0.45
103020		❑	Sickle Cell		Nil
103007		❑	Blood Film		
103025		❑	Malaria Smear		
103031		❑	PT		
103032		❑	PTT		
103033		❑	E G T		

			Result	
103012	❑ Hb. Electrophoresis			
103008	❑ DIFFERENTIAL	Neut - Band %		0
		Neut - Sig. %		40 - 75
		Eosinophil %		1 - 6
		Basophil %		0 - 1
		Lymphocyte %		20 - 45
		Monocyte %		2 - 10

LAB COMMENTS

Date Reported Reported By

HEMATOLOGY I

Clinical features of anemia

- Dizziness
- Fatigue
- Pallor
- Headache
- Hypotension
- Tachycardia
- Tachypnea
- Hemolytic anemia: jaundice, splenomegaly, bone and joint pain, growth retardation

Anemia of acute blood loss

- RBCs are rapidly lost outside circulatory system
- Body responds by shifting fluid from interstitial to intravascular space, anemia worsens by dilution
- Symptoms are related to decreased intravascular volume, might cause cardiovascular shock and death
- Erythropoietin secretion is stimulated, activating BM erythropoiesis
- Mature RBCs as well as Reticulocytes appear in blood after 5 days
- Anemia is normochromic normocytic, with reticulocytosis
- Leukocytosis (secondary to stress)

Anemia of chronic blood loss

- Frequent loss of RBCs
- Occurs when the rate of RBC loss exceeds regeneration
- Iron is lost with RBCs
- Anemia is normochromic normocytic, or hypochromic microcytic

Hemolytic Anemia

- Normally, RBCs age is around 120 days, aged RBCs are engulfed by macrophages in spleen, liver and BM
- Abnormal and premature destruction of RBCs
- Accumulation of Hg degradation products
- Retention of iron
- High erythropoietin, LDH, Retic count
- Secondary increased erythropoiesis
- Extravascular hemolysis: increased phagocytic activity
- Intravascular hemolysis: occurs inside blood vessels

Extravascular Hemolysis

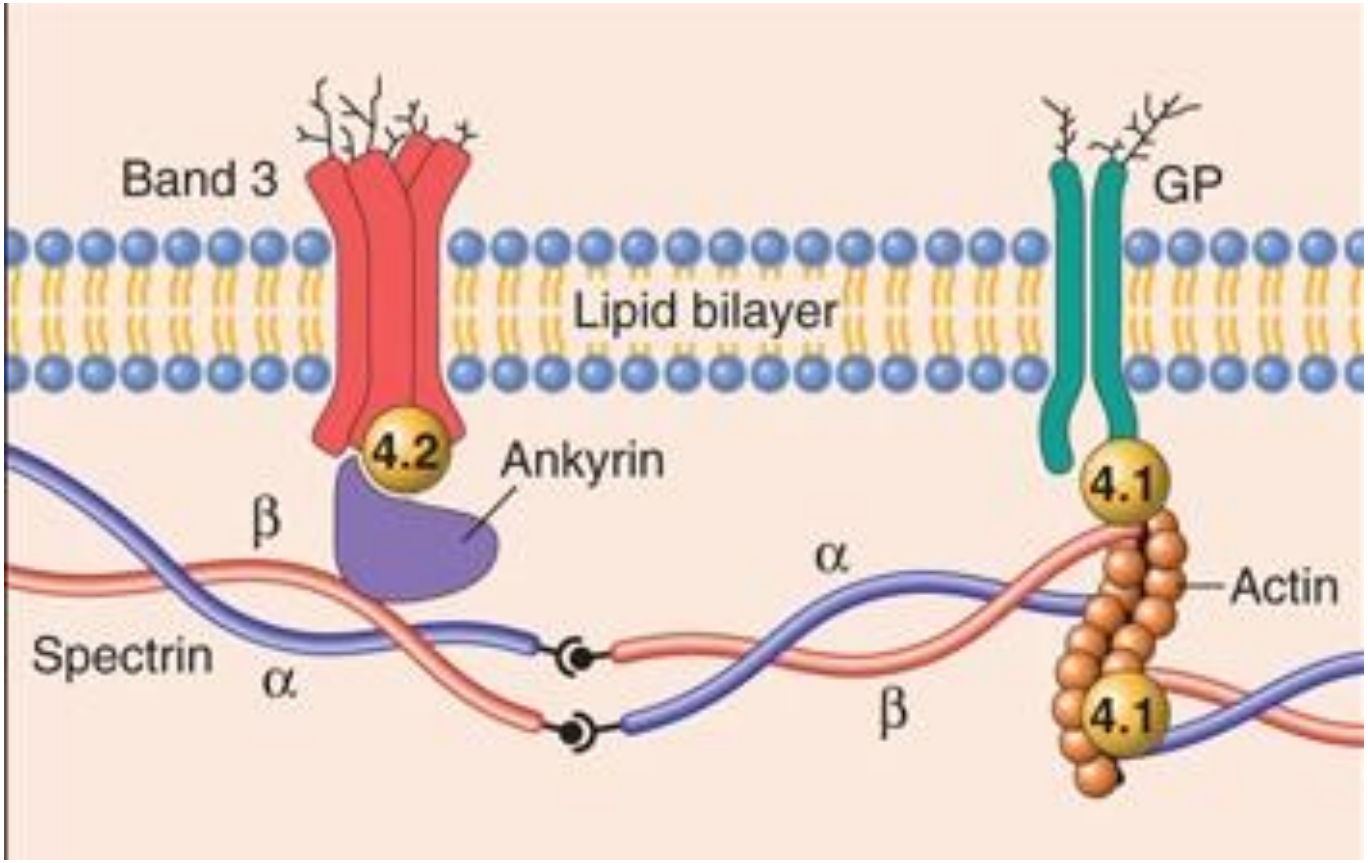
- RBC is less deformable or having abnormal shape
- Abnormal RBC movement in splenic sinusoids
- Attracts histiocytes to engulf abnormal RBCs
- Hg is converted to bilirubin in histiocytes
- Free Hg in serum binds Haptoglobin
- The triad of extravascular HA is: Anemia, splenomegaly and jaundice

Intravascular Hemolysis

- Less common, more severe symptoms
- Caused by mechanical damage, complement fixation, microorganism, exogenous toxins
- Due to large amount of free Hg, haptoglobin is cleared from the serum
- free Hg in serum is oxidized to Methemoglobin, hypoxia
- Excess free Hg and met-Hg are excreted in urine (hemoglobinuria) causing dark urine
- Renal hemosiderosis may occur

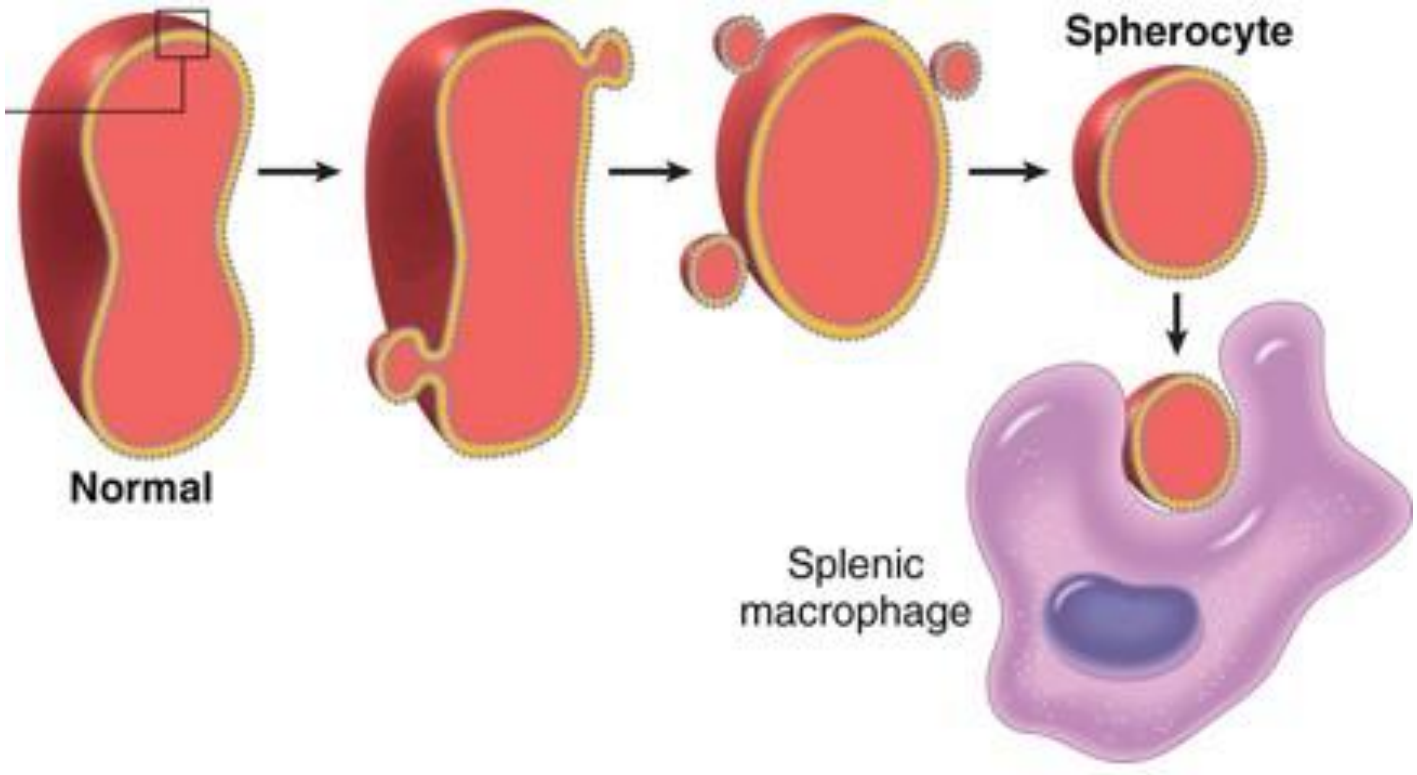
1)Hereditary spherocytosis

- Etiology: frameshift mutation



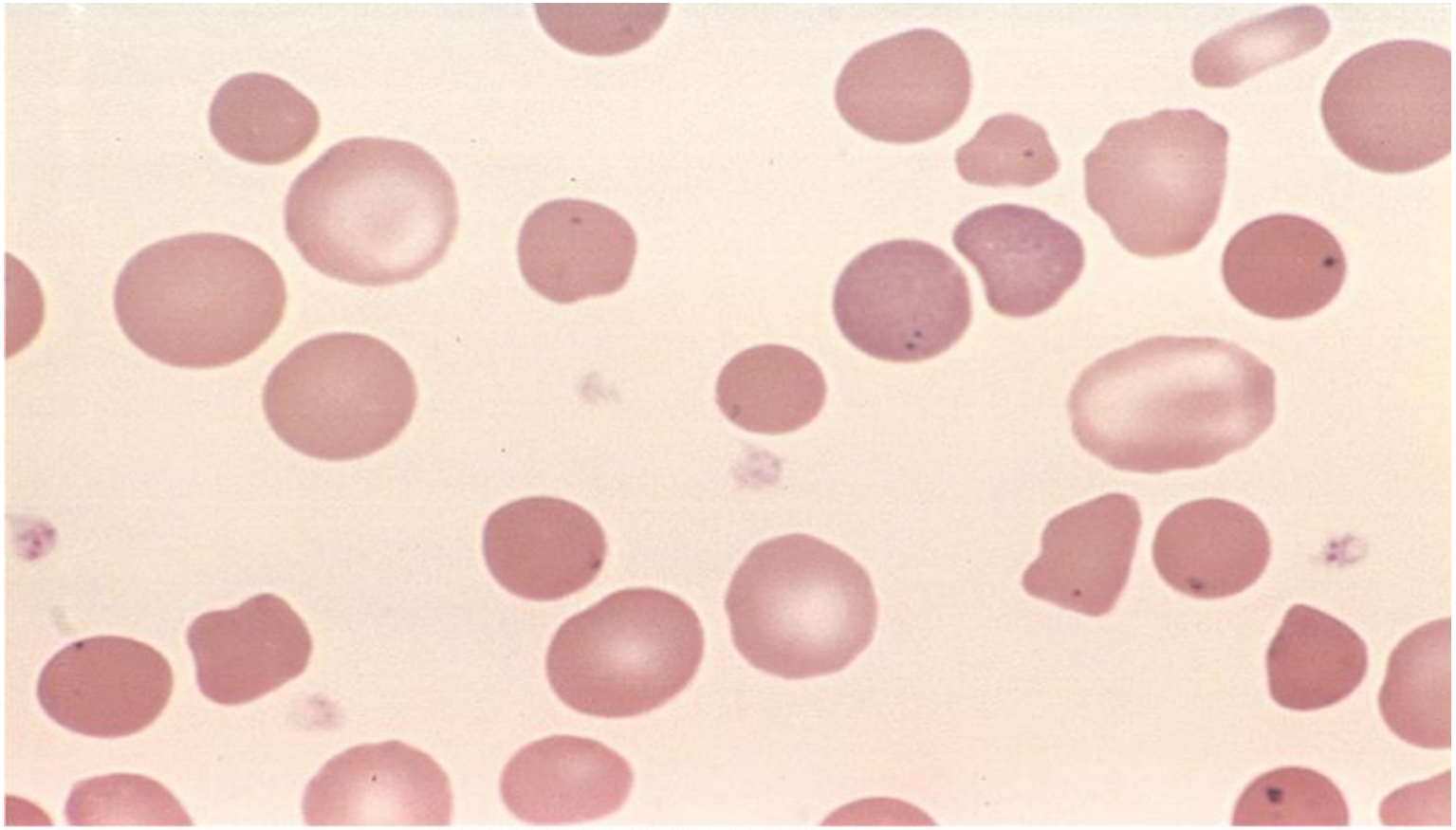
Hereditary spherocytosis

- Mode of inheritance
- Prevalence * Pathogenesis



Pathologic findings

- Blood film

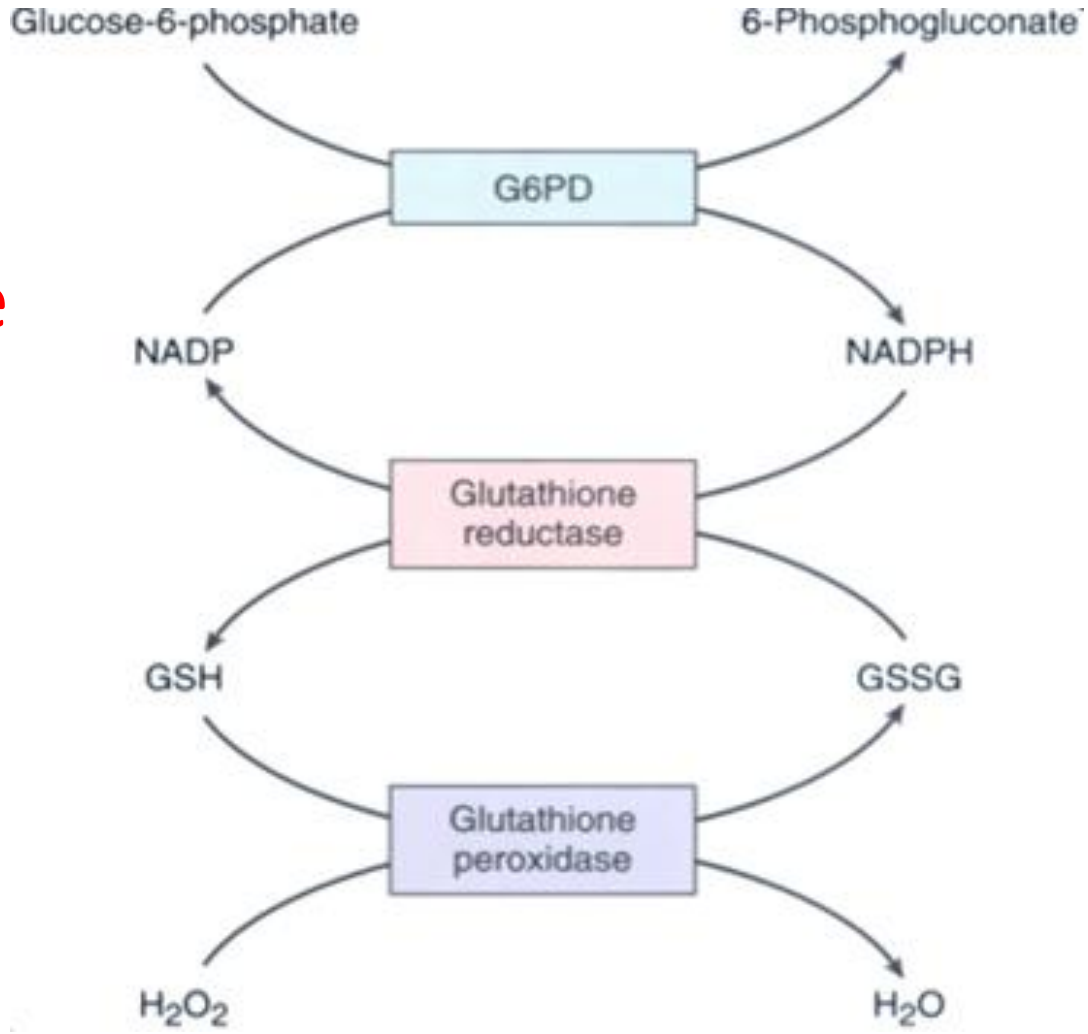


Pathologic findings

- MCHC
- Retic
- Osmotic fragility
- Family Hx
- Clinical course, signs and symptoms

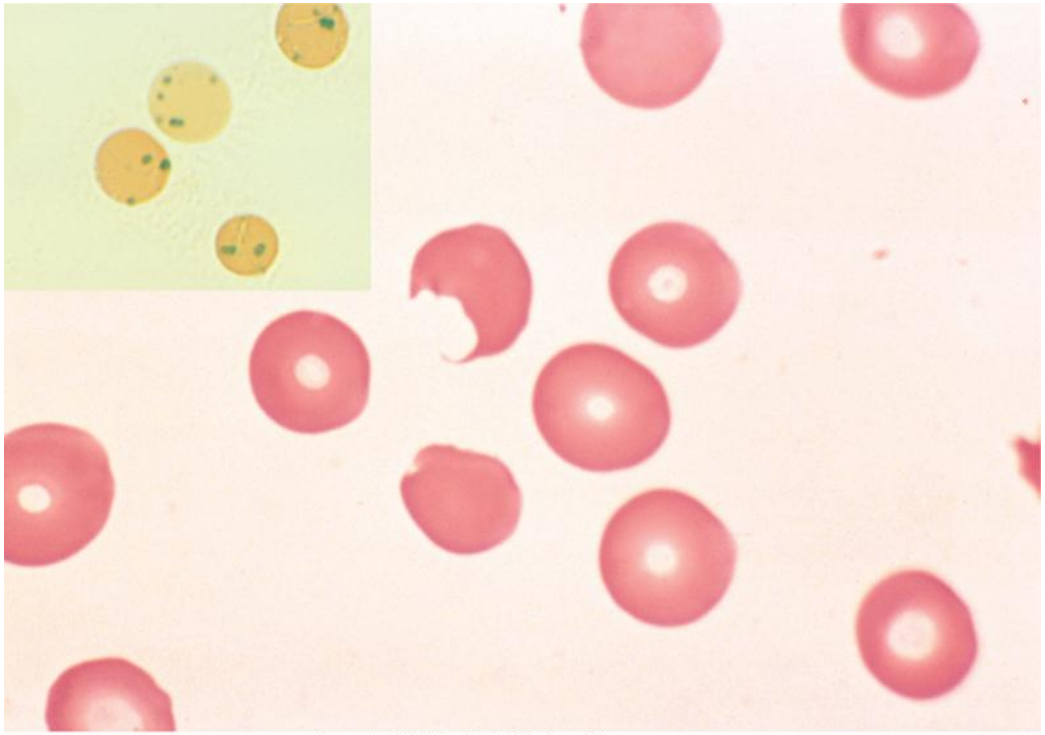
2) Glucose-6-Phosphate Dehydrogenase Deficiency

- Etiology
- Mode of inheritance
- Prevalence
- Enzymatic pathway
- Pathologic enzyme



Pathogenesis

- Site of enzyme
- RBC life
- Degree of deficiency
- Heinz bodies (crystal violet, Supravital stain)
- Bite cells
- Hemolysis (old RBCs)

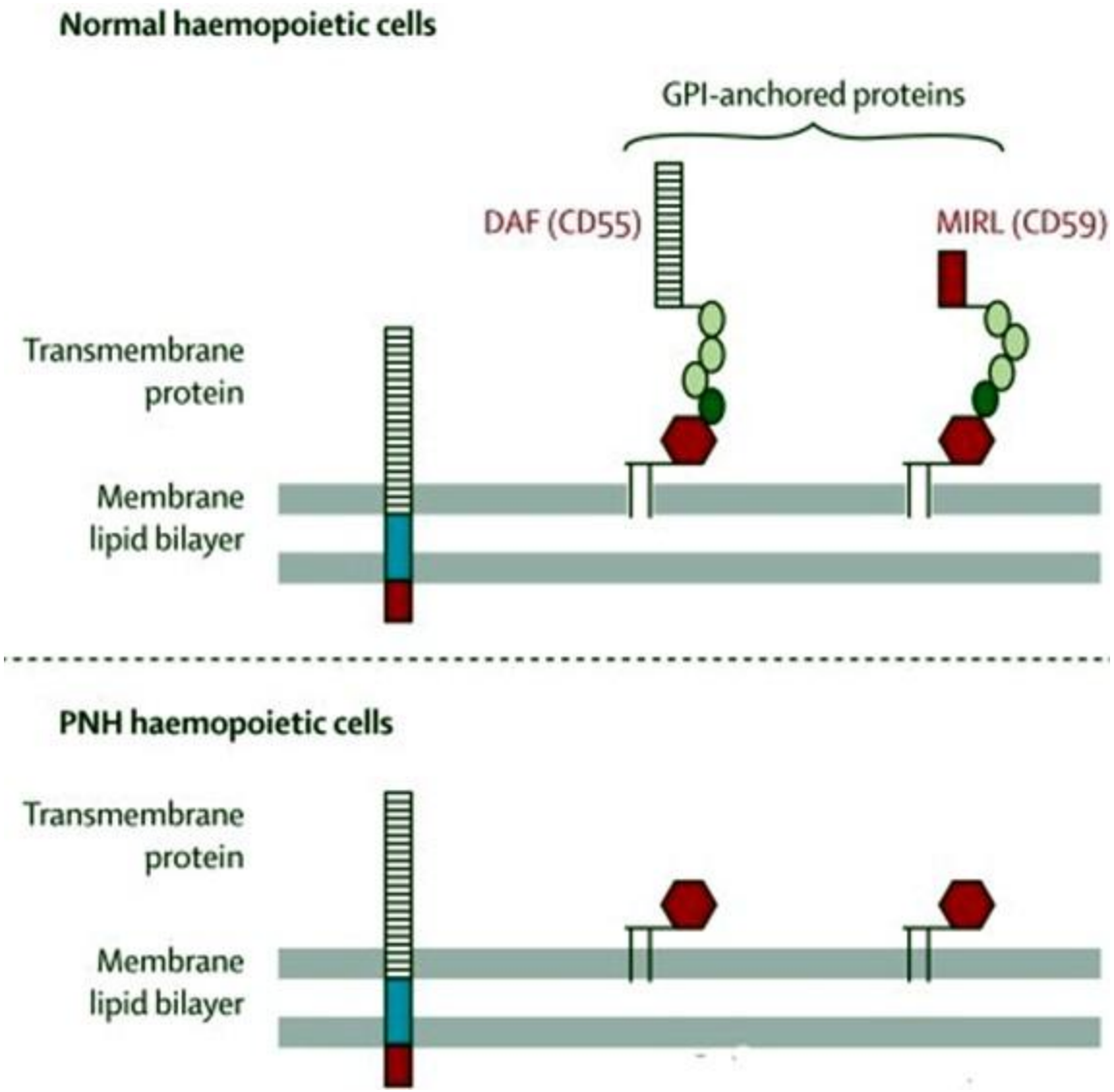


Crisis

- Drugs (sulfonamides, malaria, vitamin K, large dose aspirin)
- Infections
- Fava beans
- Clinical course (time wise, severity, signs)
- Enzymatic assay (time wise, NADPH)

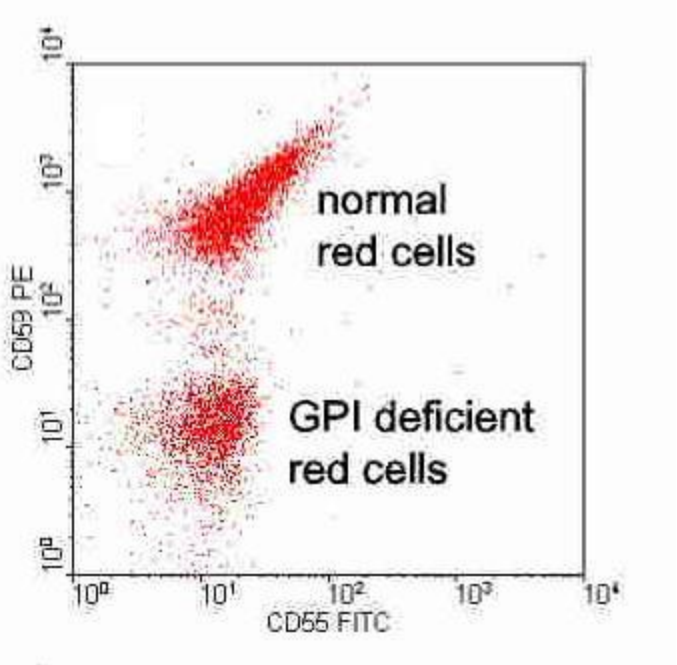
3) Paroxysmal Nocturnal Hematuria

- Etiology: mutation phosphatidylinositol glycan complementation group A gene (PIG-A)
- Absent glycosylphosphatidylinositol (GPI)



Pathogenesis

- Predominant mutant stem cell
- Deficiency in CD55, CD59
- Activation of C3-convertase (alternative pathway)
- Trilineage cell lysis
- Diagnosis: Flow cytometry



Clinical features

- Acute vs chronic hemolysis
- Thrombocytopenia
- Thrombosis
- Leukopenia
- 10% MDS, AML

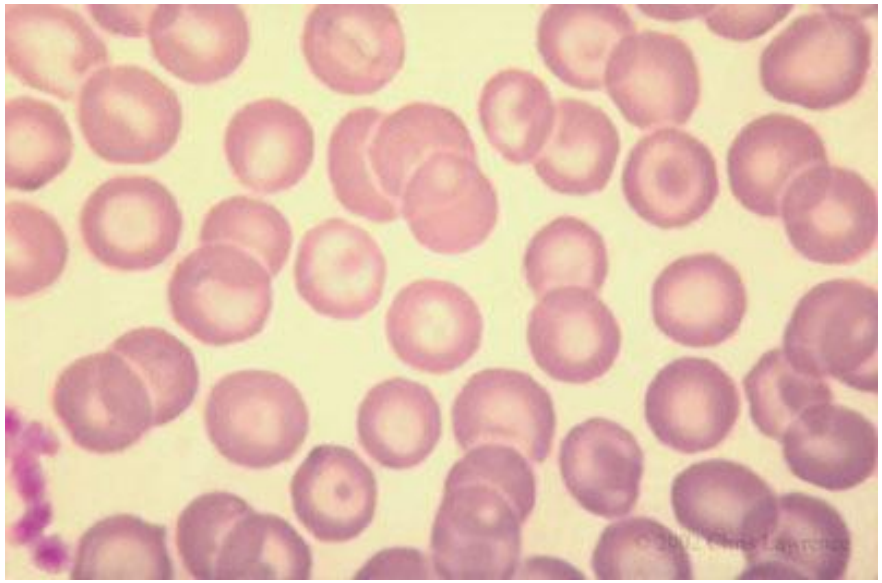
4) Thalassemia

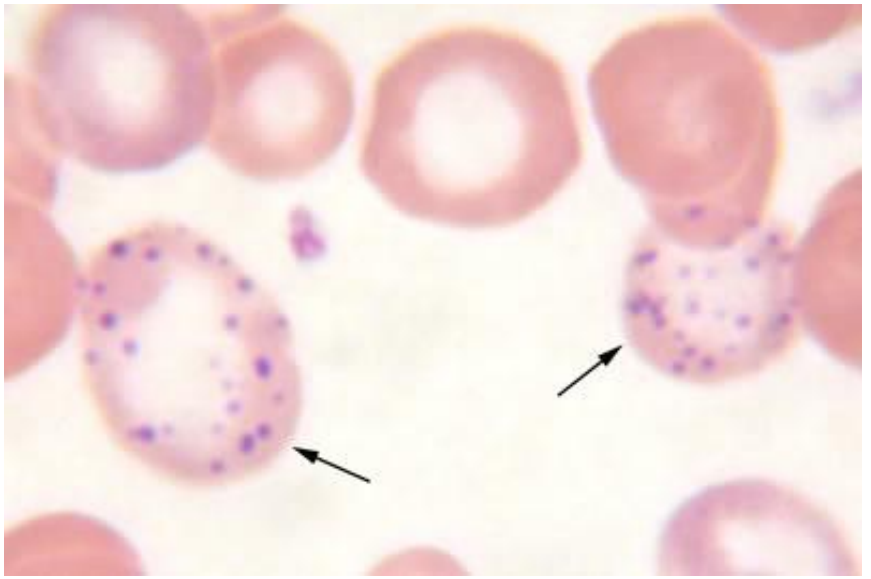
- Etiology (point mutation, deletion)
- Mode of inheritance
- Prevalence
- Types
- Beta: minor, intermedia, major
- Alpha: silent carrier, minor, intermedia, major
- Hemoglobin H Disease: deletion of 3 alpha genes, common in Asia, beta and gamma tetramer (Barts), clinically resembles β-thalassemia intermedia
- Symptoms: after 6 months

Pathogenesis

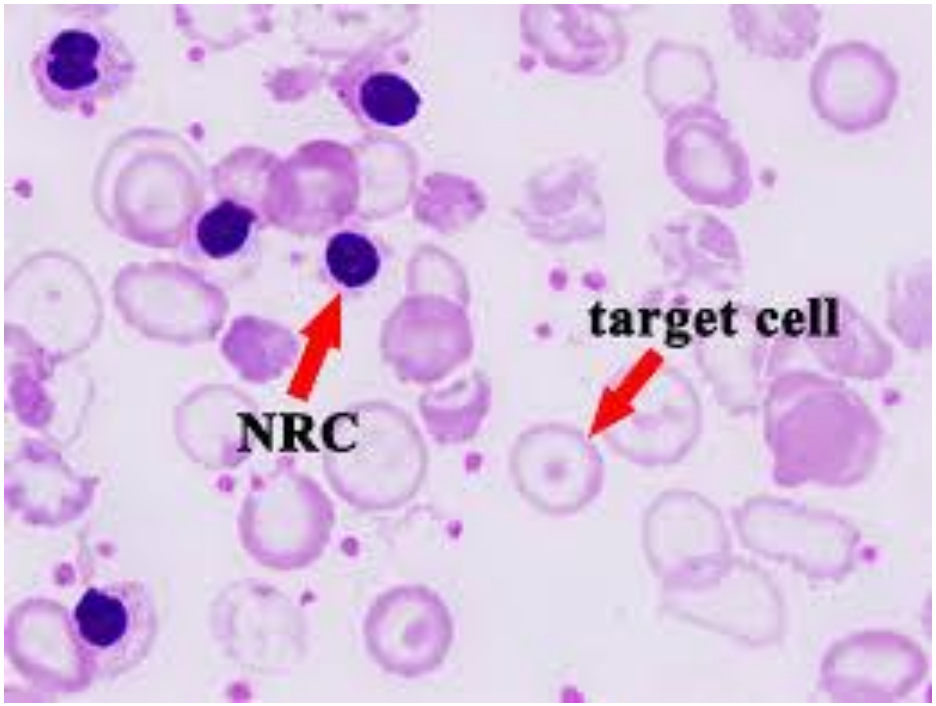
- Decreased production of hemoglobin A
- RBCs: hypochromic, microcytic (hypoxia)
- In Beta-thal: increased Hg A2, Hg F (Hg electrophoresis)
- Excess unpaired globin chains (hemichromes): membrane damage, intra and extravascular hemolysis
- Intermedia + major: chronic hypoxia, persistent high erythropoietin (inhibits Hepcidin), ineffective erythropoiesis (increased normoblasts, crew cut X-ray)
- Extramedullary hematopoiesis
- Secondary hemosiderosis (low hepcidin), skin pigmentation (melanin)
- Abnormal bone growth
- Heart failure: anemia, transfusion, hemosiderosis
- Thrombosis: deformed membrane attracts platelets and injure blood vessels

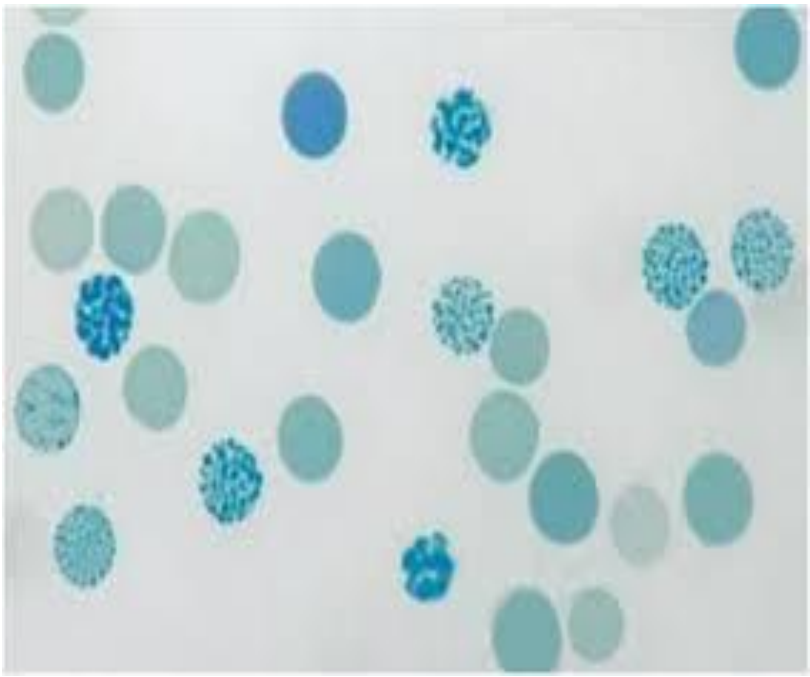
Blood film





Blood film





5) Sickle cell anemia

- Etiology (Glutamate – Valine)
- Mode of inheritance
- Prevalence
- Sickle cell trait (heterozygous): 40% HgS
- Sickle cell anemia (homozygous): 90% HgS
- Malaria
- Symptoms: 6 months

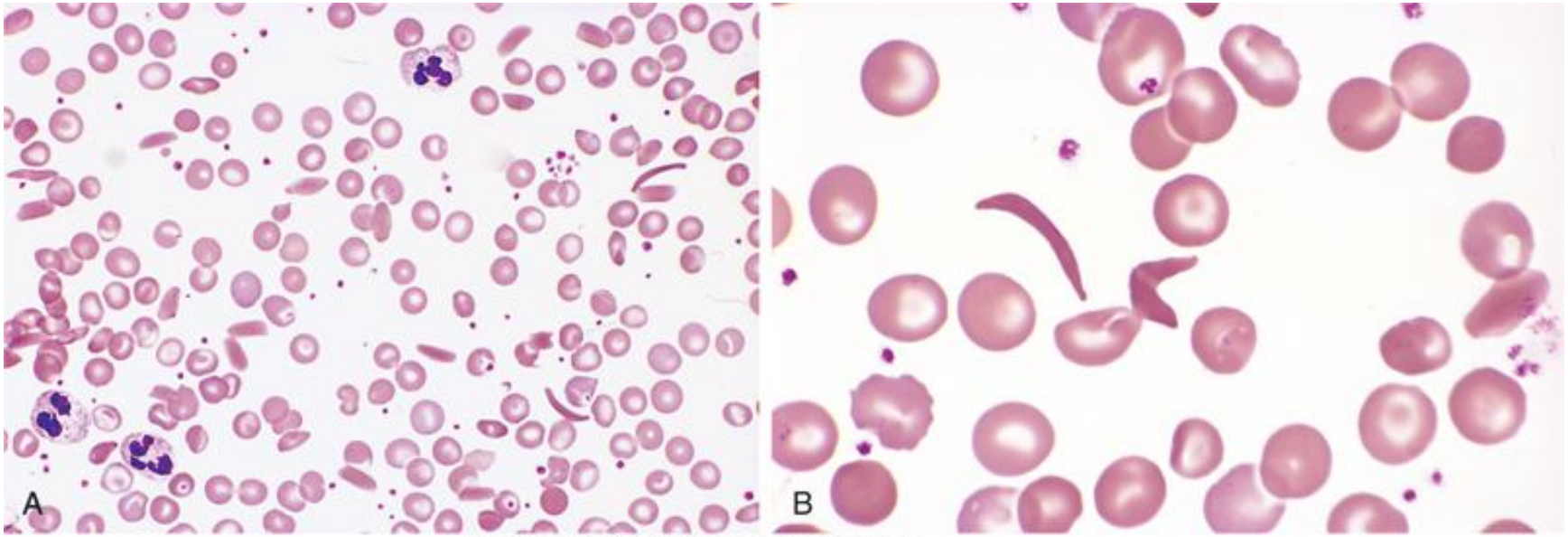
Pathogenesis

- HgS polymerizes longitudinally, needle-like
- Hypoxia, acidosis, dehydration
- Intra + extravscular hemolysis
- Ineffective erythropoiesis
- Initial hepatosplenomegaly
- Abnormal bone growth
- Secondary hemosiderosis

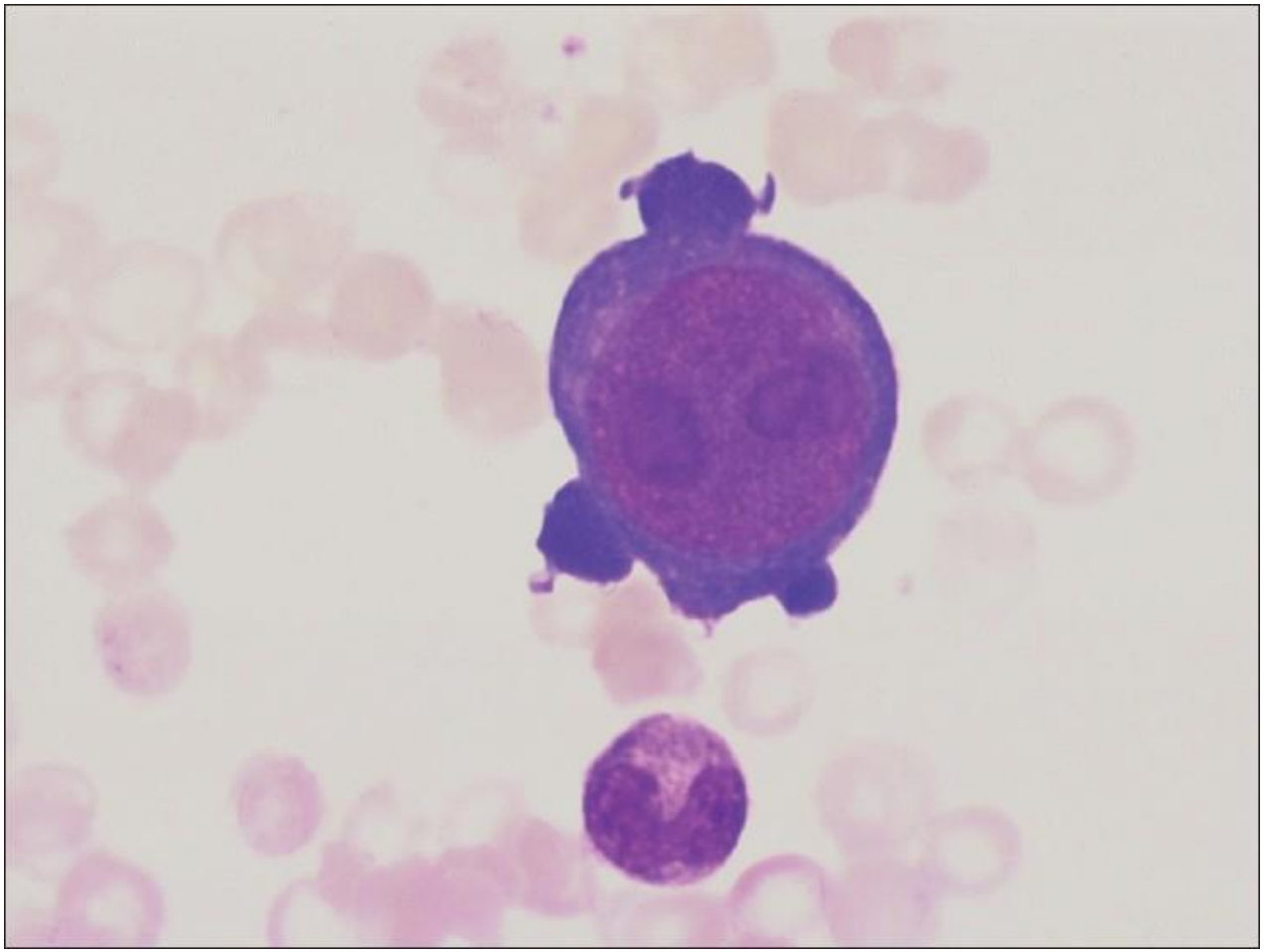
Clinical crisis

- Vaso-occlusive crisis: thrombosis
- Aplastic crisis: BM ischemia, Parvovirus B19
- Sequestration crisis: massive splenomegaly, hypovolemia
- Autosplenectomy
- Acute chest syndrome
- Priapism
- Skin ulcer

Blood film



Parvovirus B19



6) Autoimmune hemolytic anemia

- Etiology
- Coomb's test:
- the patient's blood is mixed with serum containing antibodies that are specific for human immunoglobulin. If the auto-antibody is present, agglutination of RBC occurs

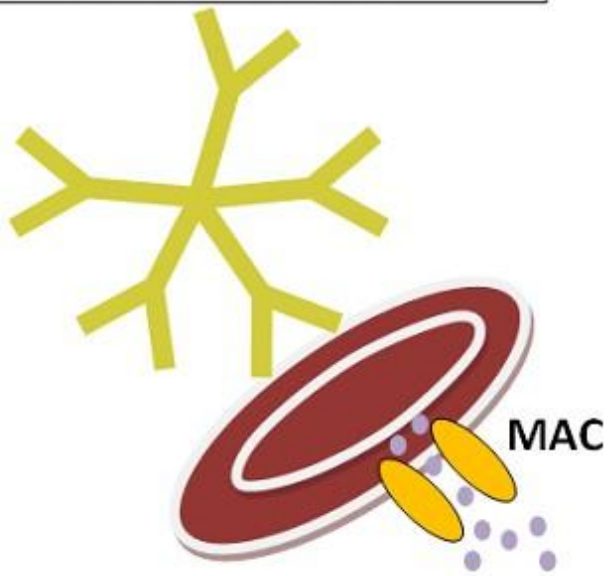
Warm Type immune HA

- IgG, IgA, core body
- 50% idiopathic
- Drugs: large IV dose (penicilline, cephalosporin, antimalaria, methyl dopa)
- 1-2 weeks
- Spherocytes
- Extravascular hemolysis

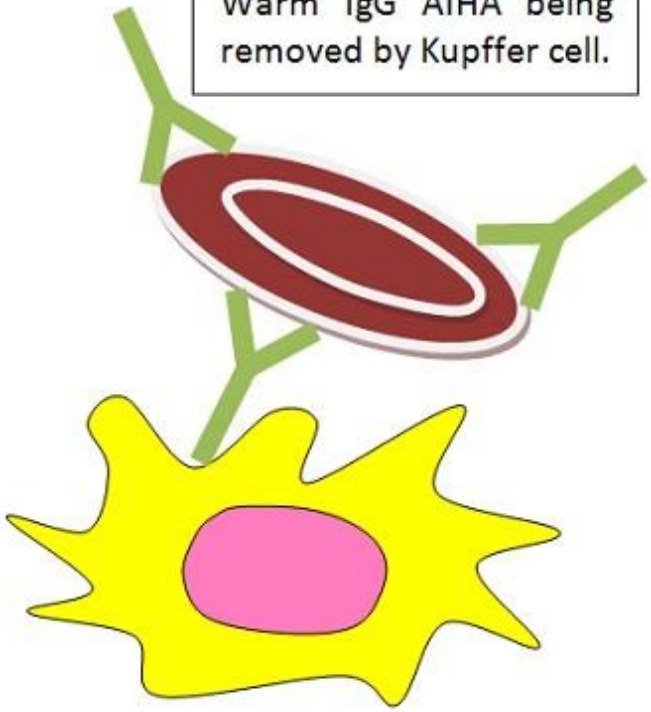
Cold type immune HA

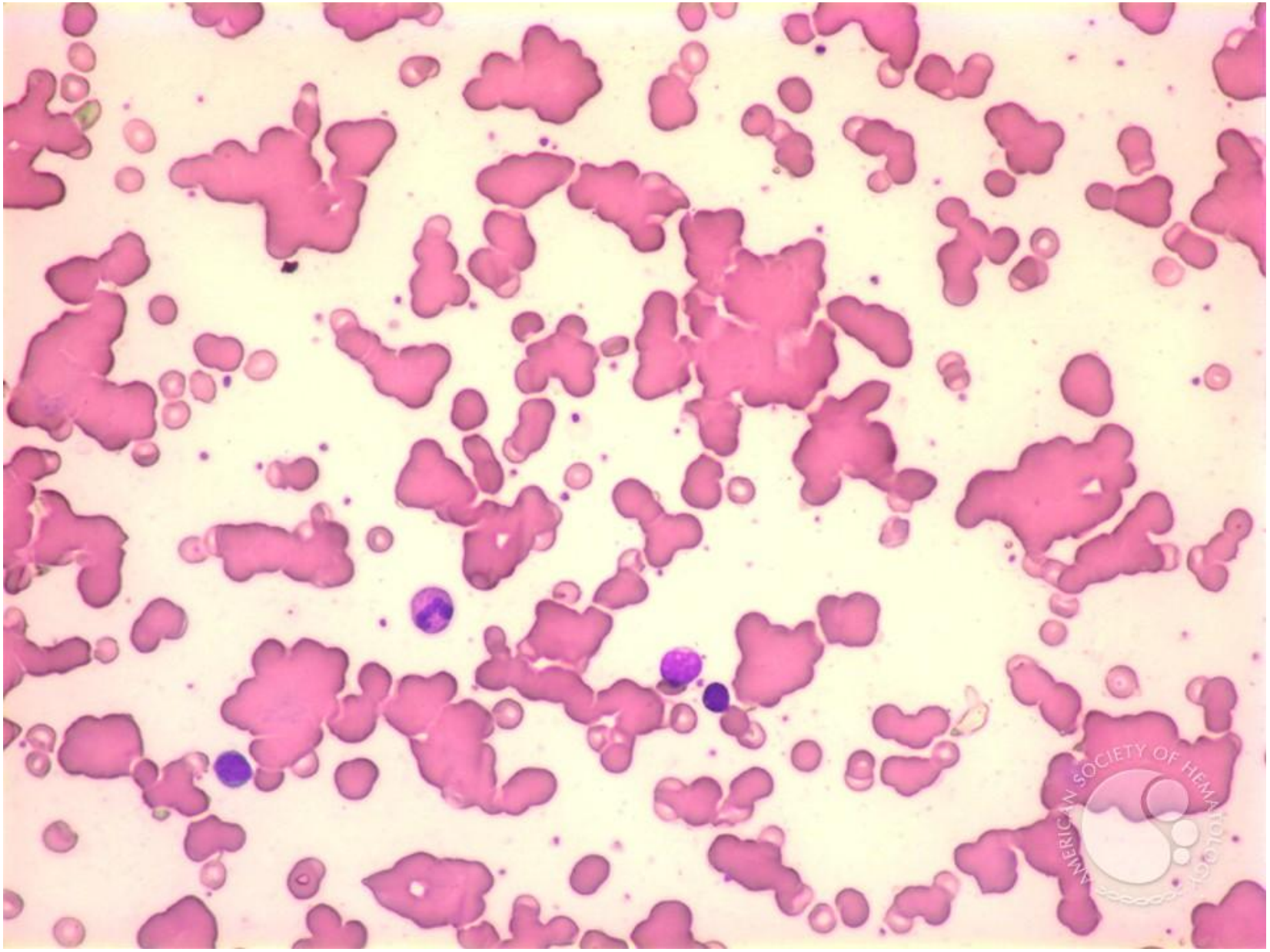
- IgM, peripheral circulation
- Acute: post infection (mycoplasma pneumonia, influenza), self limited
- Chronic: lymphoma, severe, persistent
- Subclinical complement fixation
- Spherocytes
- RBC agglutination
- Extravscular hemolysis

Cold IgM AIHA. Hemolysis through Membrane Attack Complex.



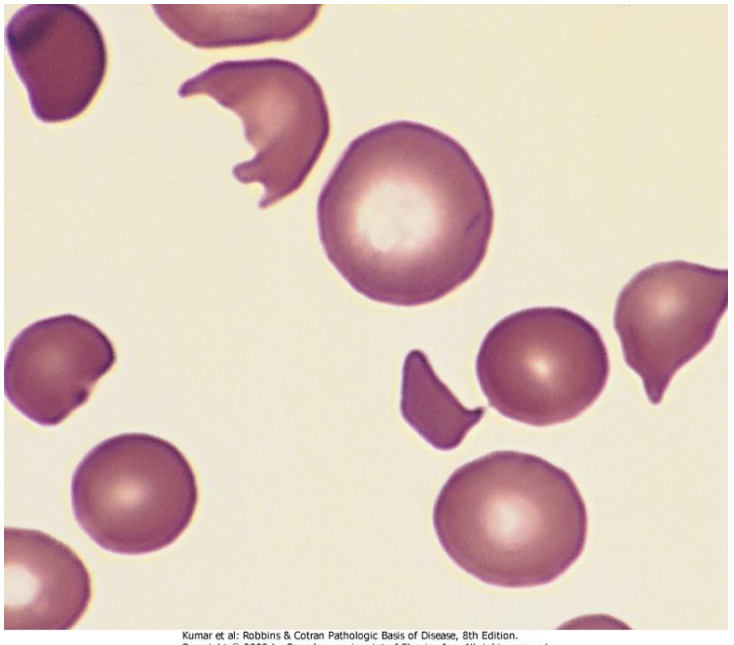
Warm IgG AIHA being removed by Kupffer cell.




AMERICAN SOCIETY OF HEMATOLOGY

7) Trauma to RBCs

- Vigorous exercise
- Prosthetic valves
- Microangiopathic disease
- Schistocytes



8) Hypersplenism

- Special status of splenomegaly
- Pancytopenia
- Rheumatologic diseases (Felty's syndrome)
- Sickle cell anemia
- Normochromic normocytic anemia

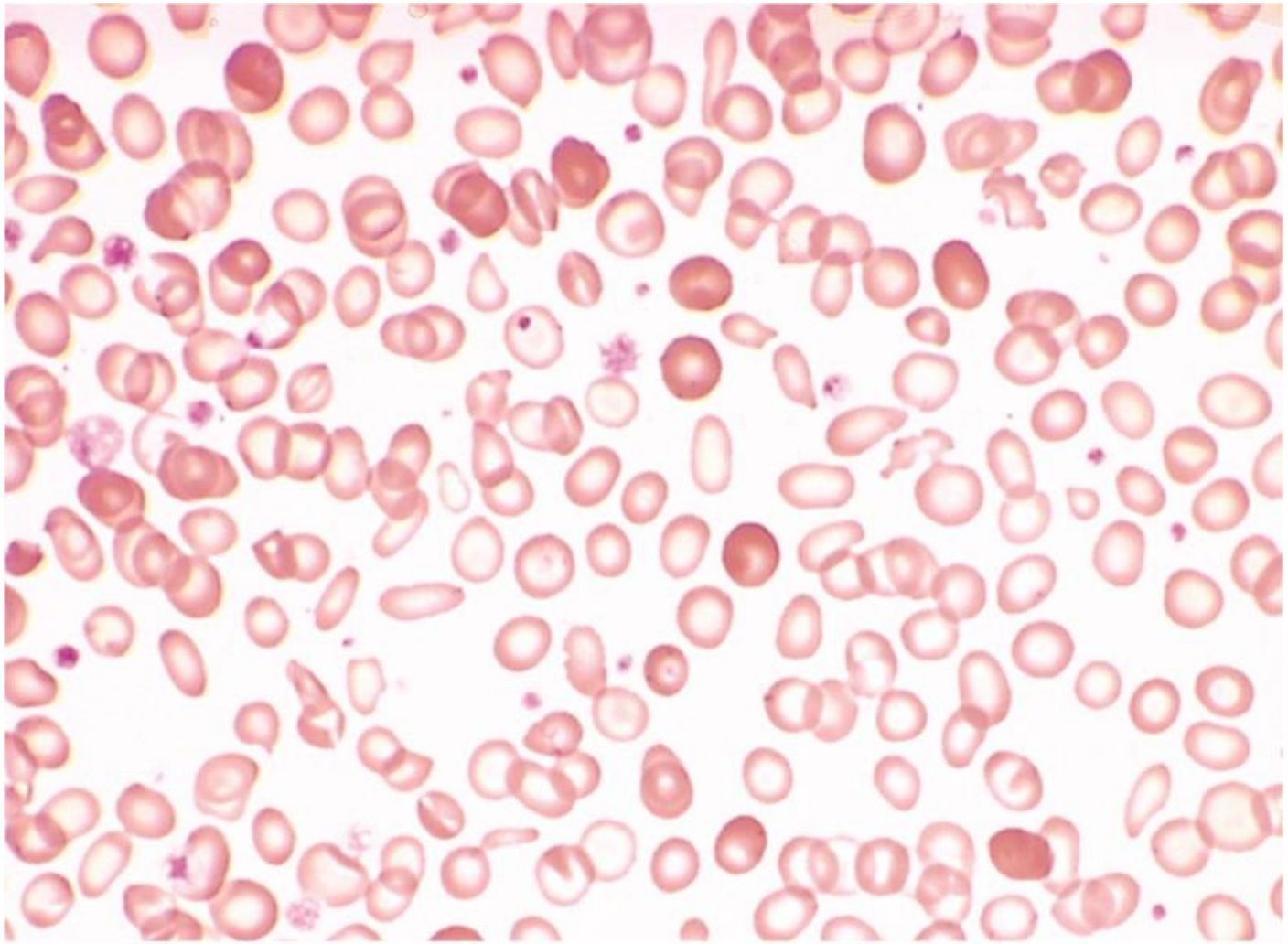
9) Iron deficiency anemia

- Causes

  Nutritional, GI disease, blood loss, increased demand
- Prevalence

Pathogenesis

- Deficient hemoglobin synthesis (hypochromic microcytic anemia)
- Iron deficiency blocks erythropoietin effect
- Small normoblasts with shortened life
- Decreased erythropoiesis
- Low iron affects membrane stability (poikelocytosis)
- Rigid membrane: minor degree of hemolysis
- Thrombocytosis



Systemic features

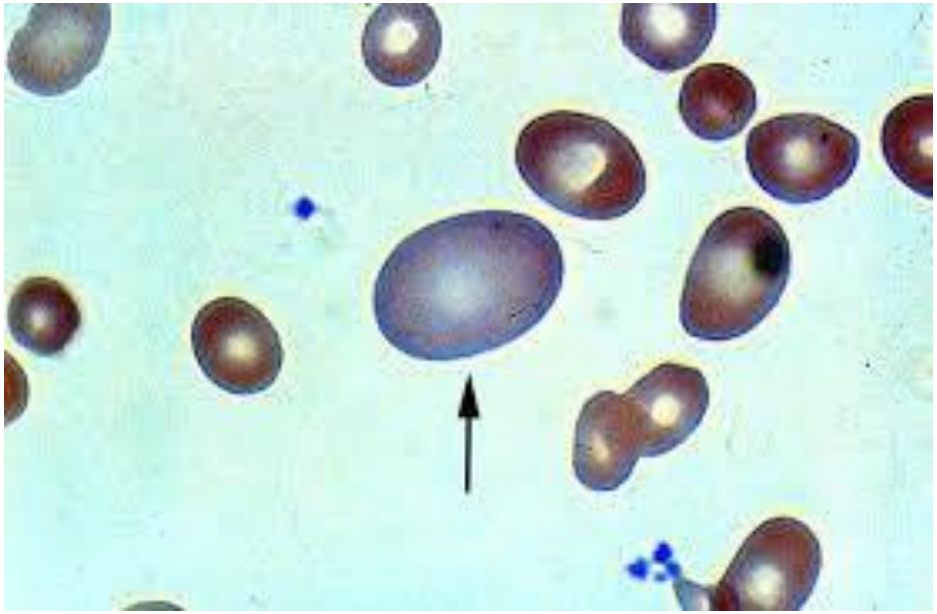
- Entire cellular defect in proliferation
- Hair loss, abnormal nails (spoon)
- Epithelial injury (glossitis, stomatitis)
- Abnormal smooth muscle function in esophagus (web)
- Blue sclera (markedly thin)
- Neurologic and cognitive impairment in children
- Pica

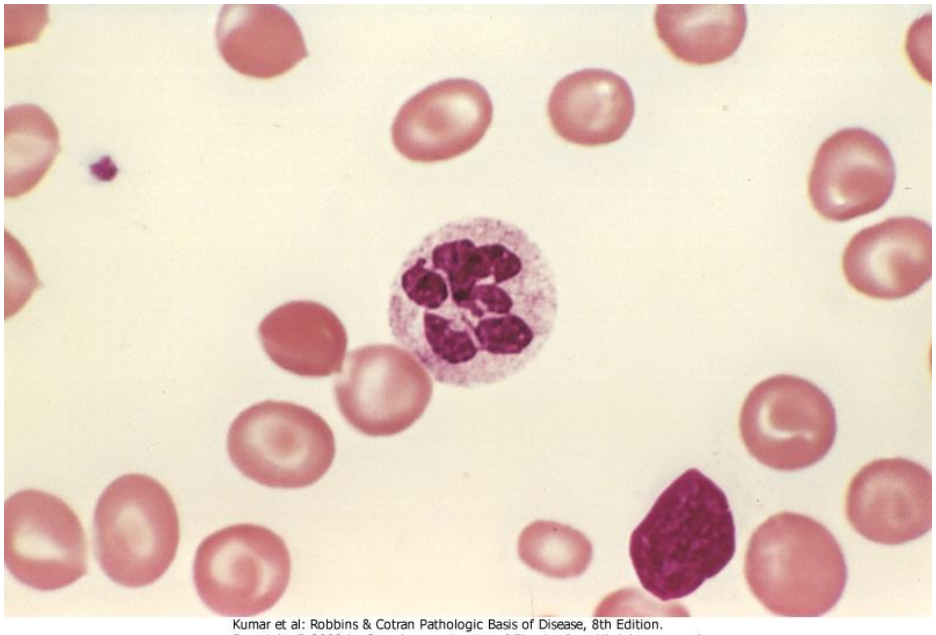
10) Megaloblastic anemia

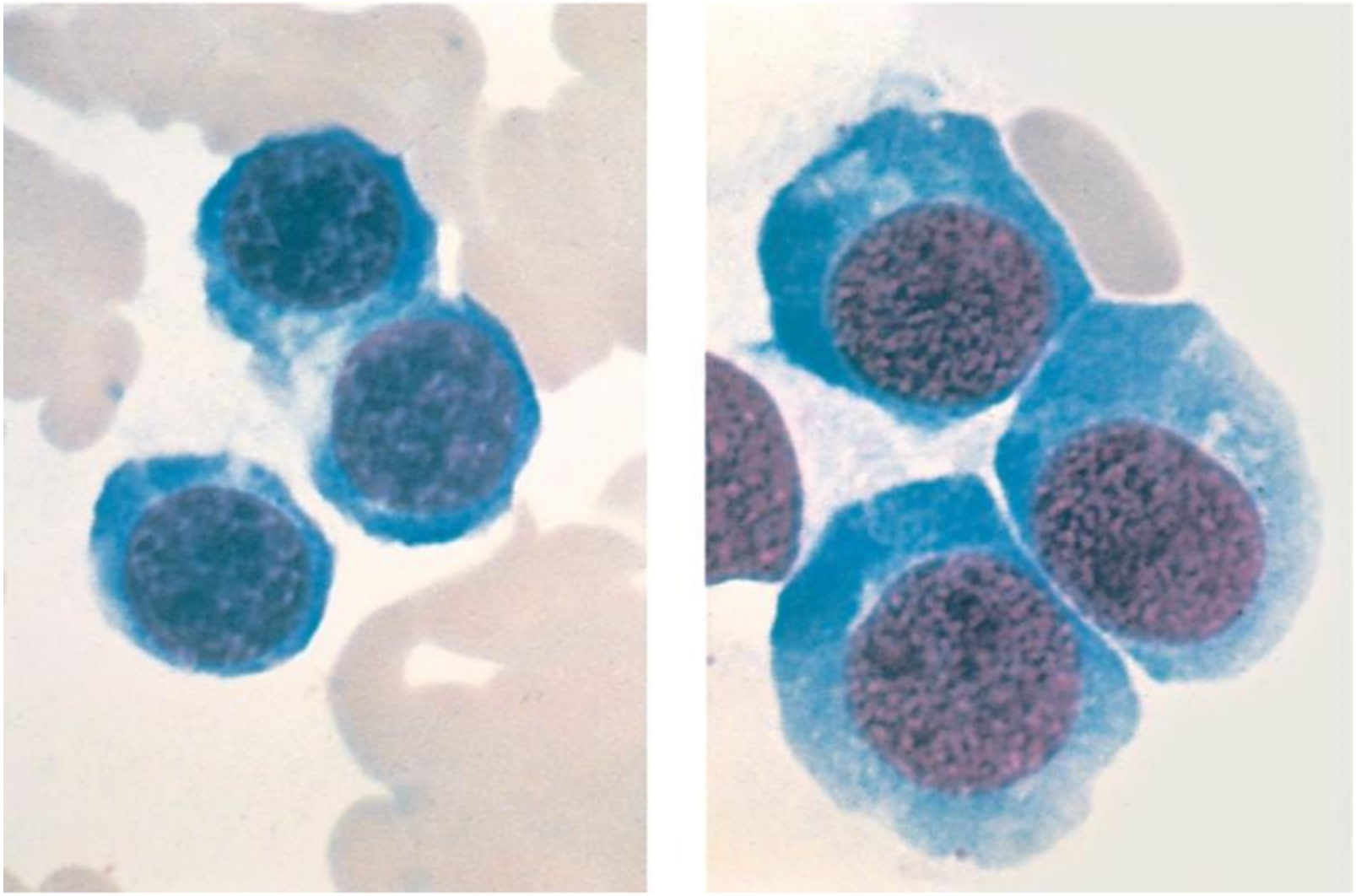
- Causes
- Vitamin B12: nutritional, pernicious anemia, GI disease
- Folate: increased demands, drugs (epilepsy, OCP, methotrexate), vitamin B12 deficiency, dialysis

Pathogenesis

- Defective thymidine, DNA synthesis
- Delayed hematopoietic cells maturation
- Large normoblasts with immature nuclei
- Macroovalocytes
- Hypersegmented neutrophils, giant meta
- Hyperlobated megakaryocytes
- Frequent apoptosis (intramedullary hemolysis)
- Defective myelin synthesis in vitamin B12







11) Anemia of Chronic Disease

- Causes

Chronic infection, cancer, rheumatologic diseases

- Prevalence
- Hospitalized patients

Pathogenesis

- High level of IL-6
- Activates Hepcidin
- Increased iron storage
- Blocks iron transfer from stores to erythroid cells
- Use of iron by macrophages

Morphology

- RBC are normochromic normocytic, or hypochromic microcytic
- Iron stores in BM are markedly increased
- Serum ferritin is increased
- Treatment: treat the underlying cause

12) Aplastic Anemia

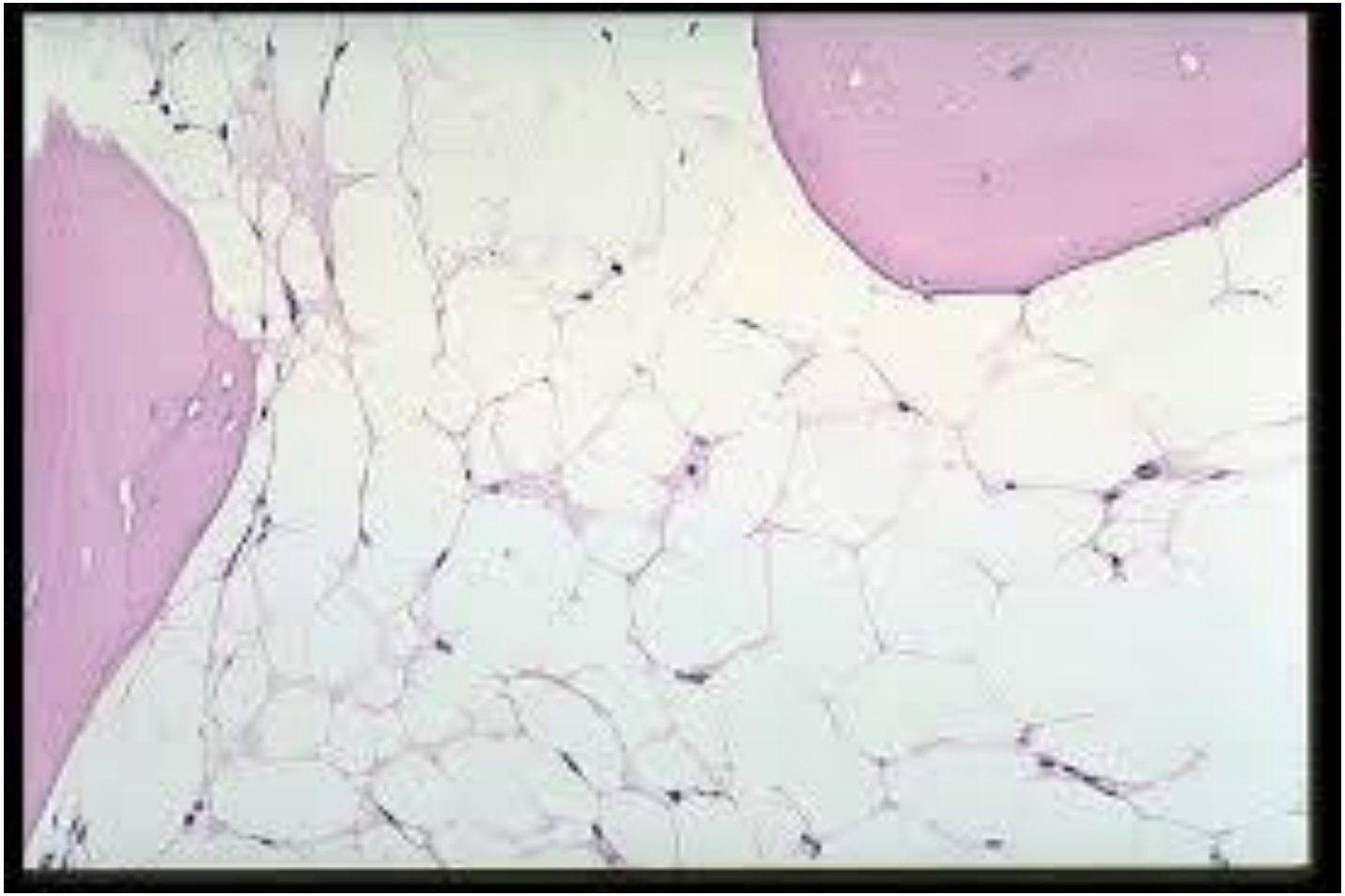
- Etiology

Idiopathic, autoimmune diseases, drugs (chloramphenicol), viral hepatitis

- Prevalence
- Acquired
- Congenital: Fanconi, pure red cell aplasia

Pathogenesis and morphology

- Destruction of stem cells by aberrant T-cells
- Normochromic normocytic anemia
- Pancytopenia
- Hypocellular bone marrow, predominance of fat



13) Myelophthisic anemia

Causes

- Infiltrative disease
- Malignancy: leukemia, myeloma, metastasis
- Granulomas
- Storage disorders

Morphology

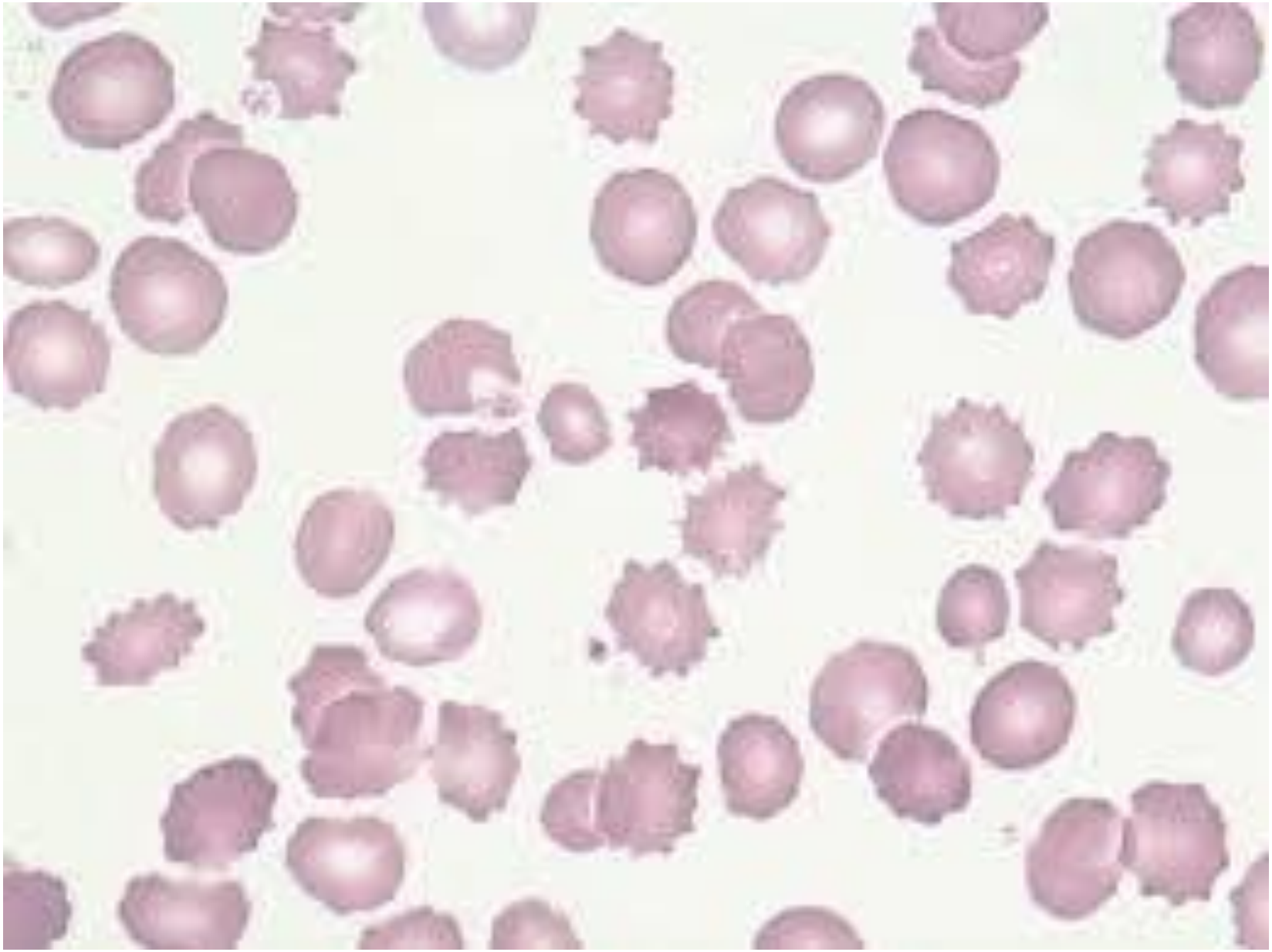
- Normochromic normocytic anemia
- pancytopenia

14) Hypothyroidism

- Slow cell growth and maturation
- Macrocytic anemia

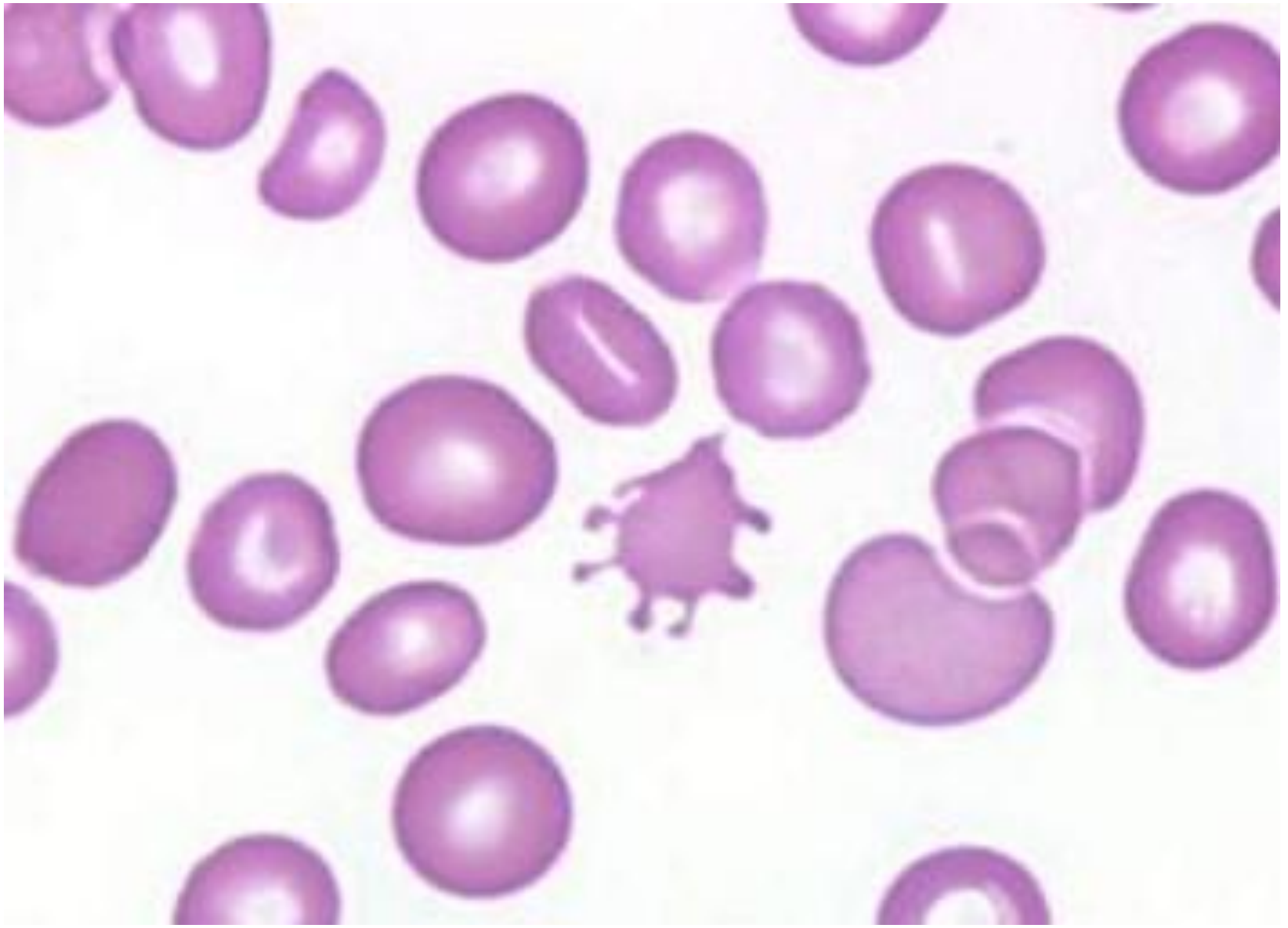
15) Chronic renal failure

- Early disease
- Deficient erythropoietin
- Normochromic normocytic anemia
- Uremic stage
- ecchinocytes



16) Chronic liver disease

- Multifactorial anemia
- Hemorrhage
- Nutritional (vitamin B12)
- Defective lipid synthesis (acanthocytes)



17) Myelodysplastic syndrome

- Acquired mutations in stem cells
- Defective cellular maturation and egress
- Normochromic normocytic anemia, or macrocytic anemia

Polycythemia

Polycythemia

- Increased RBCs mass above normal level
- Erythrocytosis: high RBC count, seen in polycythemia and hemolytic anemia

Polycythemia vera

- Primary polycythemia
- Neoplastic disease of erythroid cells
- Low erythropoietin
- Splenomegaly
- Plethora, cyanosis, itching
- Sluggish circulation, thrombosis
- gout

Secondary polycythemia

- Chronic hypoxia
- Chronic lung disease, chronic heart disease (septal defect), alcoholism, smoking, high altitude
- Renal cell carcinoma
- Surreptitious
- Reversible
- High erythropoietin
- No splenomegaly