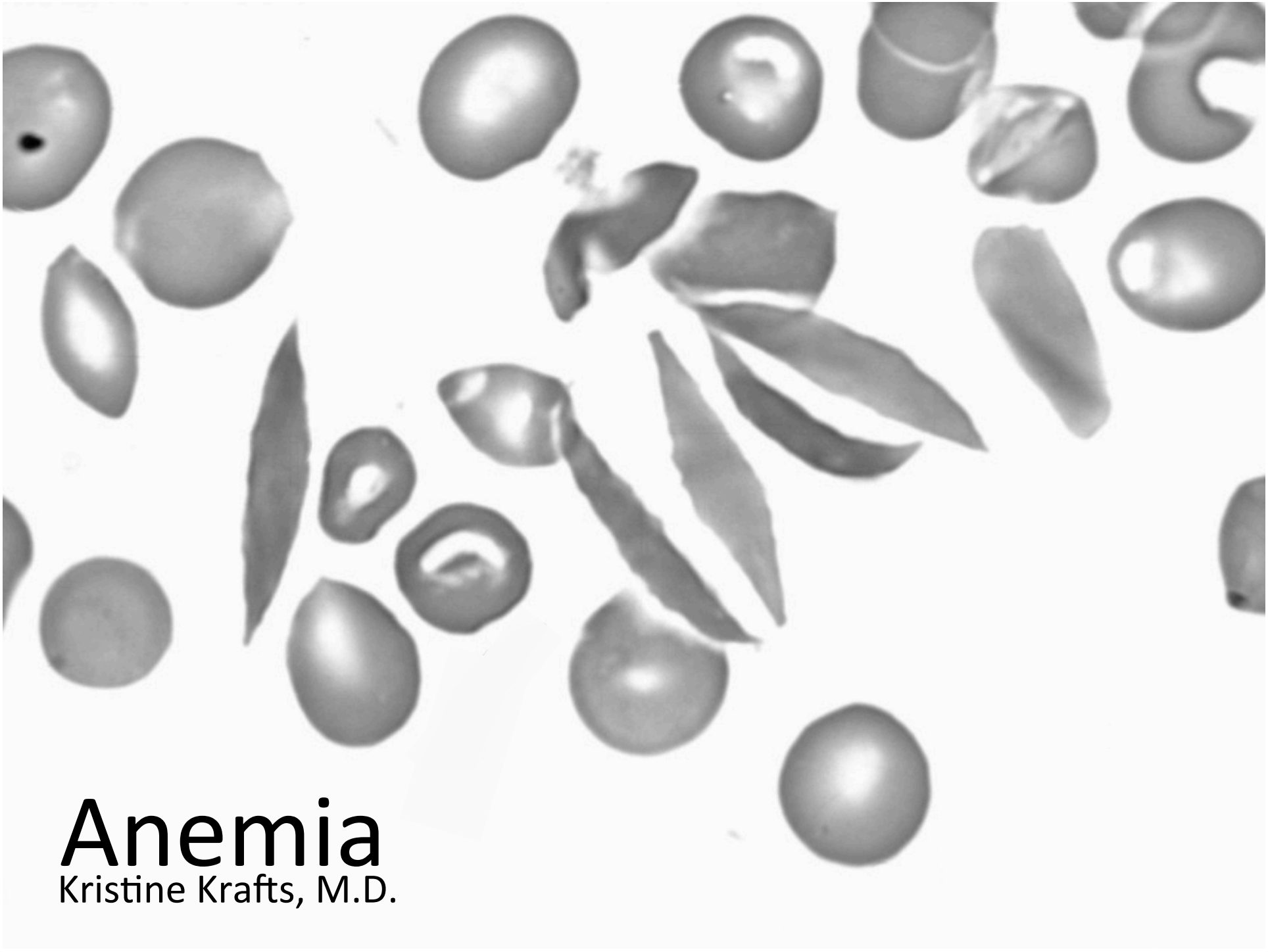


Anemia

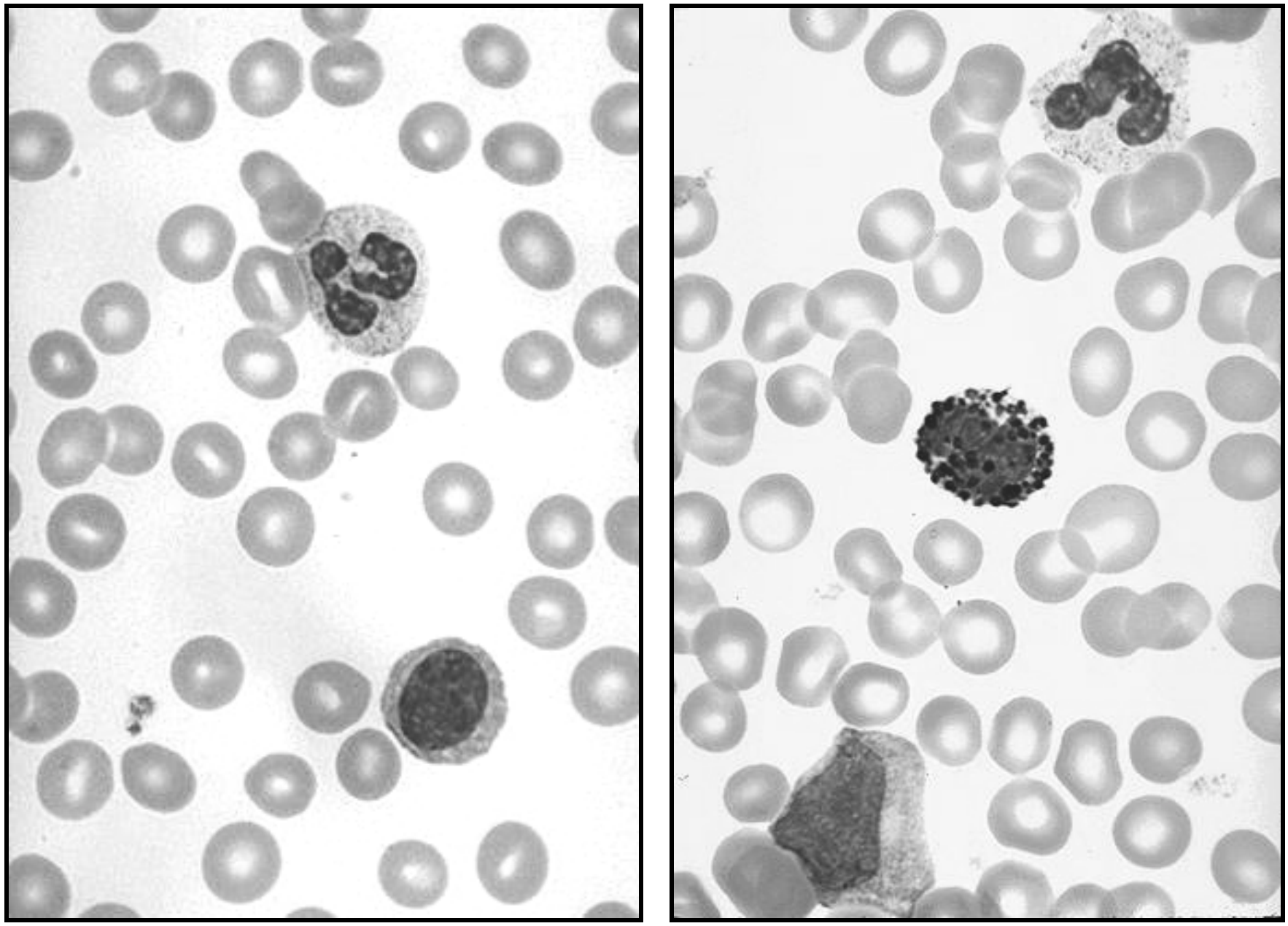
Kristine Krafts, M.D.

Anemia Outline

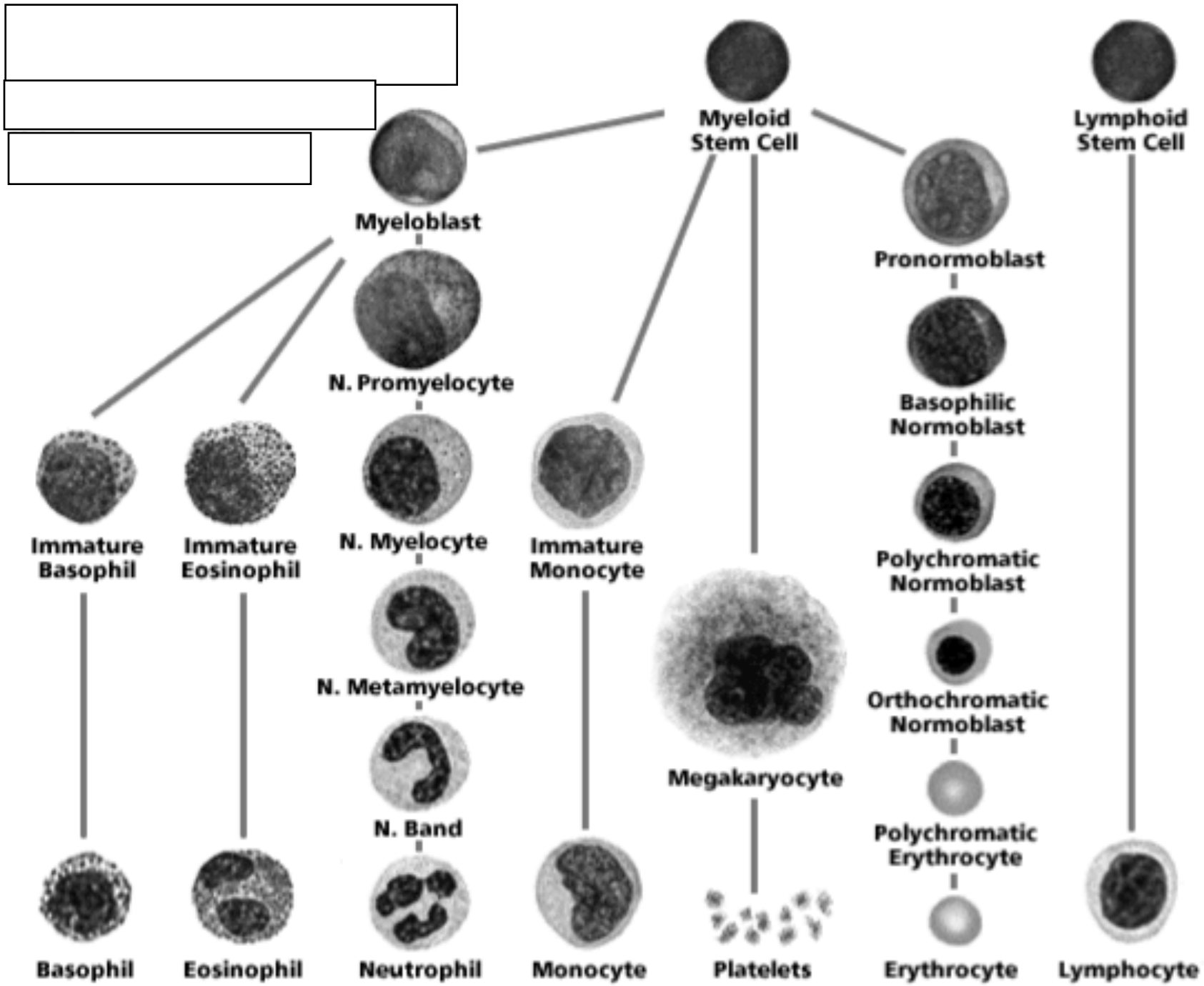
- Background facts about blood
- Anemia: general information
- Anemia: specific types

Anemia Outline

- Background facts about blood

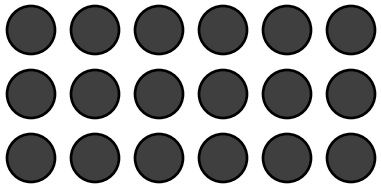


Normal blood cells


Myeloid Stem Cell
Lymphoid Stem Cell
Myeloblast
Pronormoblast
N. Promyelocyte
Basophilic Normoblast
Immature Basophil
Immature Eosinophil
N. Myelocyte
Immature Monocyte
Polychromatic Normoblast
N. Metamyelocyte
Megakaryocyte
Orthochromatic Normoblast
N. Band
Polychromatic Erythrocyte
Basophil
Eosinophil
Neutrophil
Monocyte
Platelets
Erythrocyte
Lymphocyte

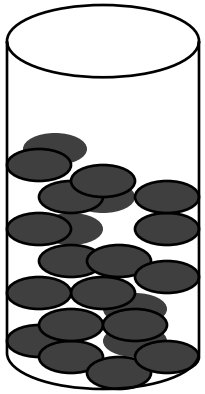
Complete Blood Count (CBC)

RBC

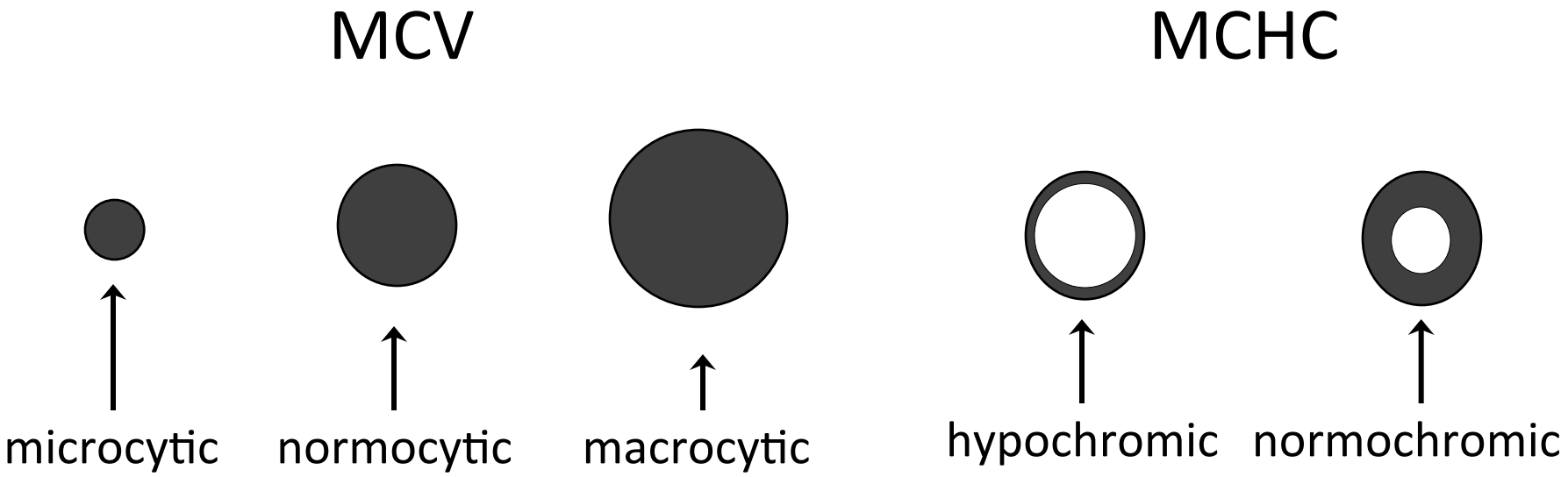


Hemoglobin

Hematocrit

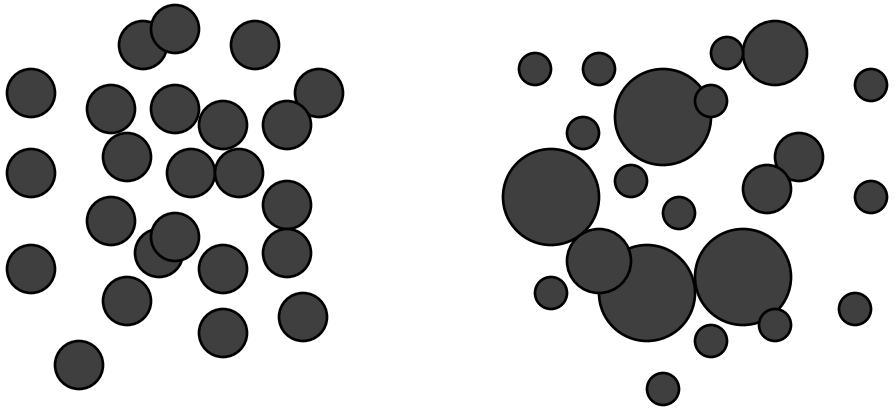


Complete Blood Count (CBC)



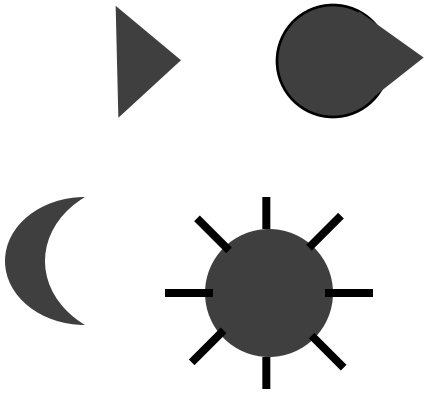
Additional Red Blood Cell Properties

Size variation

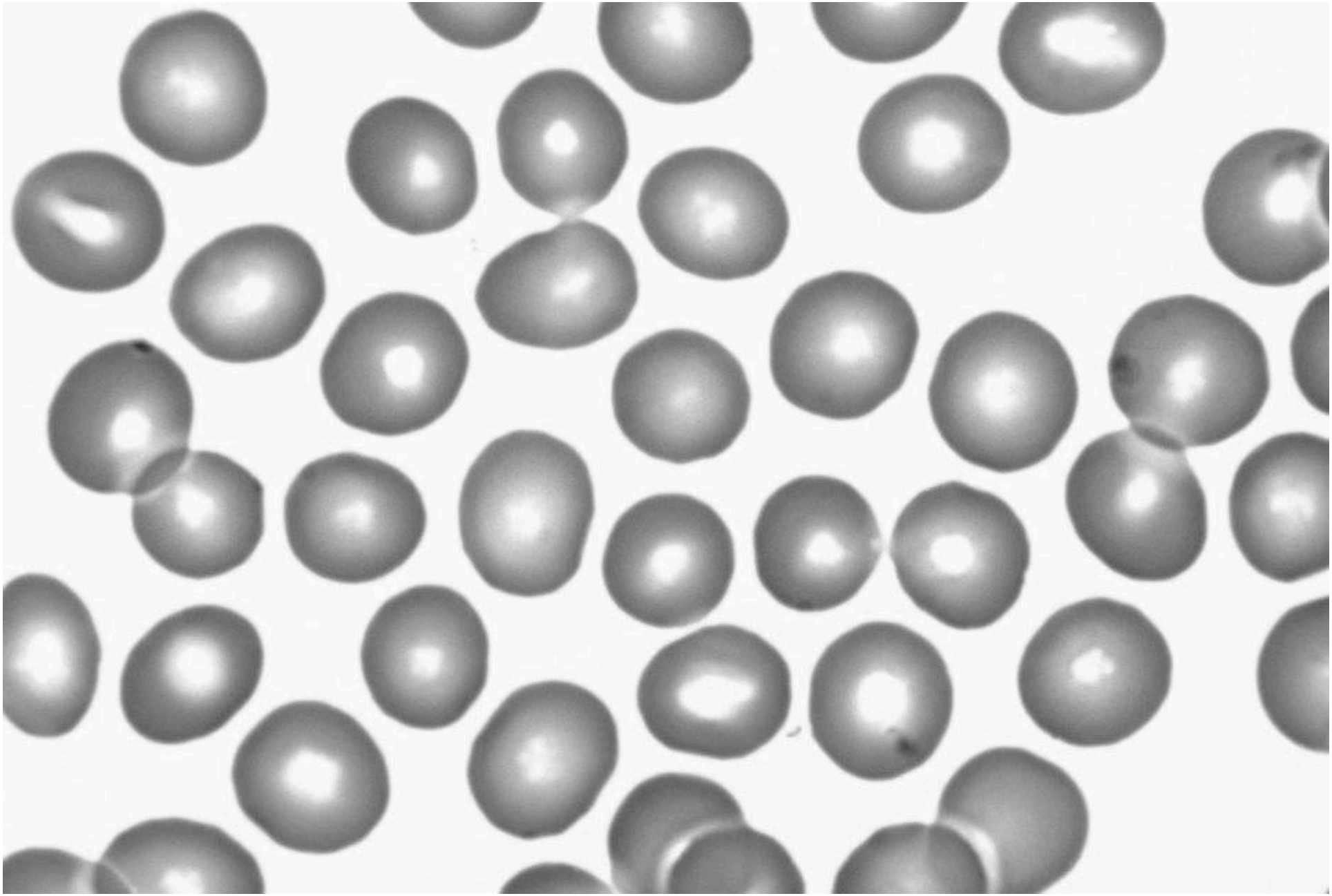


anisocytosis

Shape



poikilocytosis



Normal red blood cells

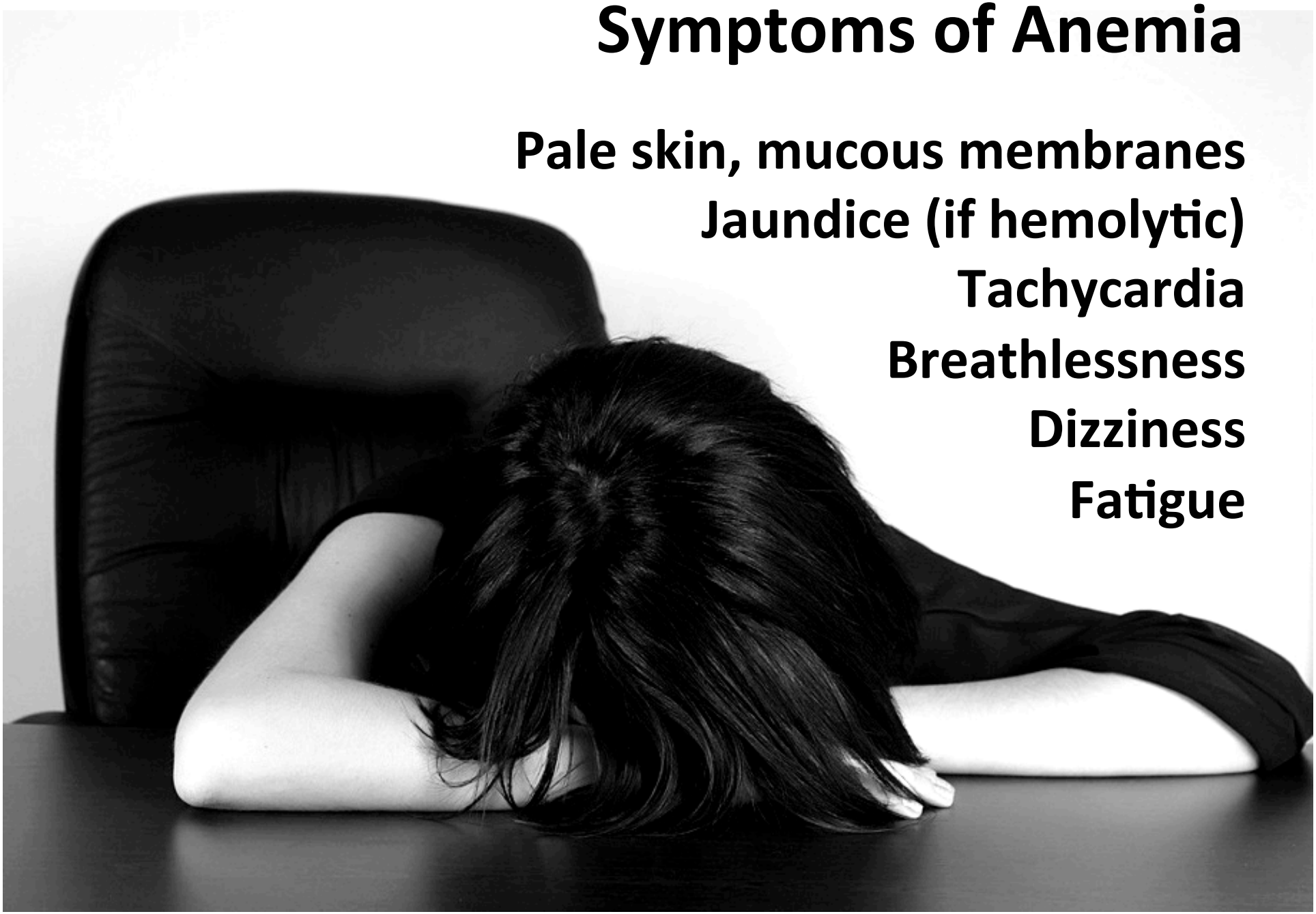
Anemia Outline

- Background facts about blood
- Anemia: general information

An (without) -*emia* (blood):

a reduction below normal
in hemoglobin or red blood cell number.

Symptoms of Anemia



Pale skin, mucous membranes

Jaundice (if hemolytic)

Tachycardia

Breathlessness

Dizziness

Fatigue

Anemia Outline

- Background facts about blood
- Anemia: general information
- Anemia: specific types

Three Ways to Get Anemic

Lose blood

Destroy too much blood

- Extracorpuscular reasons
- Intracorpuscular reasons

Make too little blood

- Too few building blocks
- Too few erythroblasts
- Not enough room

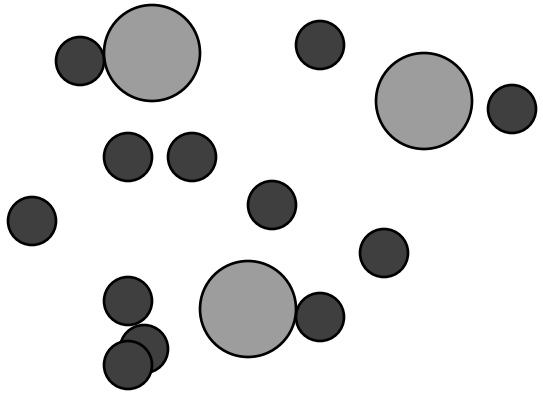
Three Ways to Get Anemic

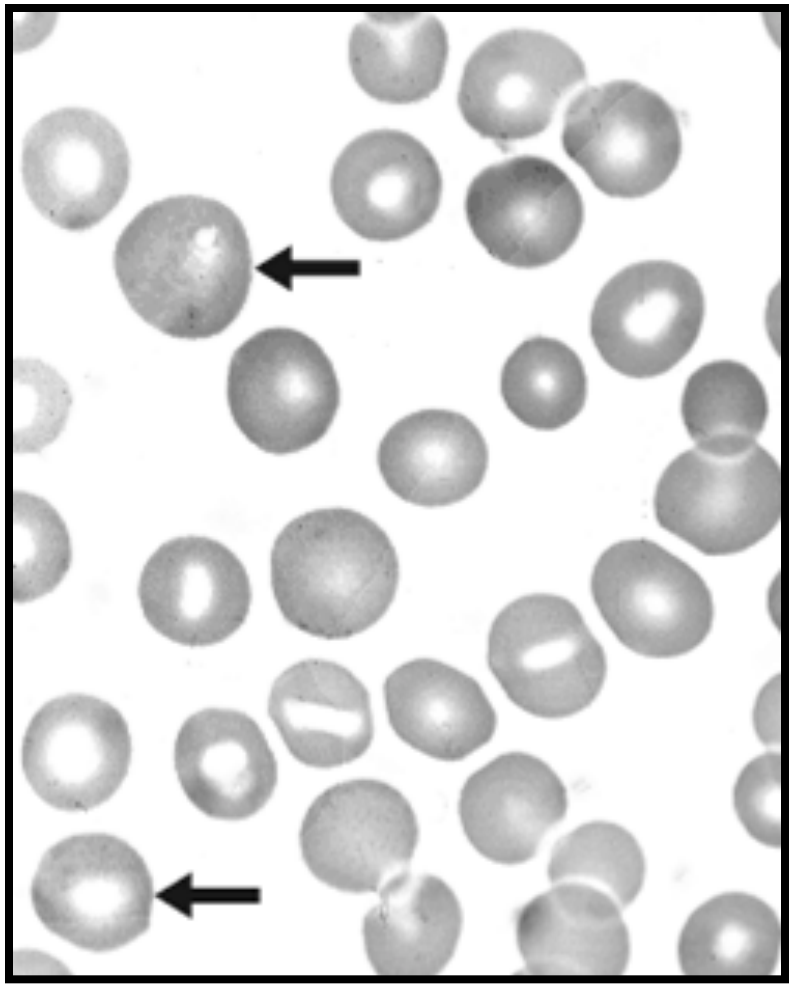
Lose blood

Anemia of Blood Loss

Things you must know

- Cause: traumatic, acute blood loss
- At first, hemoglobin is normal!
- After 2-3 days, see reticulocytes
- Chronic blood loss is different
  (it causes iron deficiency anemia).





Reticulocytes

Three Ways to Get Anemic

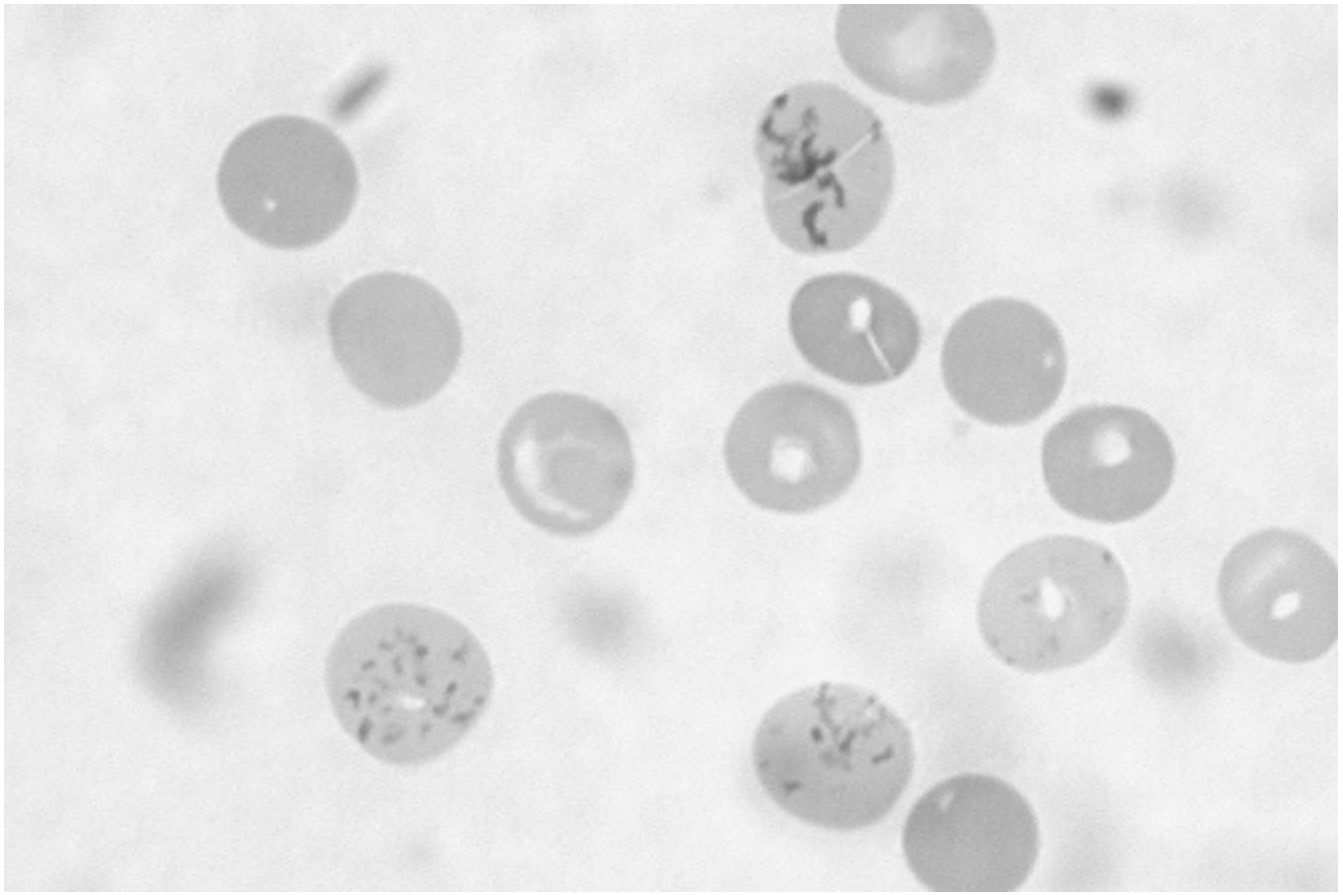
Lose blood

Destroy too much blood

- Extracorpuscular reasons
- Intracorpuscular reasons

Hemolytic Anemias

- Intracorpuscular vs. extracorpuscular
- Chronic vs. acute
- Signs of destruction:
  ↓ haptoglobin
- Signs of production: ↑ reticulocytes, nucleated red cells in blood



Reticulocytes (supravital stain)

Three Ways to Get Anemic

Lose blood

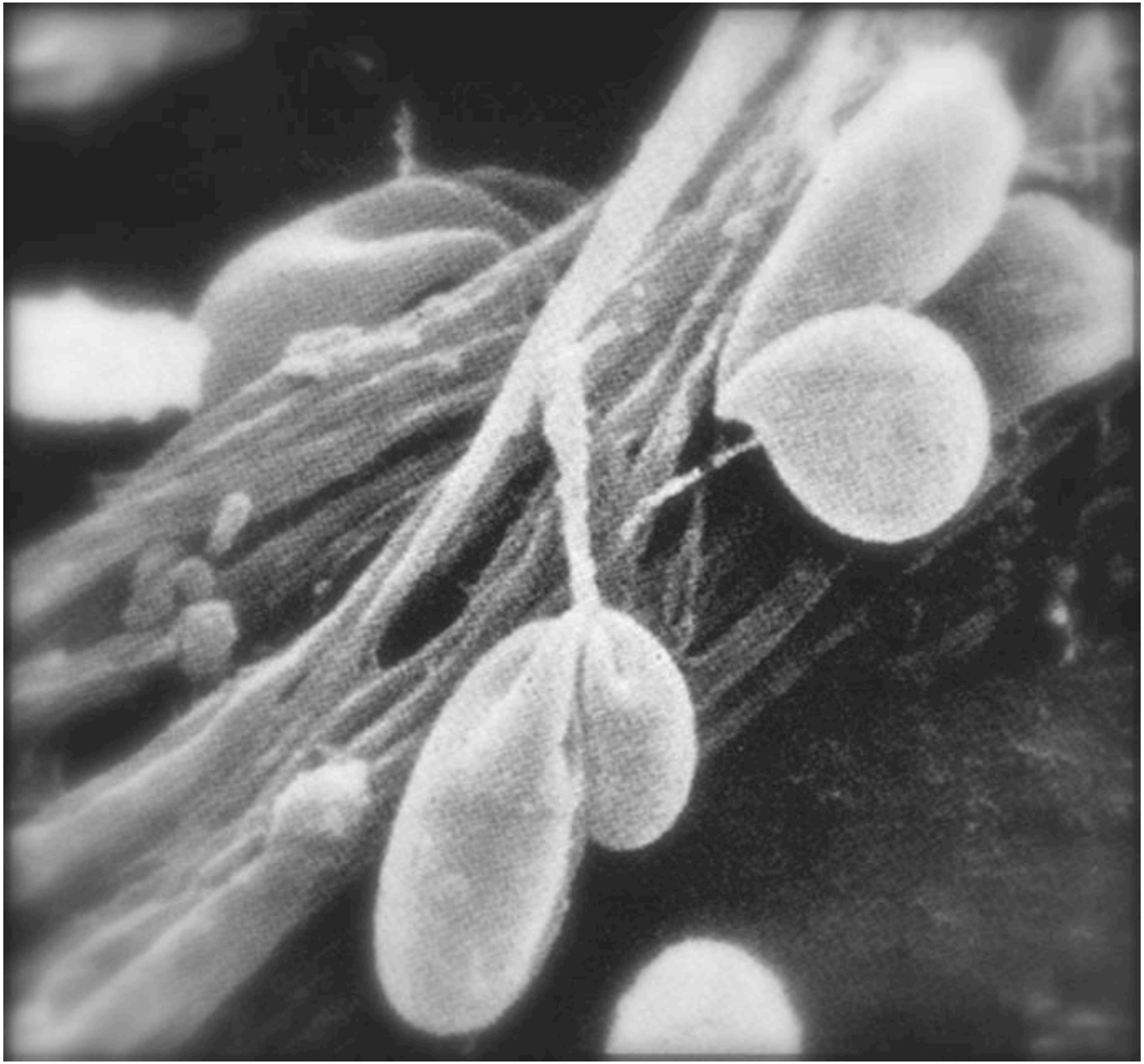
Destroy too much blood

- Extracorpuscular reasons

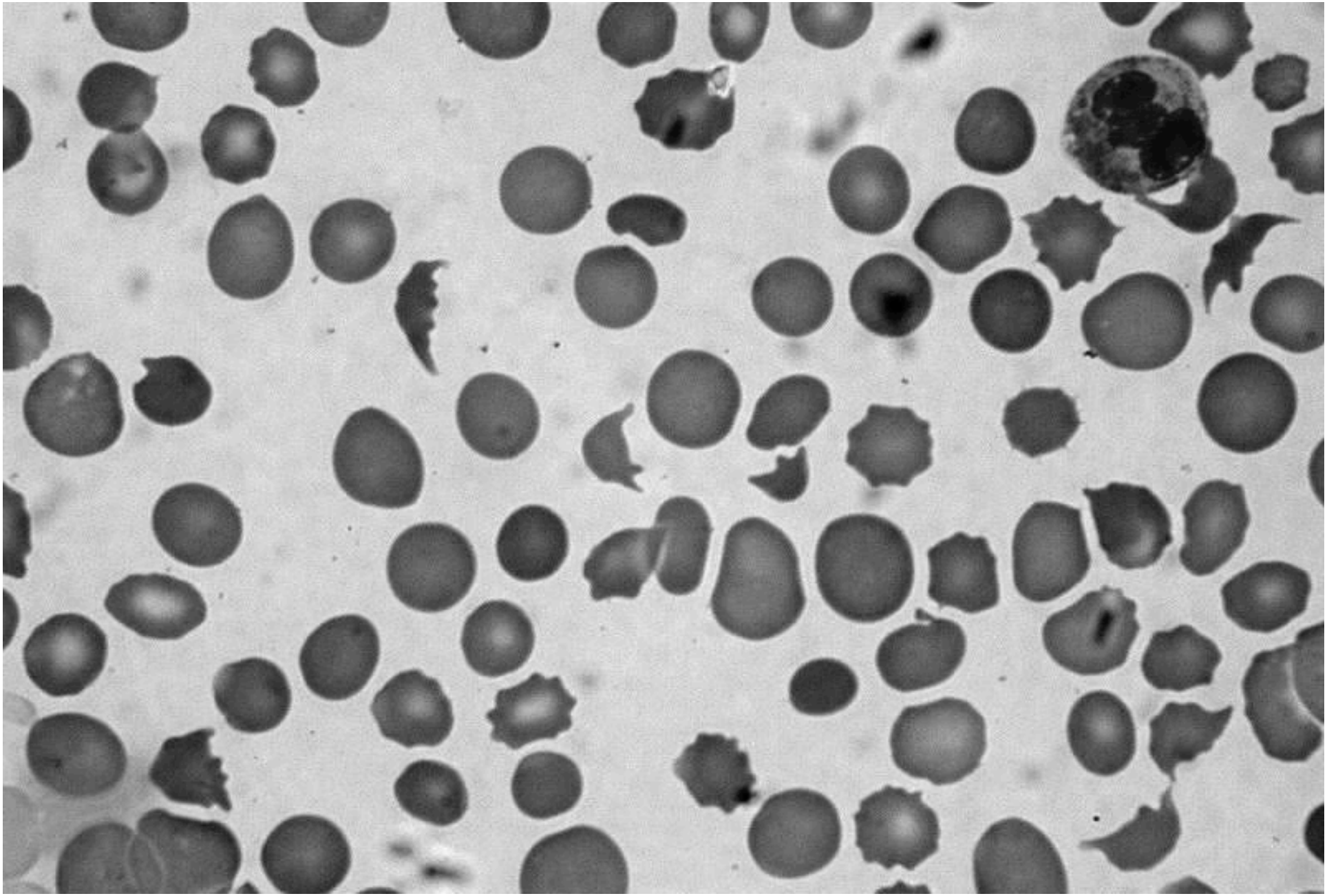
Microangiopathic Hemolytic Anemia

Things You Must Know

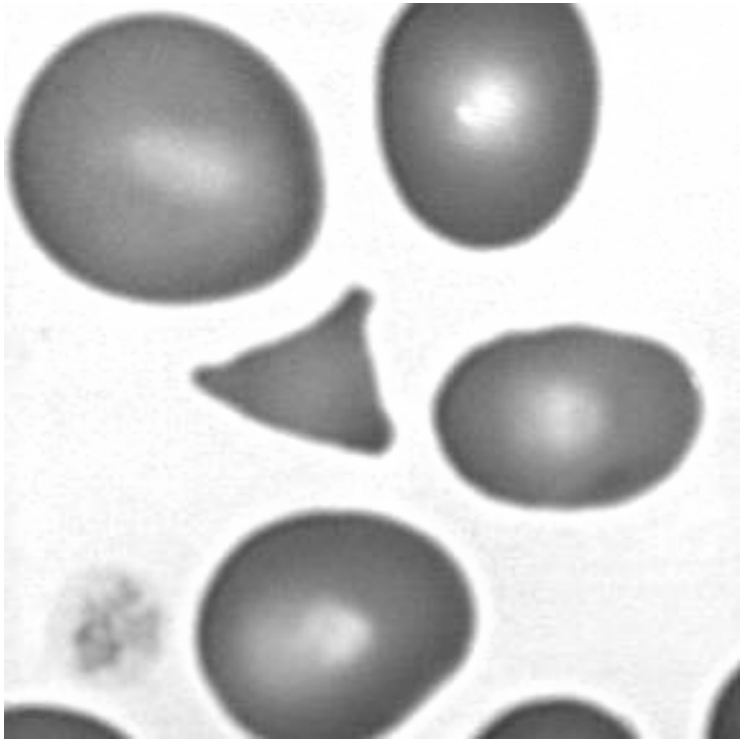
- Physical trauma to red cells
- Schistocytes
- Find out why!



Red cells snagged on fibrin strand



Schistocytes



Triangulocyte

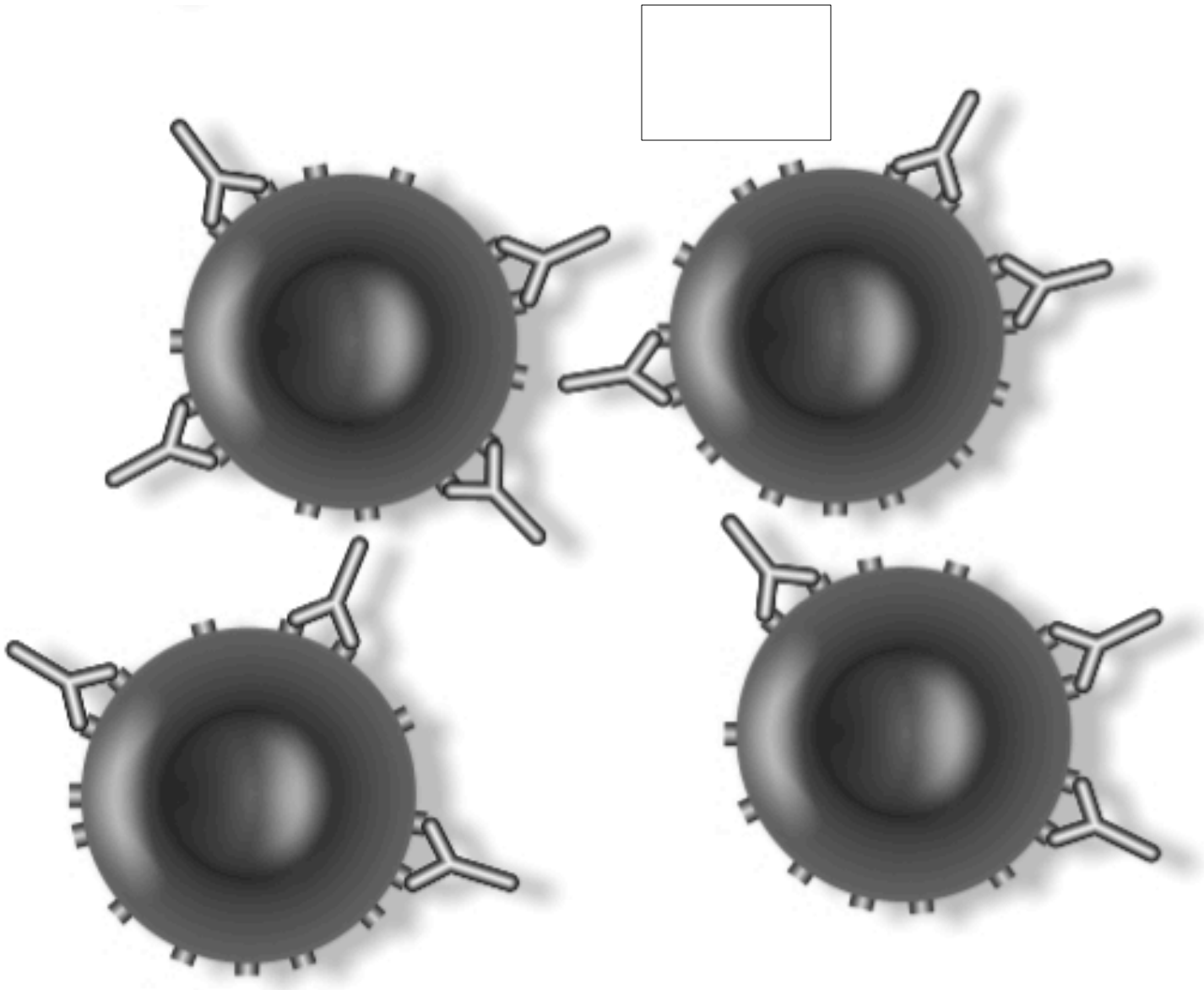
Causes of MAHA

- Artificial heart valve
- Malignancy
- Obstetric complications
- Sepsis
- Trauma

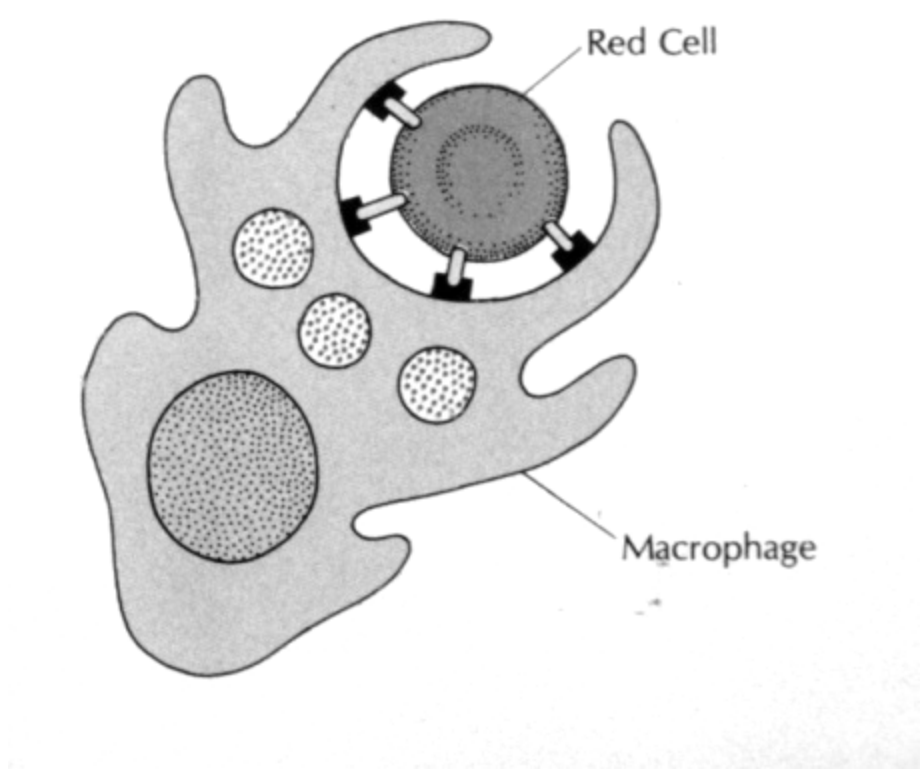
Autoimmune Hemolytic Anemia

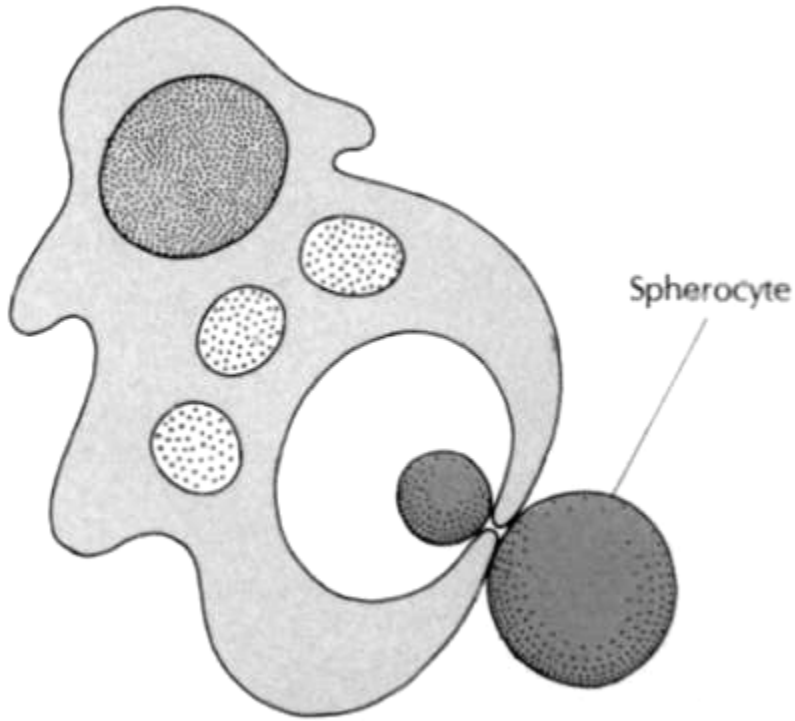
Things You Must Know

- Warm AIHA
  - IgG
  - Spleen
  - Spherocytes
- Cold AIHA
  - IgM, complement
  - Intravascular hemolysis
  - Agglutination

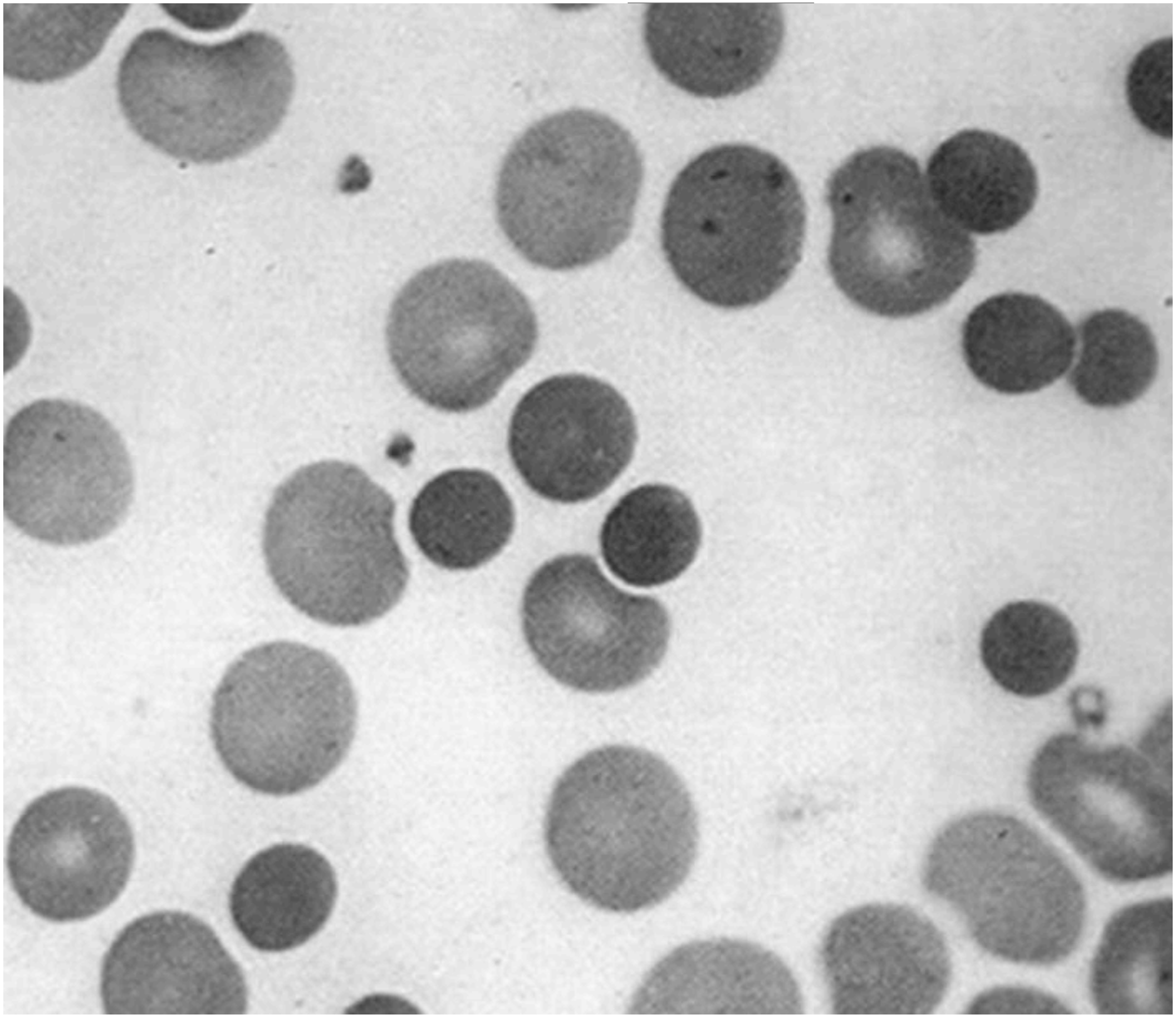


Warm AIHA

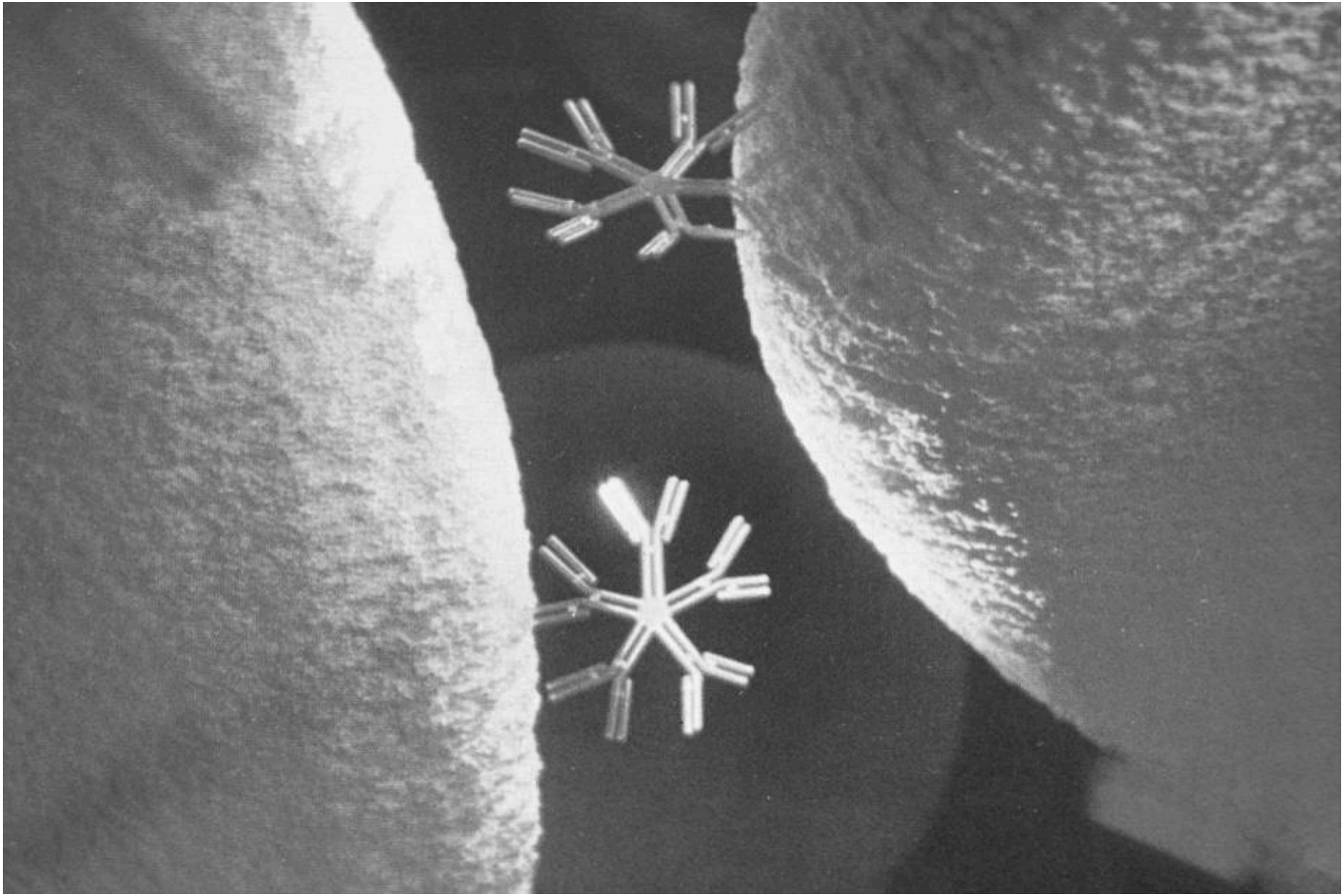




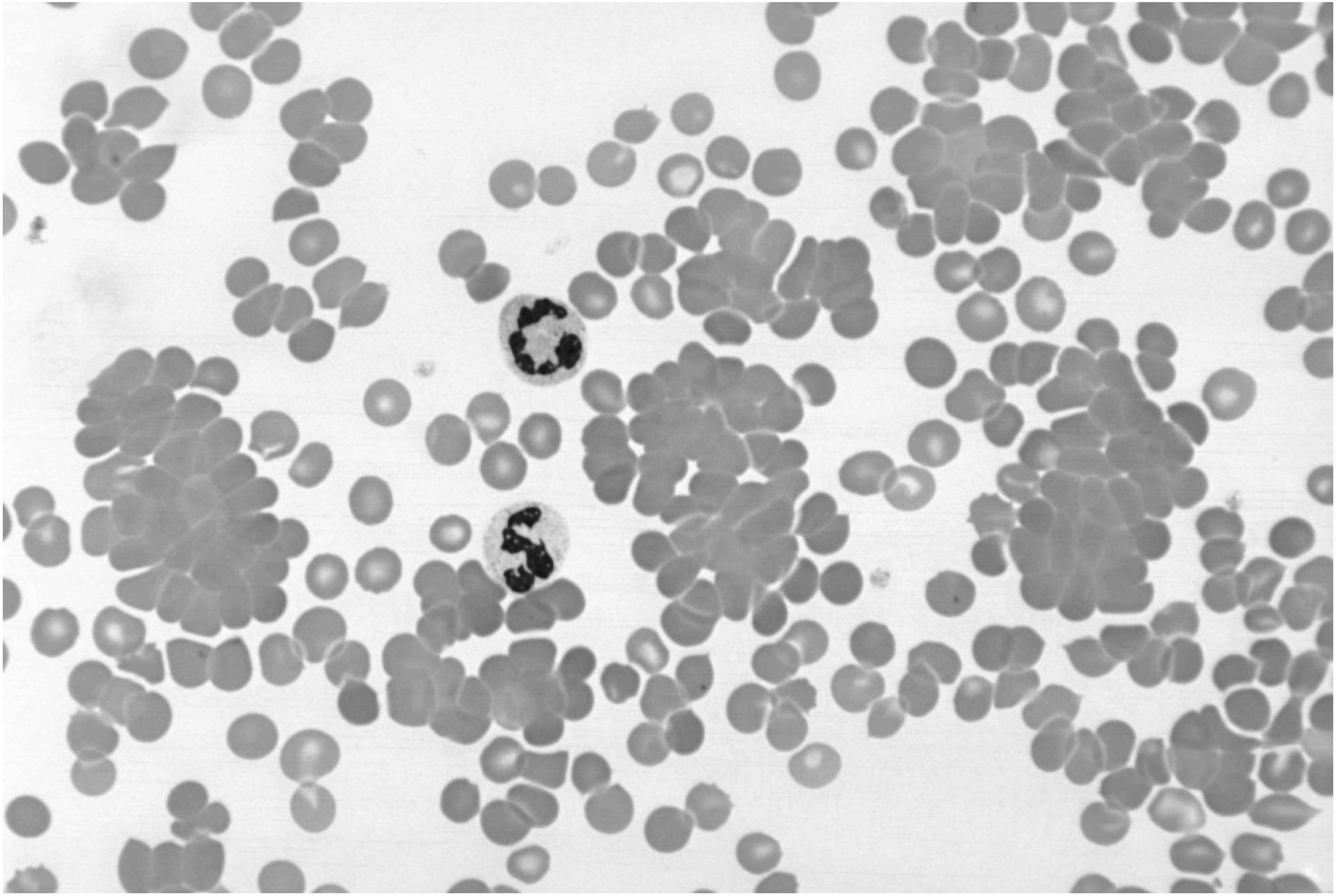
Warm AIHA



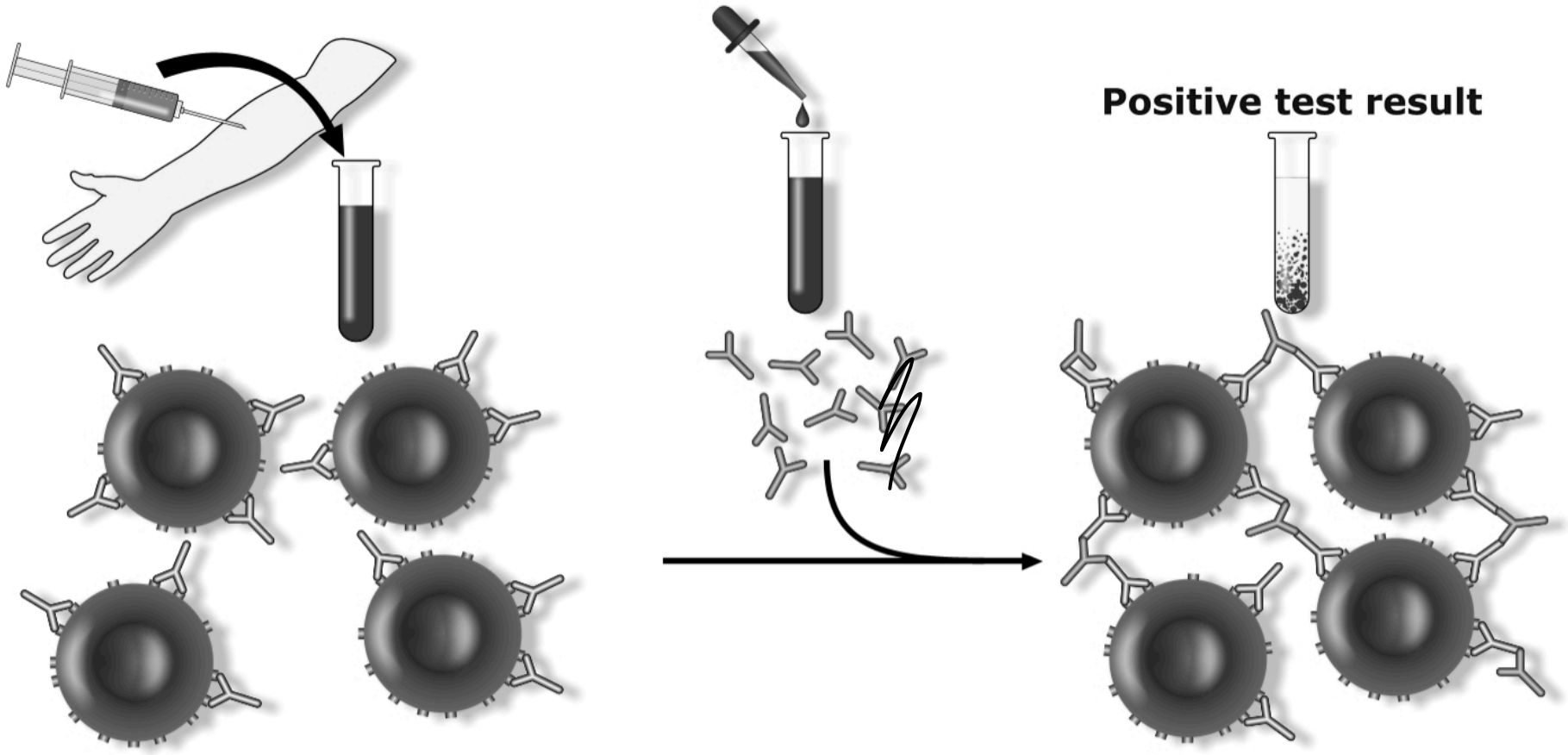
Warm AIHA



Cold AIHA



Cold AIHA



patient red cells + AHG = agglutination

Direct antiglobulin test (DAT)

Three Ways to Get Anemic

Lose blood

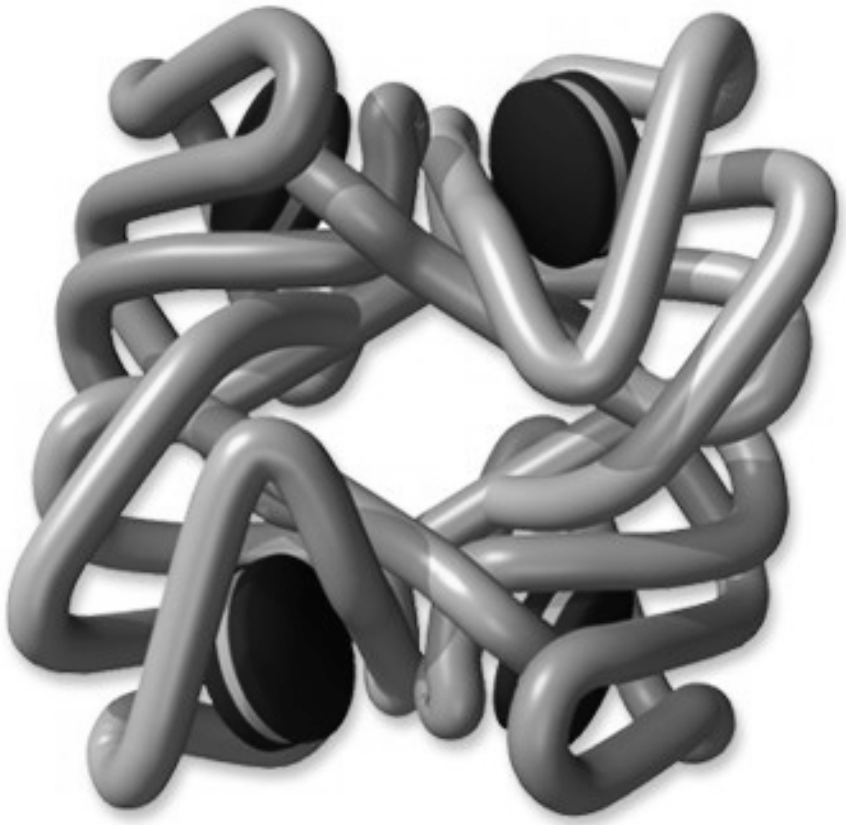
Destroy too much blood

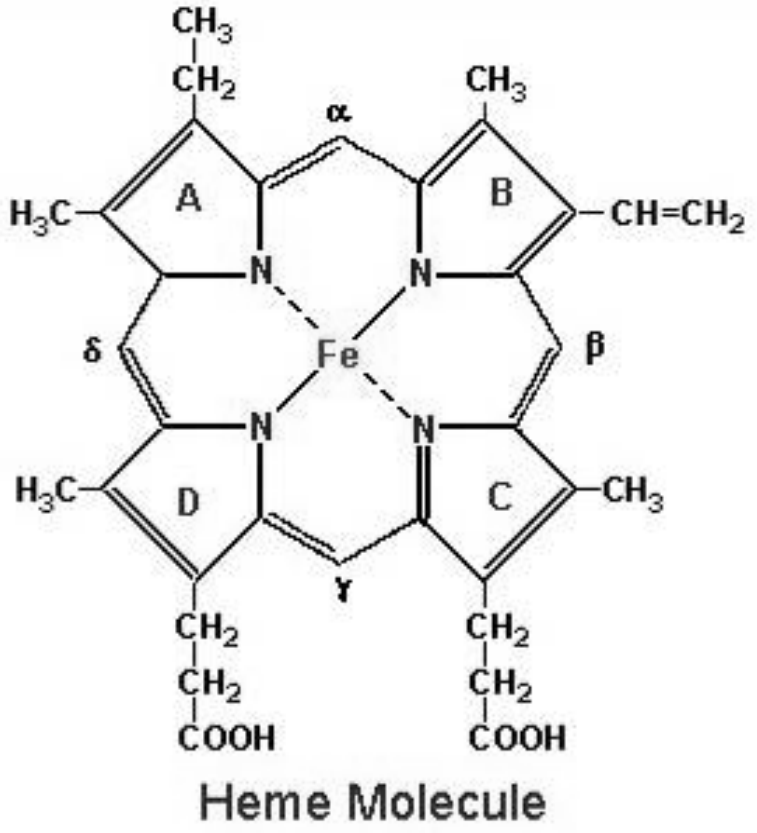
- Extracorpuscular reasons
- Intracorpuscular reasons

Sickle Cell Anemia

Things You Must Know

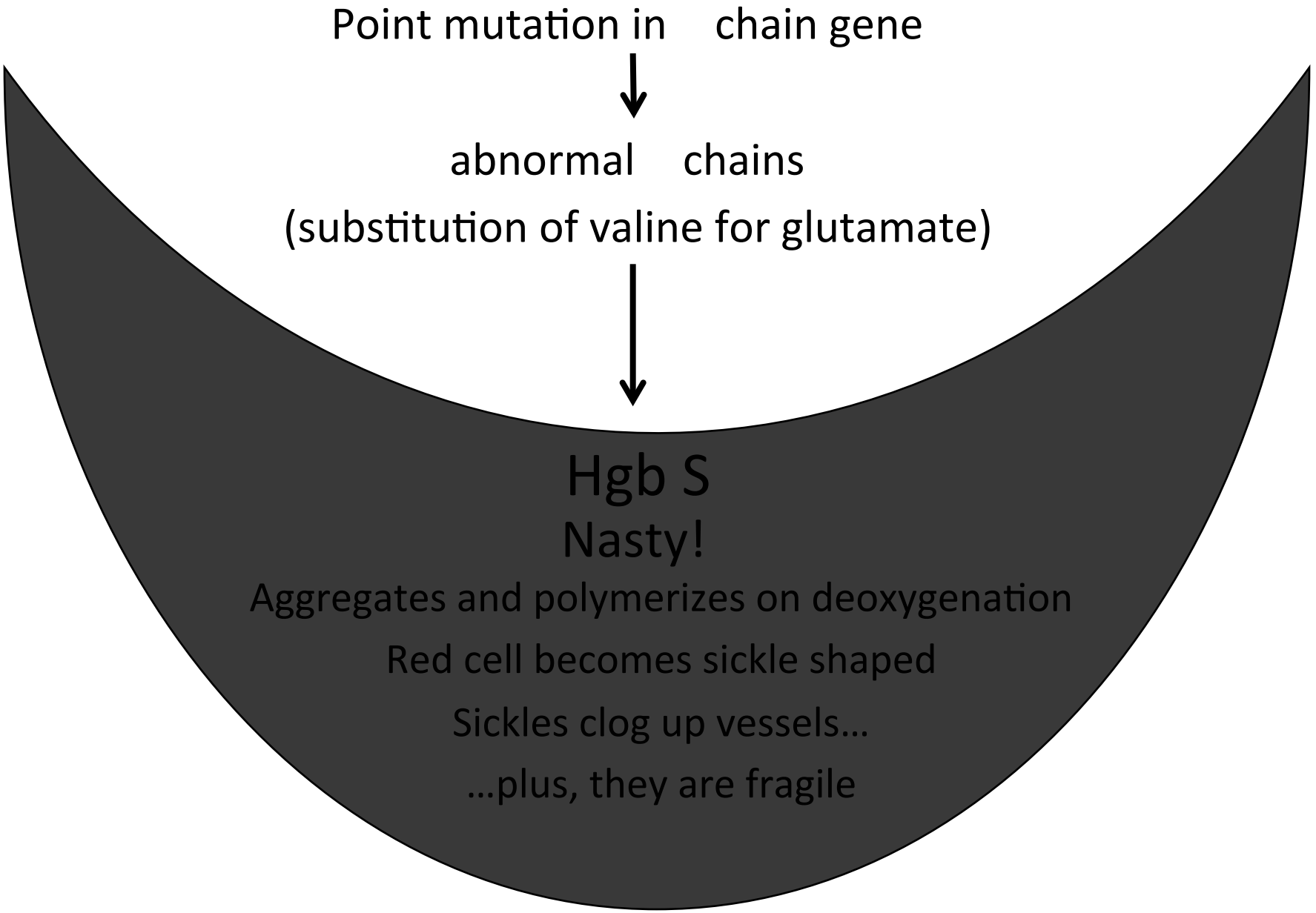
- Hemoglobinopathy (qualitative defect in hemoglobin)
- Single amino acid substitution in beta chain of hemoglobin
- Can be heterozygous or homozygous
- Sickle cells are nasty:
  - Fragile (burst easily)
  - Get stuck in vessels

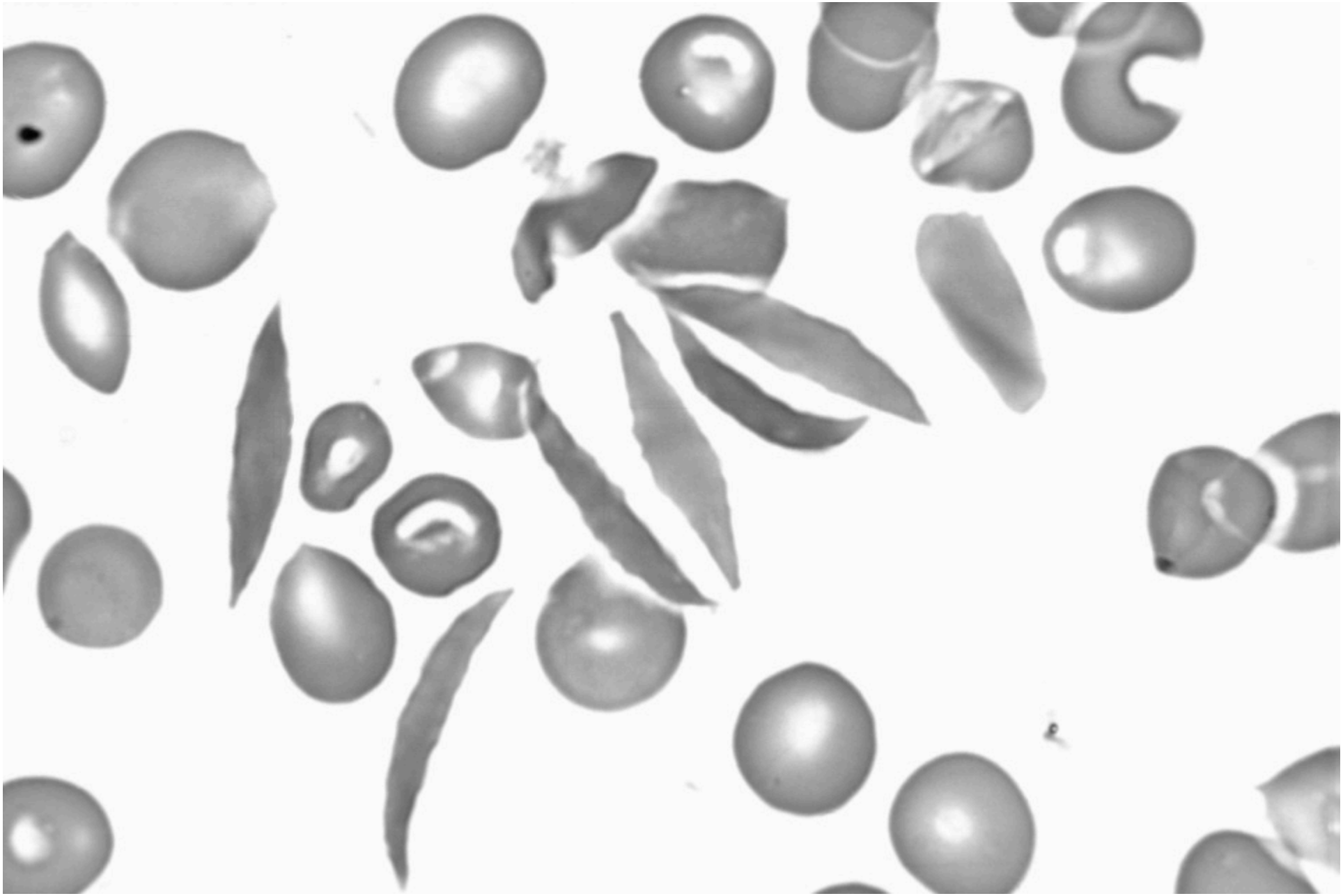




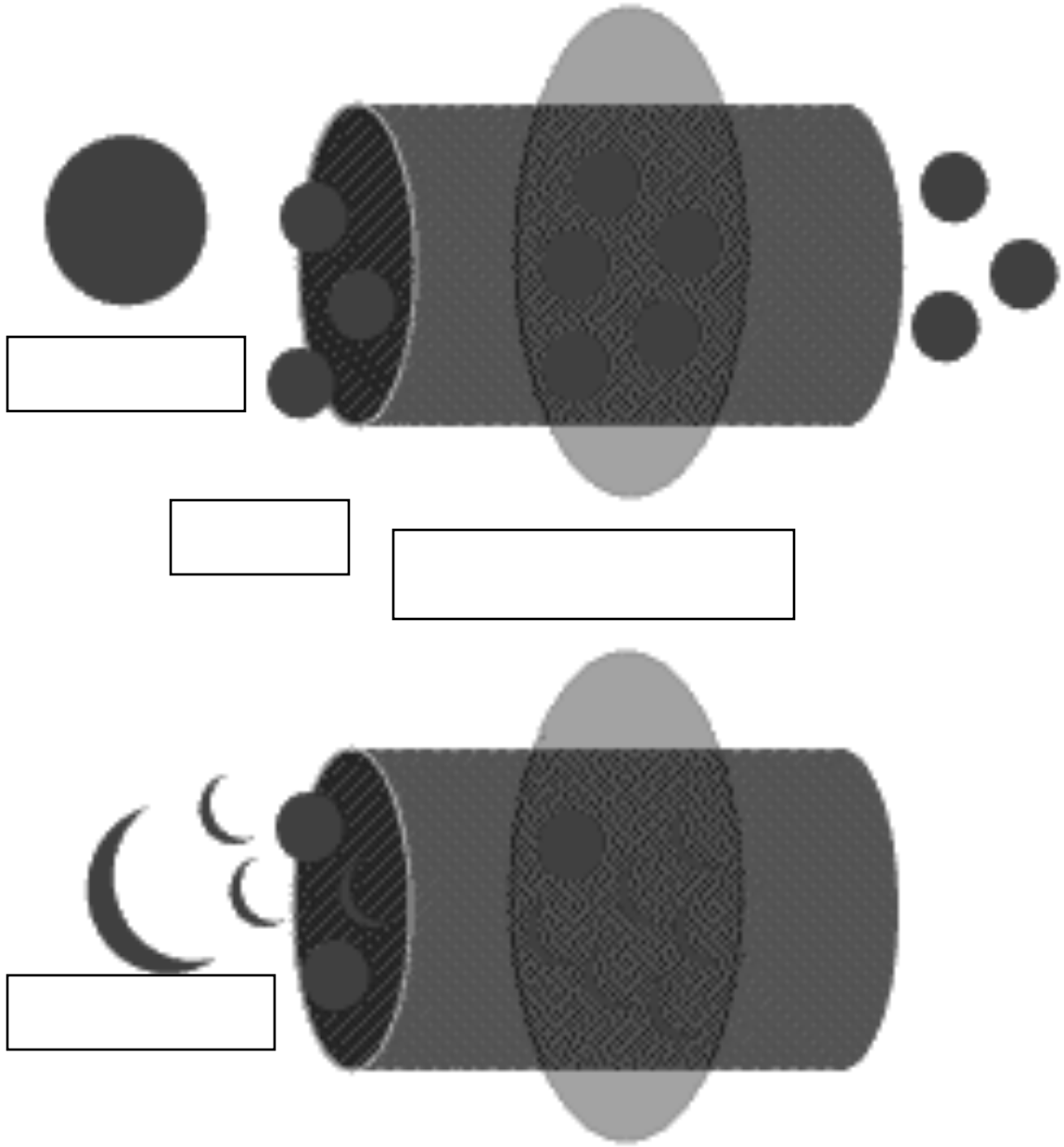
Heme Molecule

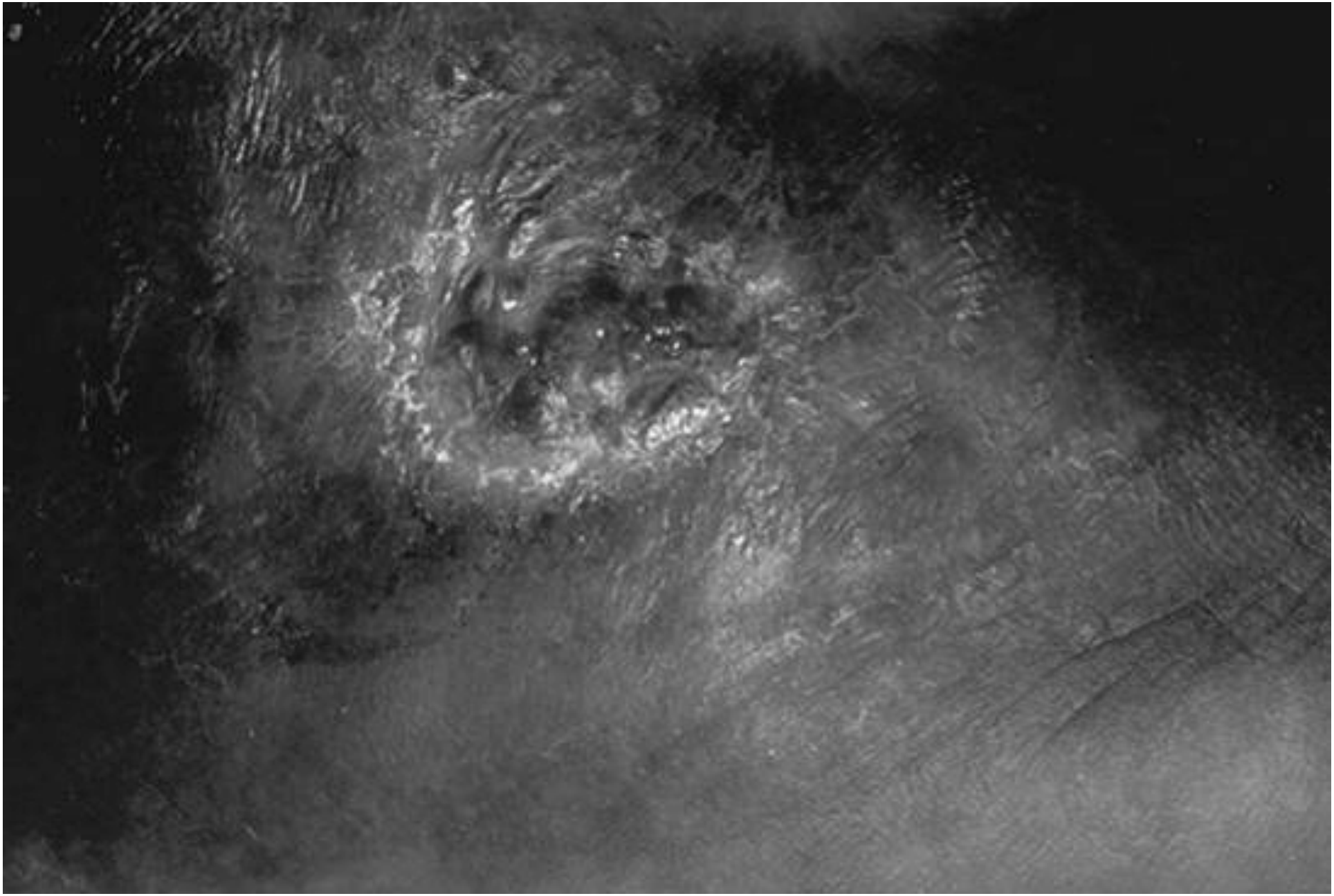
Hemoglobin


Point mutation in chain gene
abnormal chains
(substitution of valine for glutamate)
Hgb S
Nasty!
Aggregates and polymerizes on deoxygenation
Red cell becomes sickle shaped
Sickles clog up vessels…
…plus, they are fragile

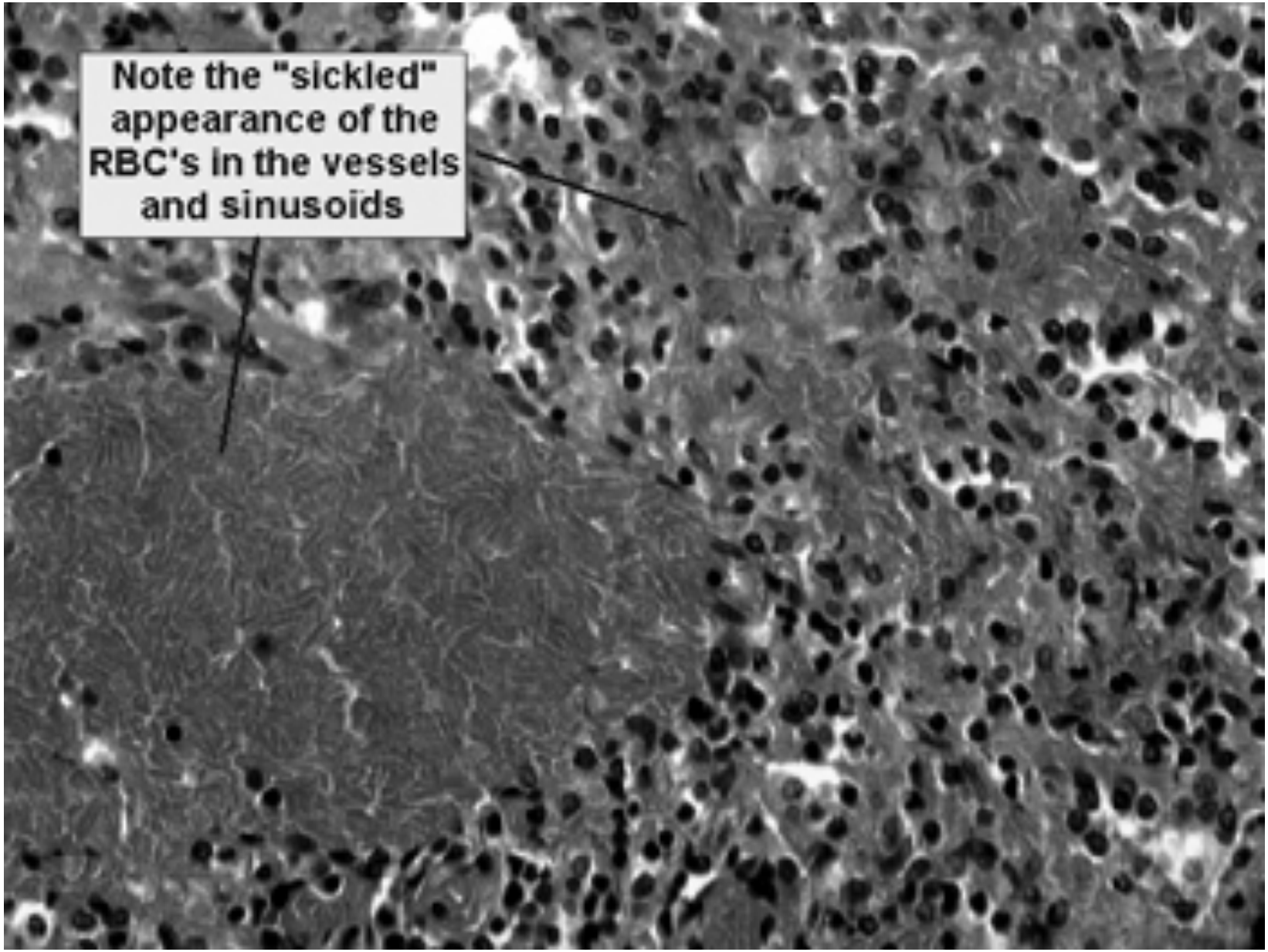


Sickle cell anemia





Sickle cell anemia: foot lesion



Sickle cell anemia: spleen

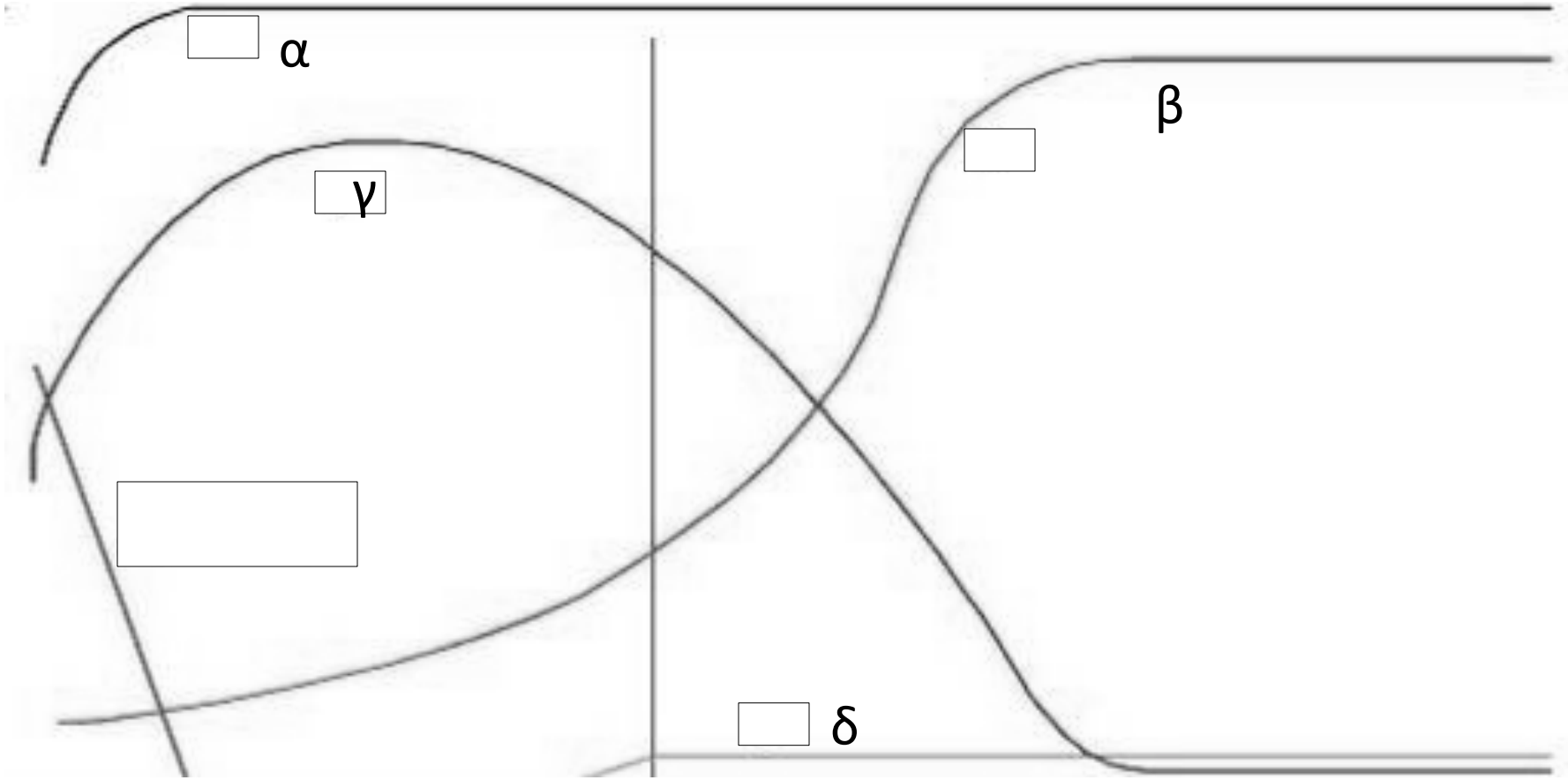
Clinical Findings in Sickle Cell Anemia

- Blacks (8% are heterozygous)
- Severity of disease is variable
- Chronic hemolysis, vaso-occlusive disease, and infections (autosplenectomy)
- Treatment: prevent triggers, vaccinate, transfuse

Thalassemia

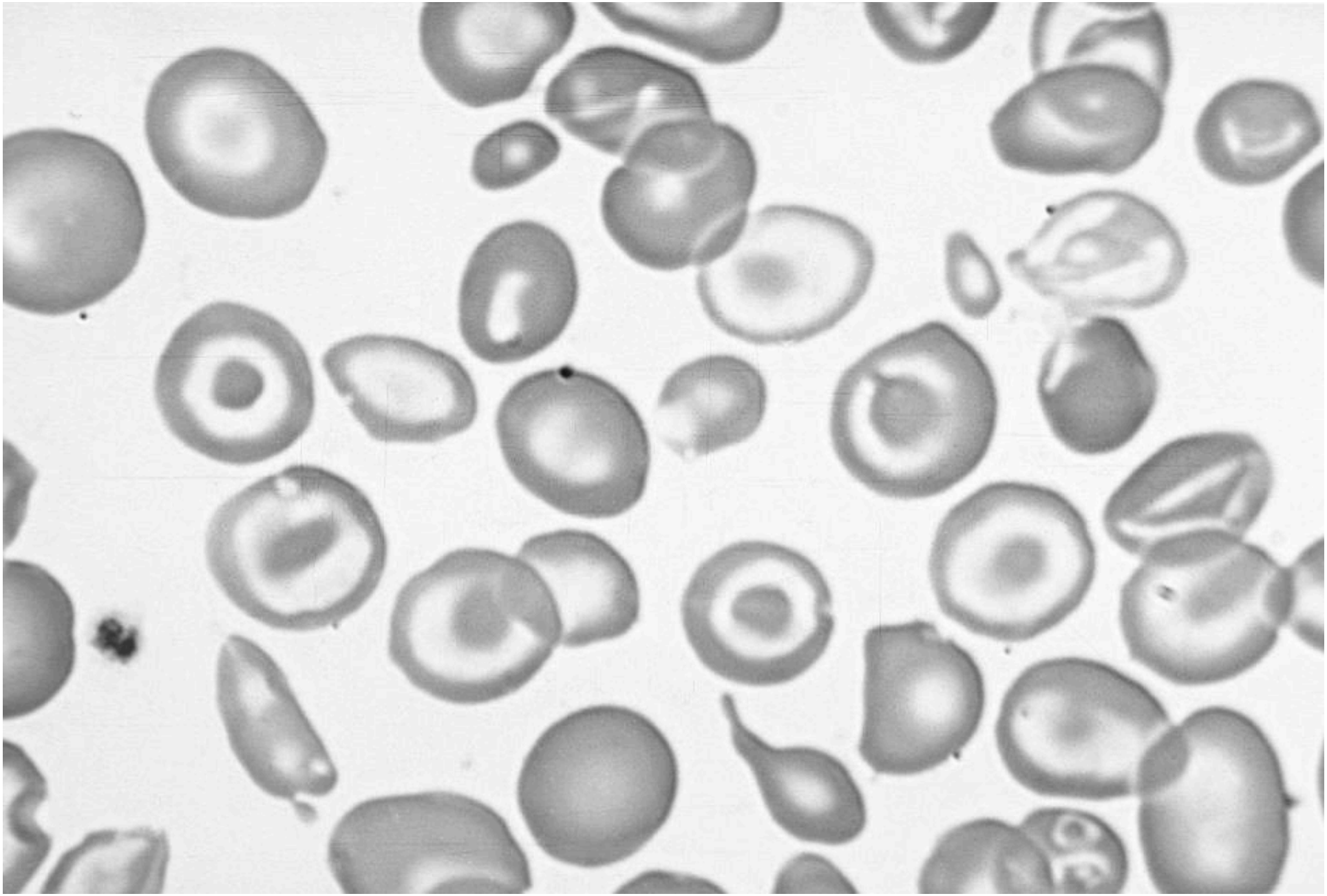
Things You Must Know

- Quantitative defect in hemoglobin
- Can't make enough α or β chains
- Variable disease severity
- Hypochromic, microcytic anemia with increased RBC and target cells

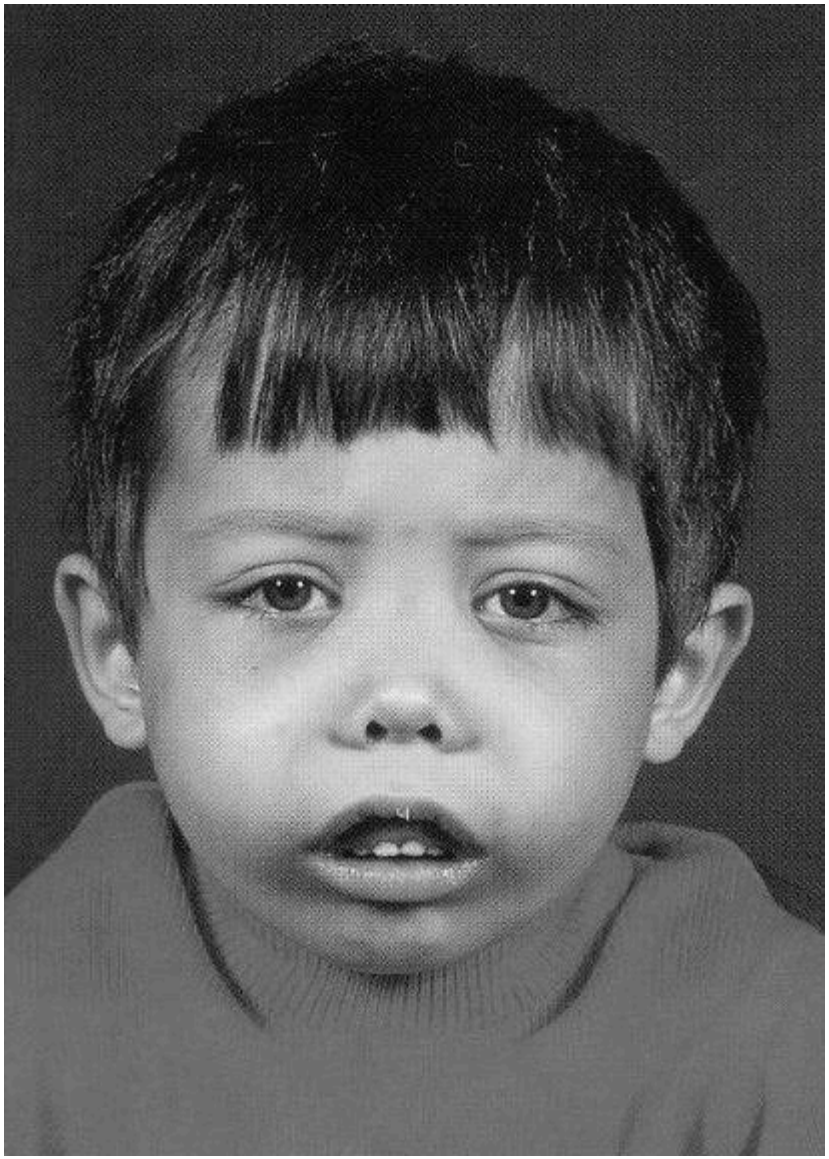


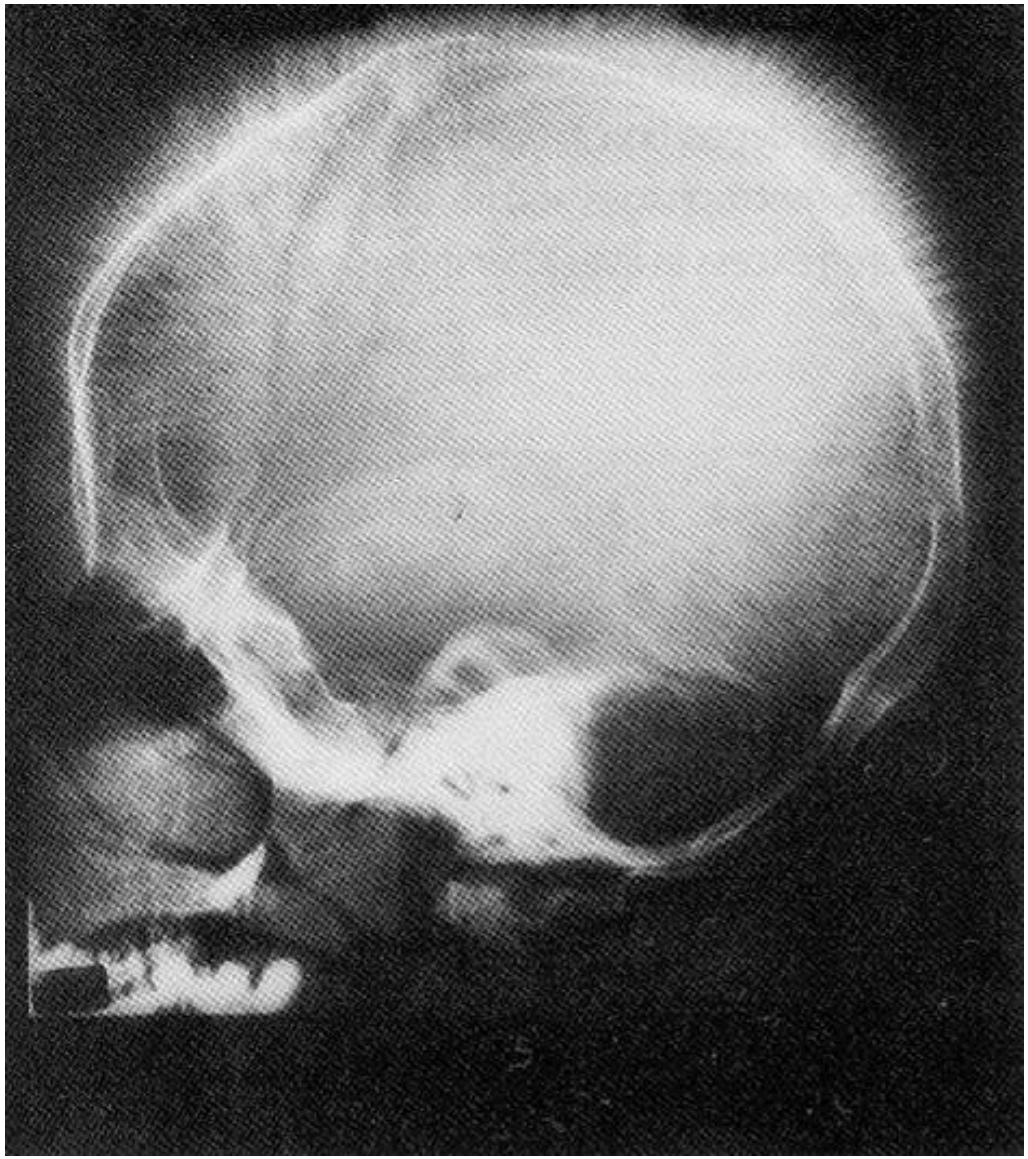
Hgb F = $\alpha_2\gamma_2$ Hgb A_2 = $\alpha_2\delta_2$ Hgb A = $\alpha_2\beta_2$

Hemoglobin chain development



Thalassemia



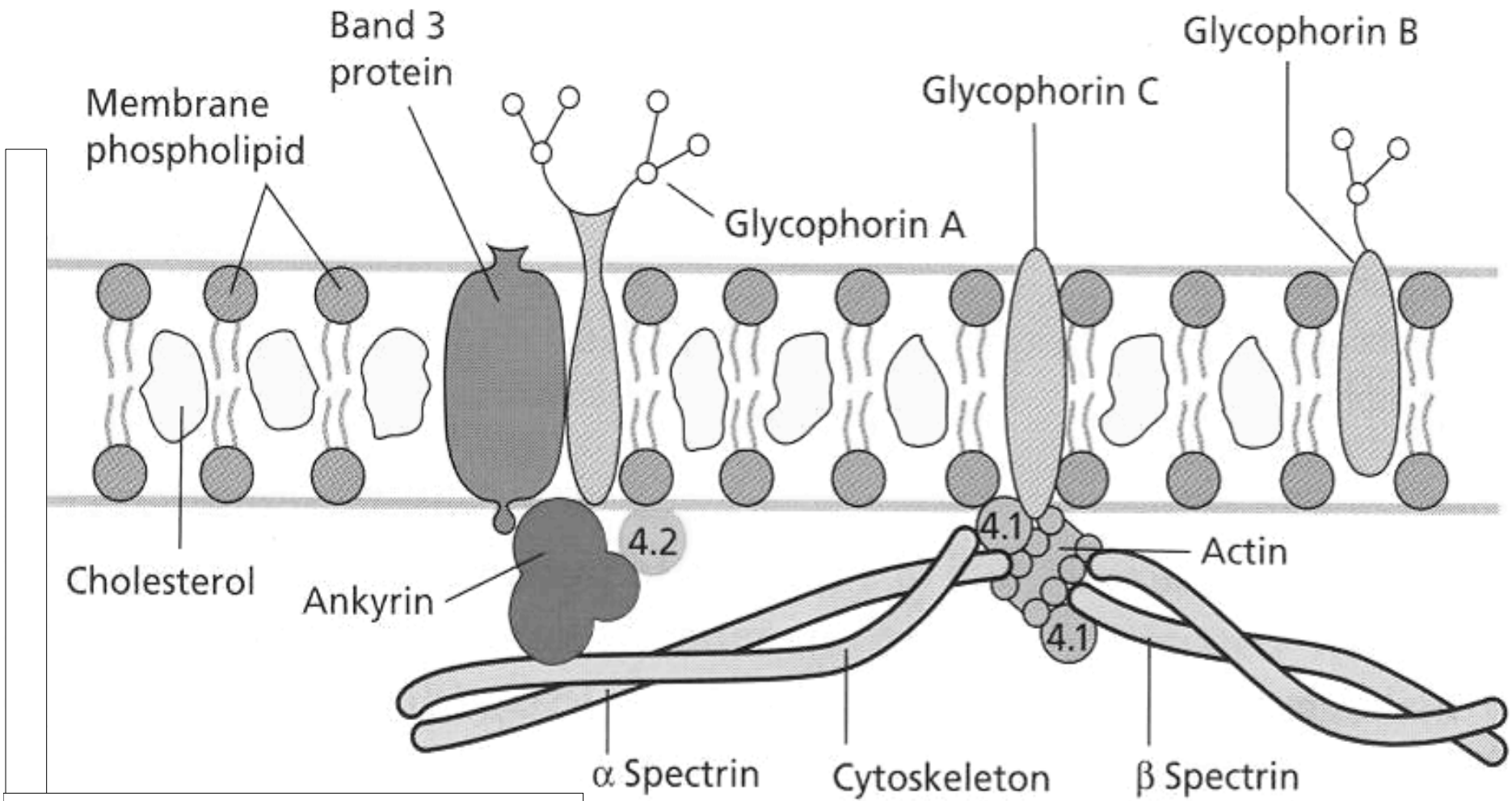


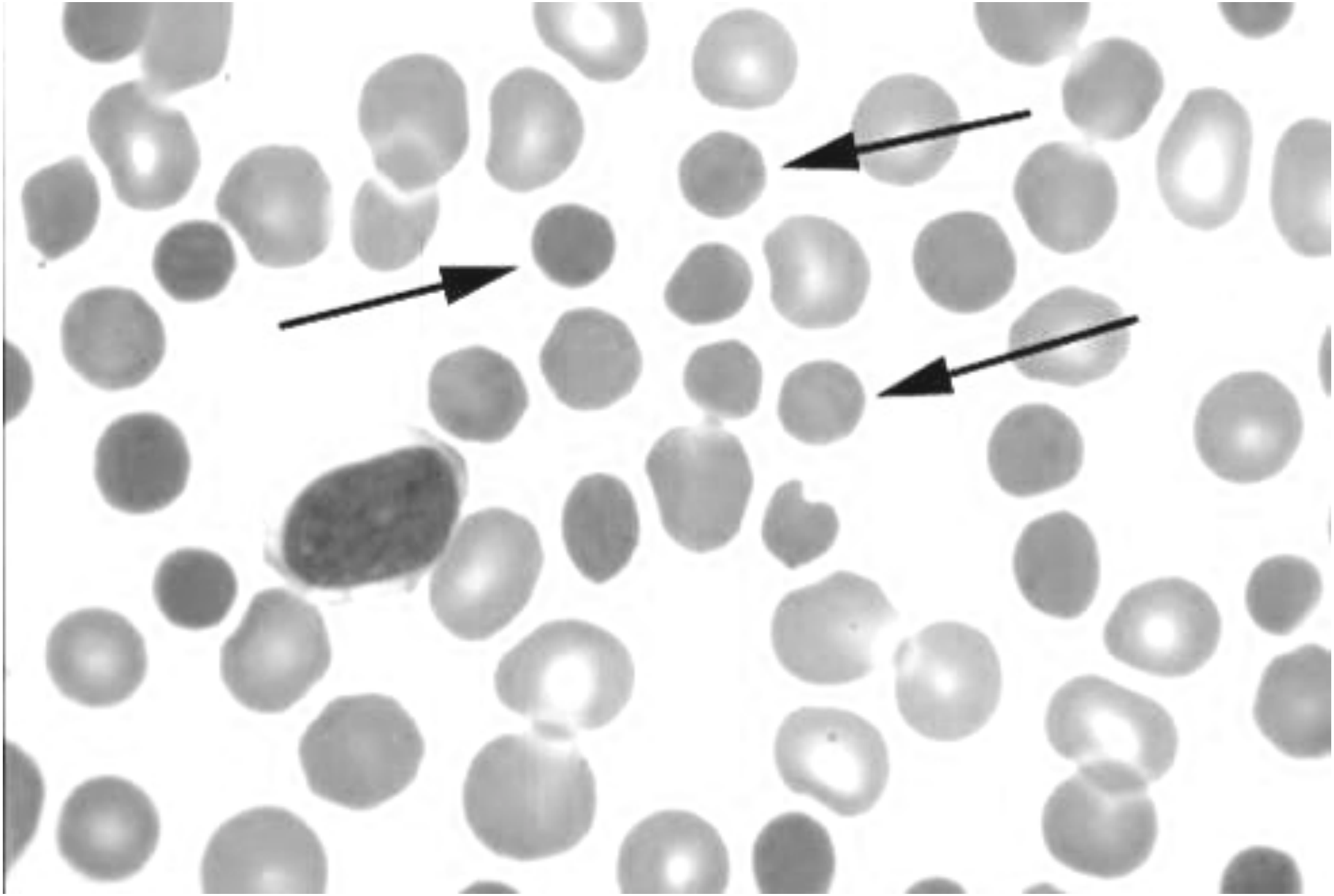
Thalassemia: Medullary expansion

Hereditary Spherocytosis

Things You Must Know

- Tons of spherocytes
- Spectrin defect
- Splenectomy is curative


Band 3
protein
Glycophorin B
Membrane
phospholipid
Glycophorin C
Glycophorin A
4.2
4.1
Actin
Cholesterol
Ankyrin
4.1
α Spectrin
Cytoskeleton
β Spectrin



Hereditary spherocytosis

Splenomegaly in hereditary spherocytosis

Glucose-6-Phosphate Dehydrogenase Deficiency

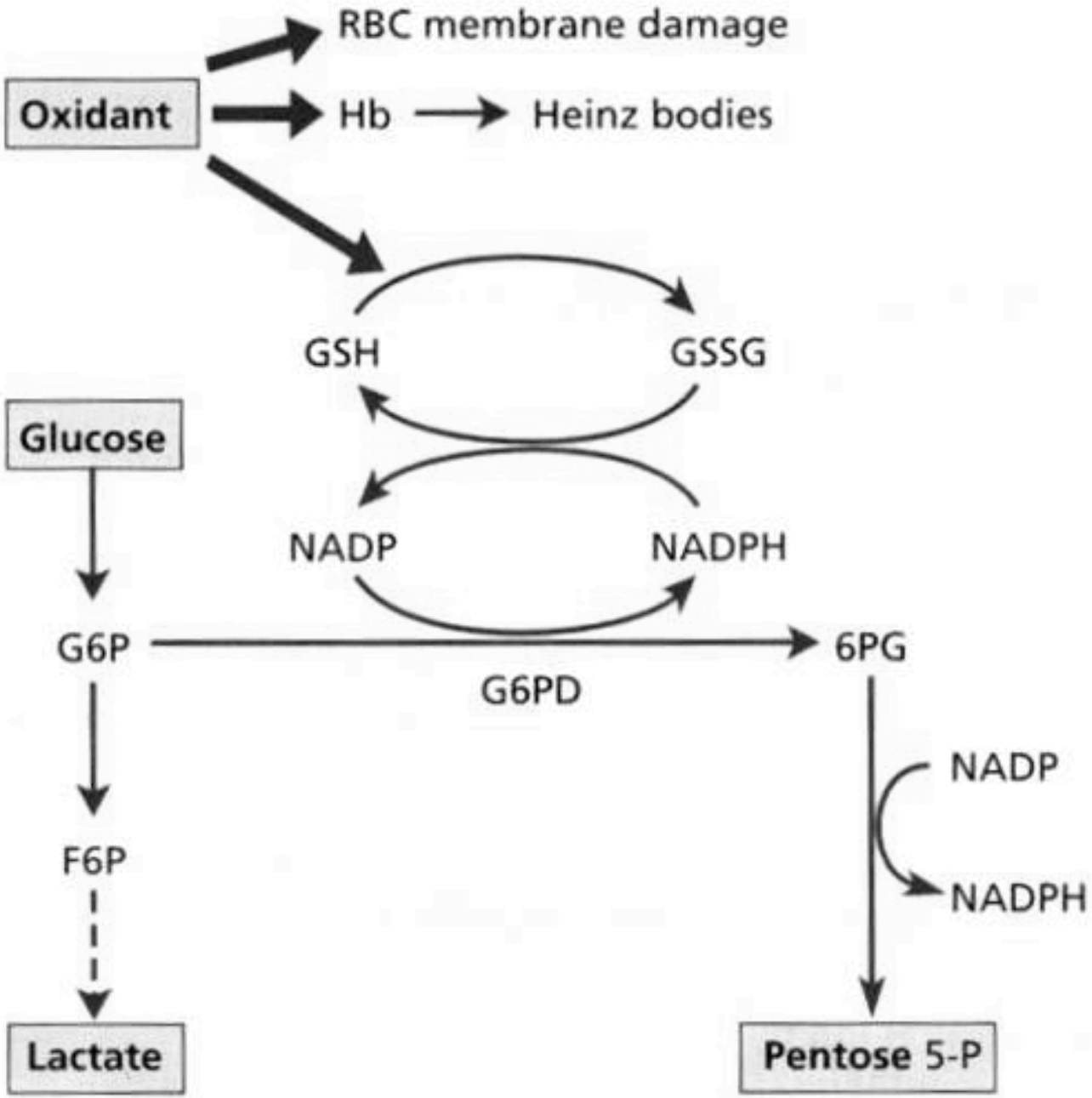
Things You Must Know

- ↓ G6PD → ↑ peroxides → cell lysis
- Oxidant exposure
- Bite cells (removal of Heinz bodies)
- Self-limiting

Clinical Findings in G6PD Deficiency

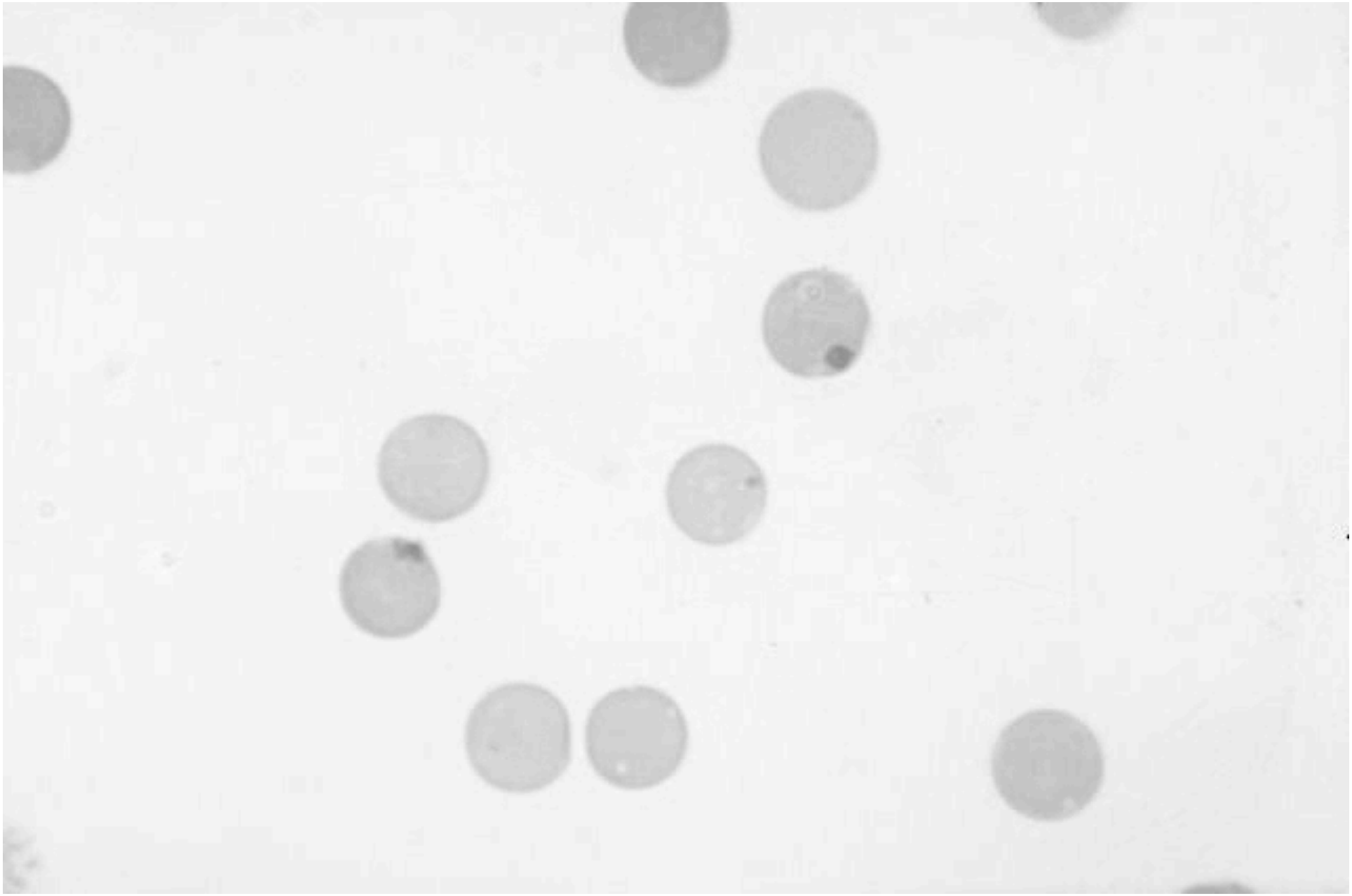
- Some patients asymptomatic
- Others have episodic hemolysis
- Triggers: broad beans (favism), drugs (antibiotics, aspirin)
- Spontaneous resolution

Child with G6PD deficiency: jaundiced sclera

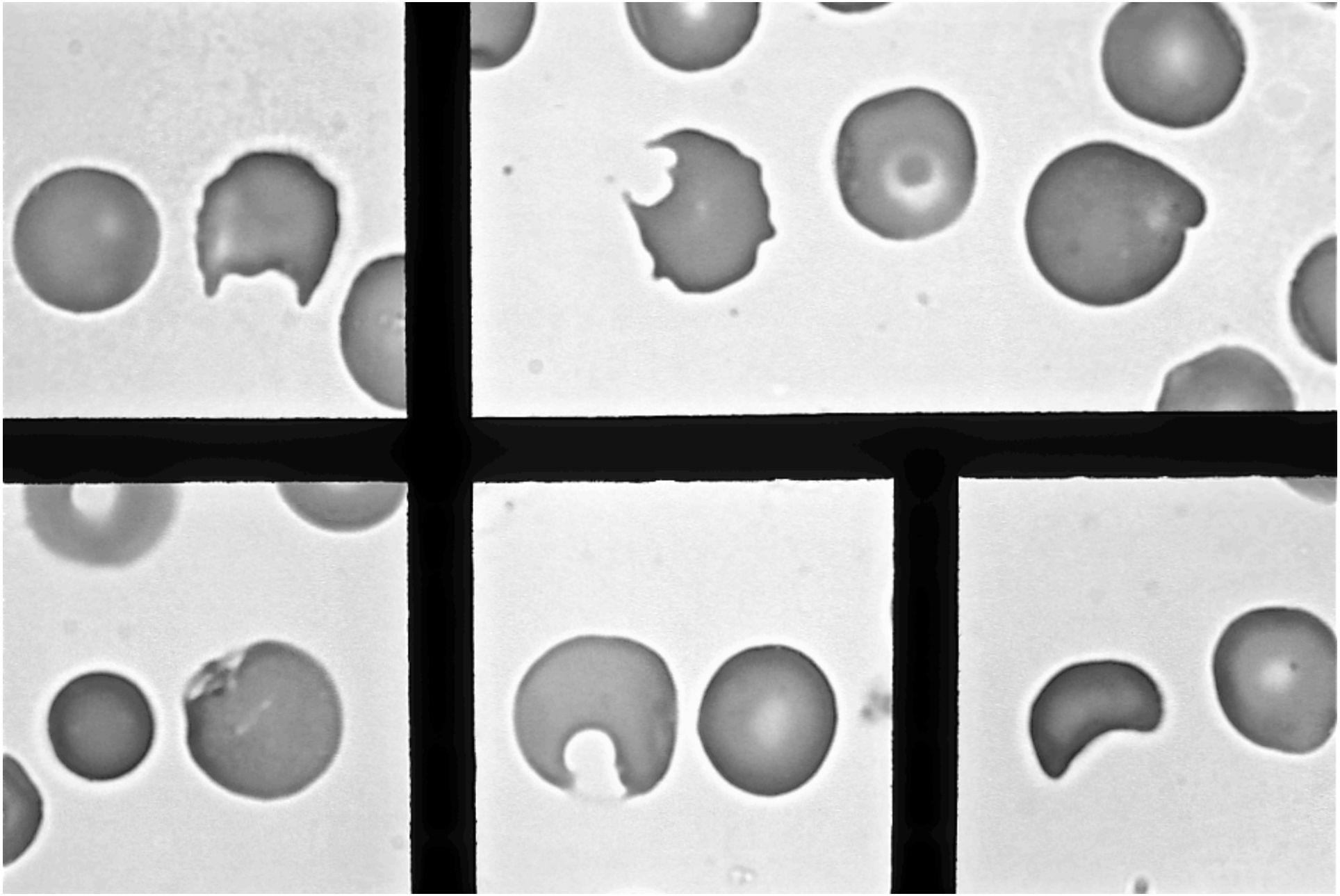

RBC membrane damage
Oxidant
Hb
Heinz bodies
GSH
GSSG
Glucose
NADP
NADPH
G6P
6PG
G6PD
NADP
F6P
NADPH
Lactate
Pentose 5-P

Why Do G6PD-Deficient Red Cells Die?

- They can't reduce nasties
- Nasties attack hemoglobin bonds
- Heme breaks away from globin
- Globin denatures, sticks to red cell membrane ("Heinz body")
- Spleen bites out Heinz bodies



G6PD deficiency: Heinz bodies



G6PD deficiency: bite cells

Three Ways to Get Anemic

Lose blood

Destroy too much blood

- Extracorpuscular reasons
- Intracorpuscular reasons

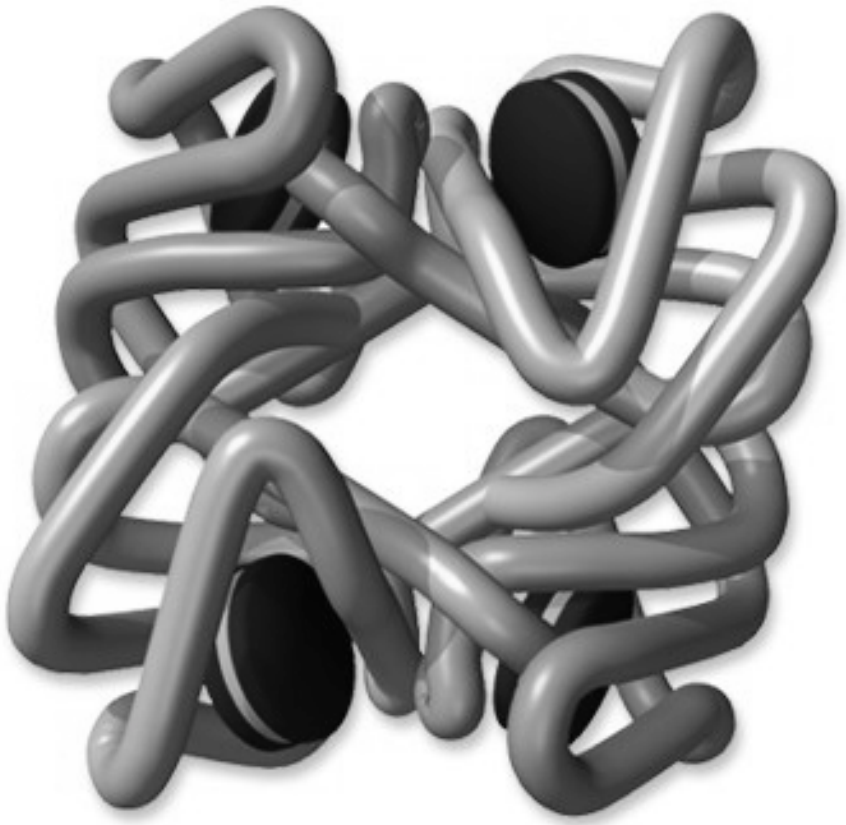
Make too little blood

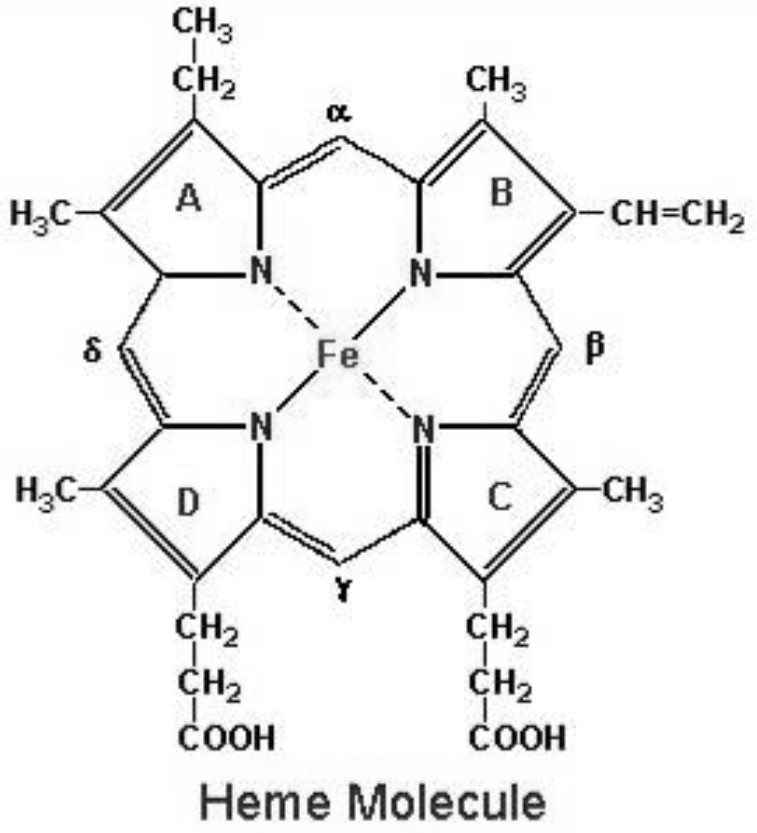
- Too few building blocks

Iron-Deficiency Anemia

Things You Must Know

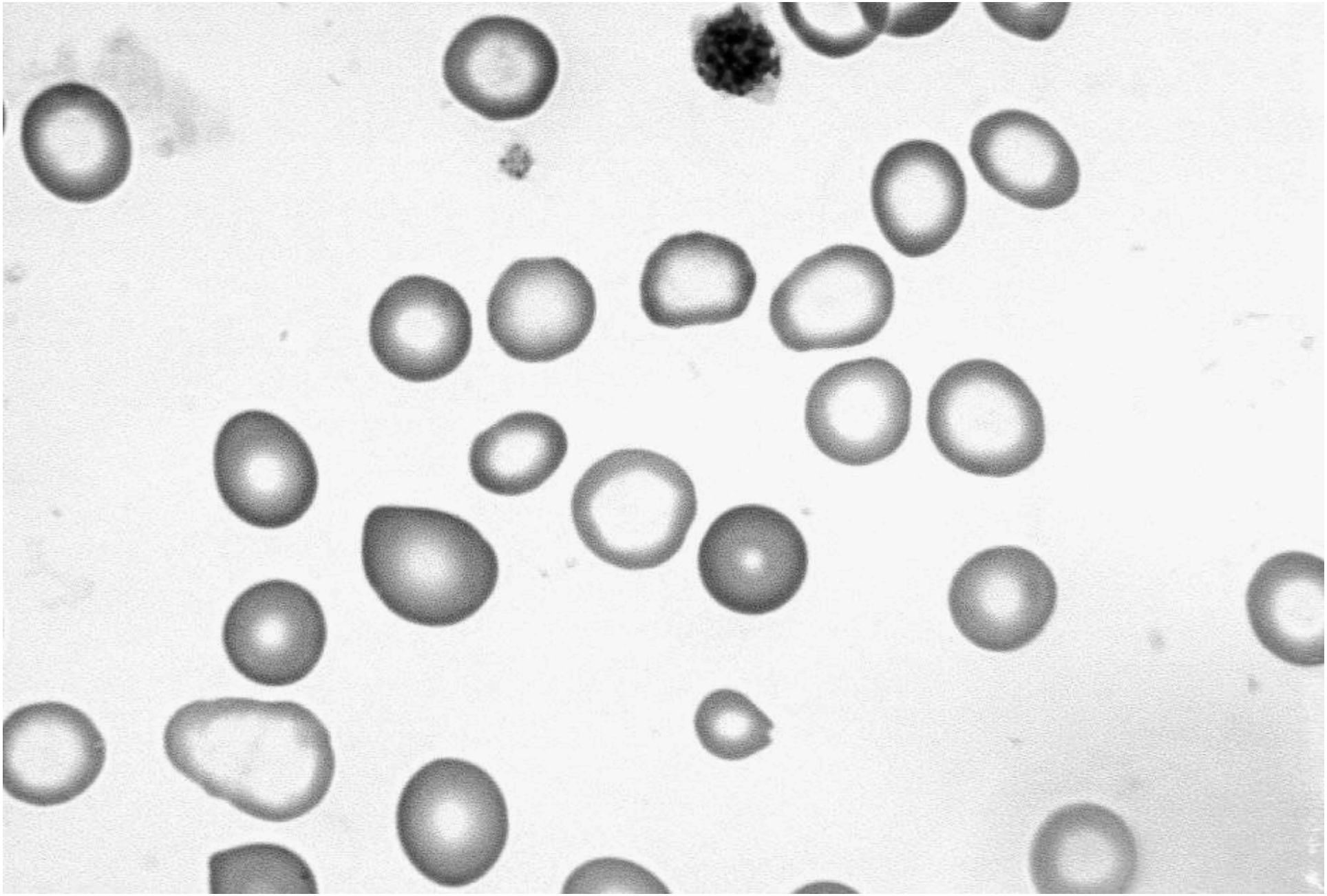
- Most important cause: GI bleeding
- Microcytic, hypochromic anemia
- Must find out why patient is iron deficient!



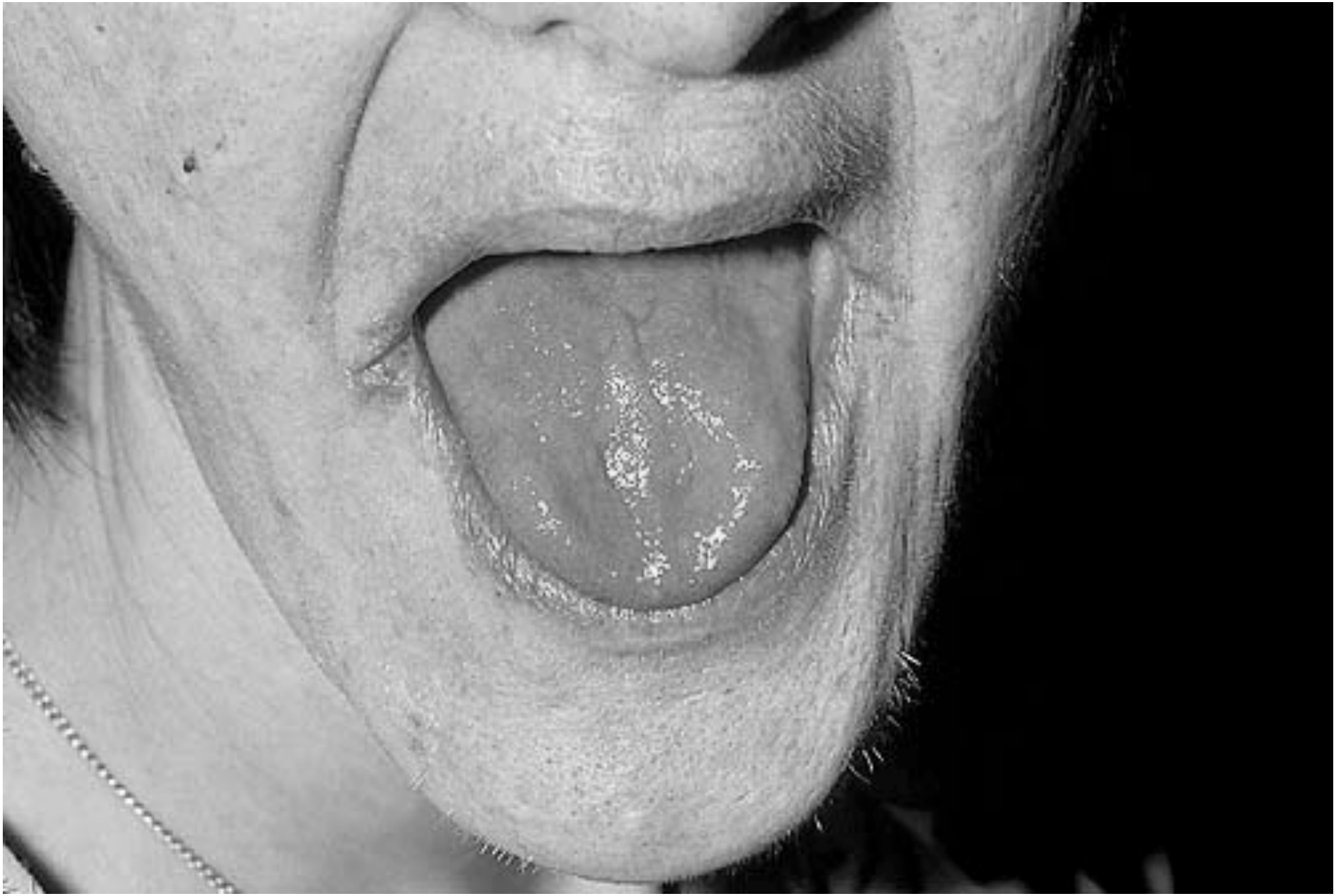


Heme Molecule

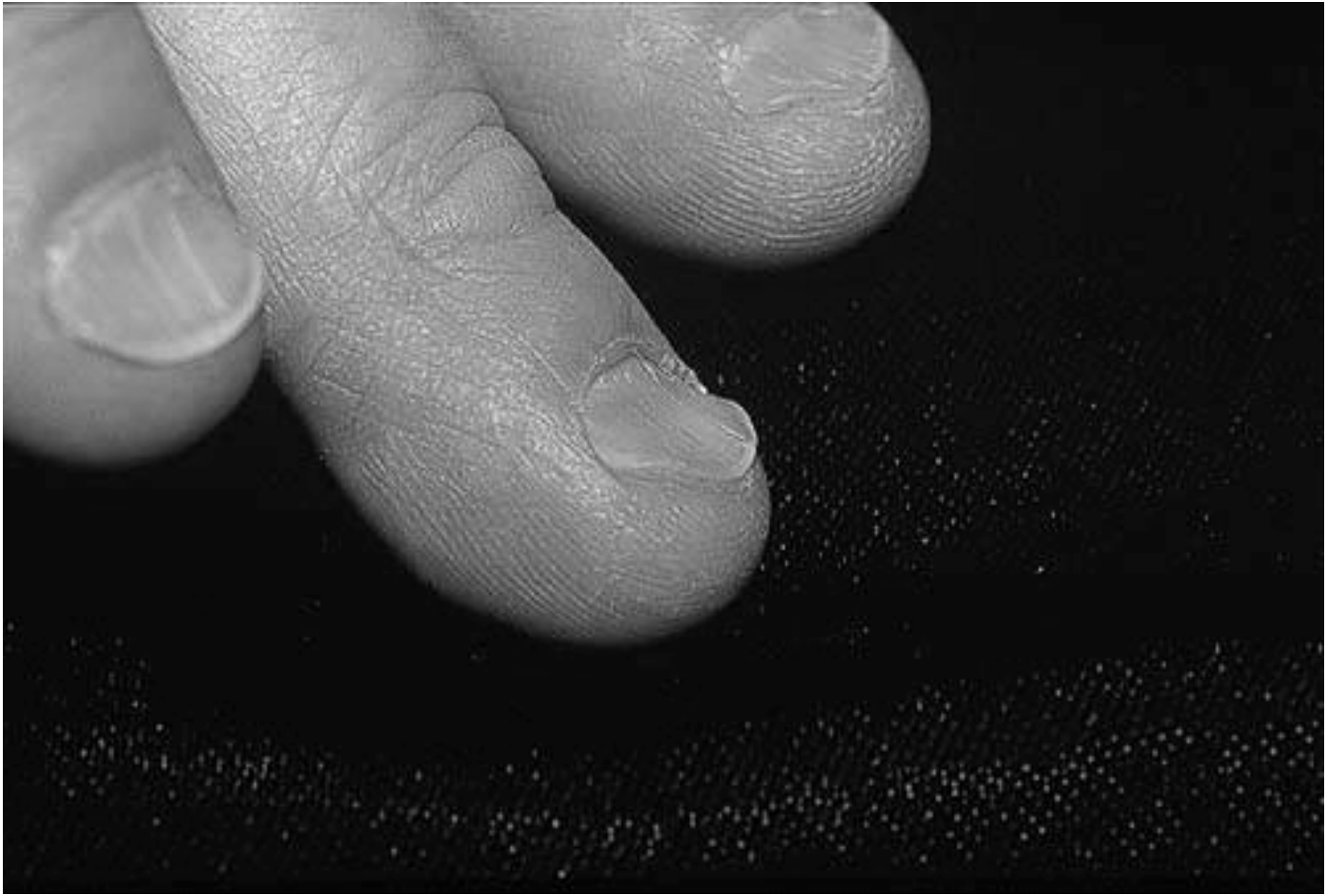
Hemoglobin



Iron-deficiency anemia



Atrophic glossitis in iron-deficiency anemia



Koilonychia in iron-deficiency anemia

Causes of Iron Deficiency

- Decreased iron intake
  - bad diet
  - bad absorption
- Increased iron loss
  - GI bleed
  - menses
  - hemorrhage
- Increased iron requirement
  - pregnancy

Anemia of Chronic Disease

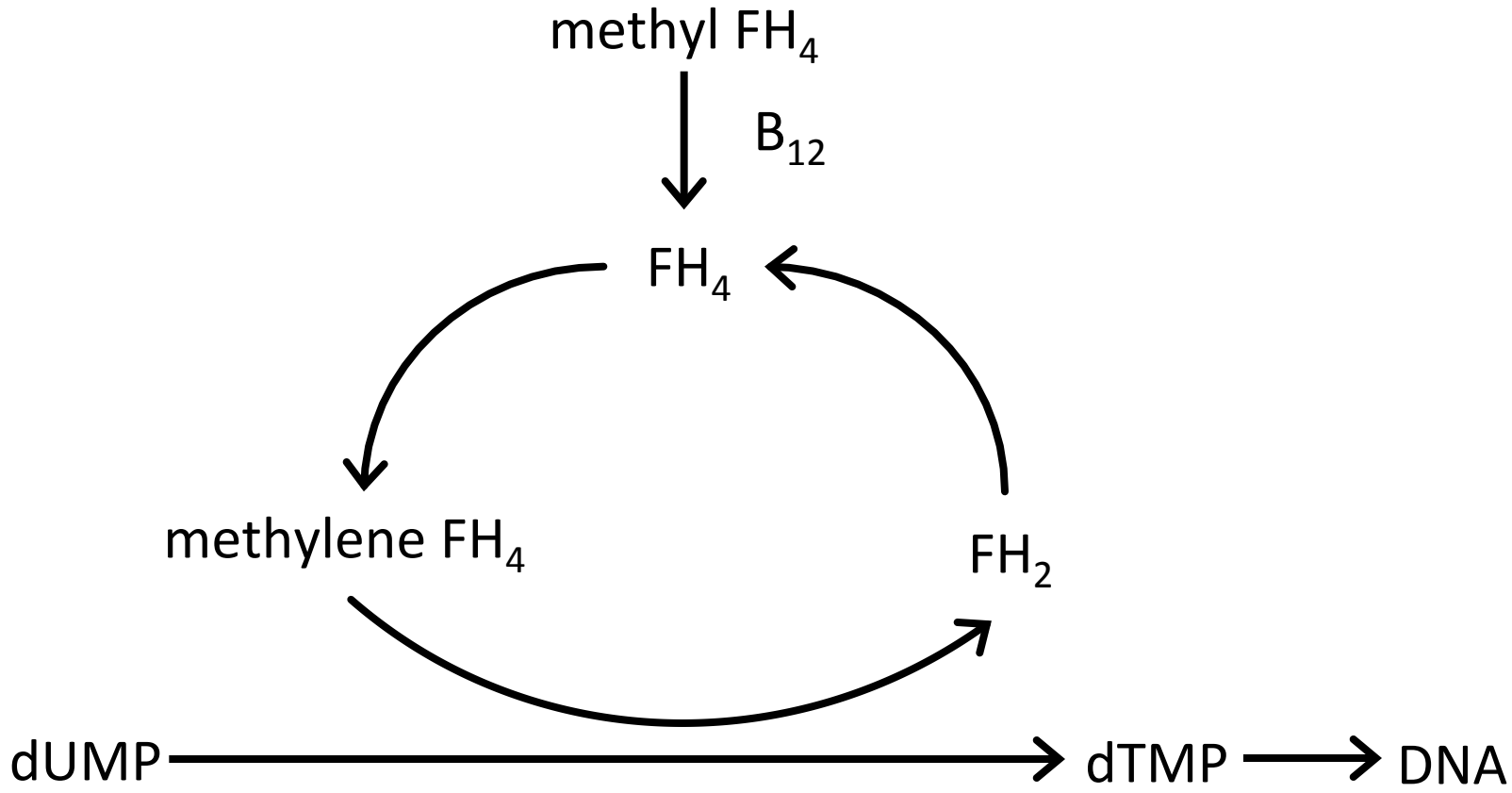
Things You Must Know

- Infections, inflammation, malignancy
- Iron metabolism disturbed
- Normochromic, normocytic anemia
- Anemia usually mild

Megaloblastic Anemia

Things You Must Know

- Defective DNA synthesis
- Nuclear/cytoplasmic asynchrony
- ↓ B_{12}/folate
- Macrocytic anemia with oval macrocytes and hypersegmented neutrophils

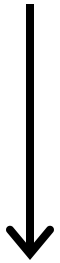


Need B_{12} to make DNA!

Megaloblastic Anemia

retarded DNA synthesis

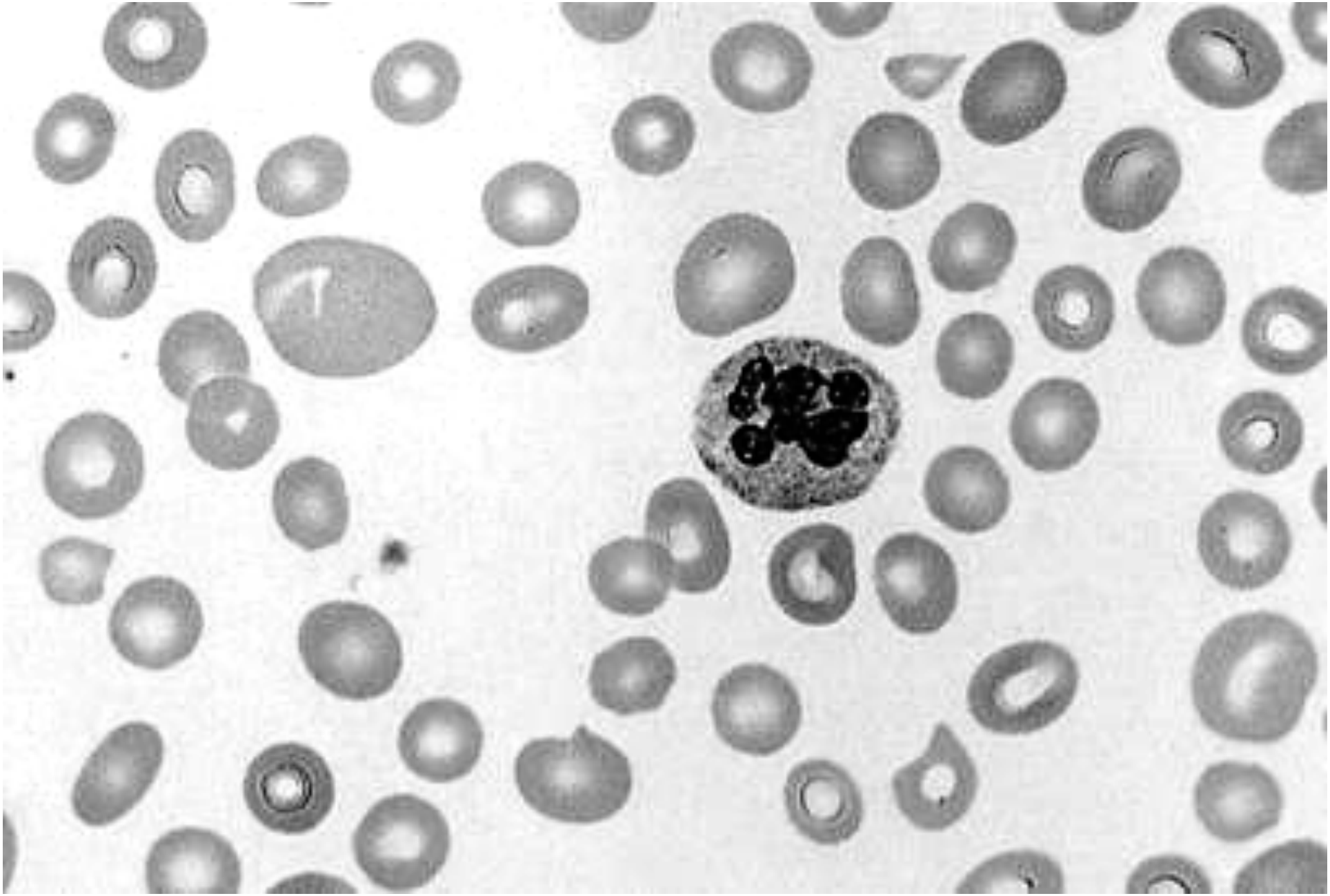
unimpaired RNA synthesis



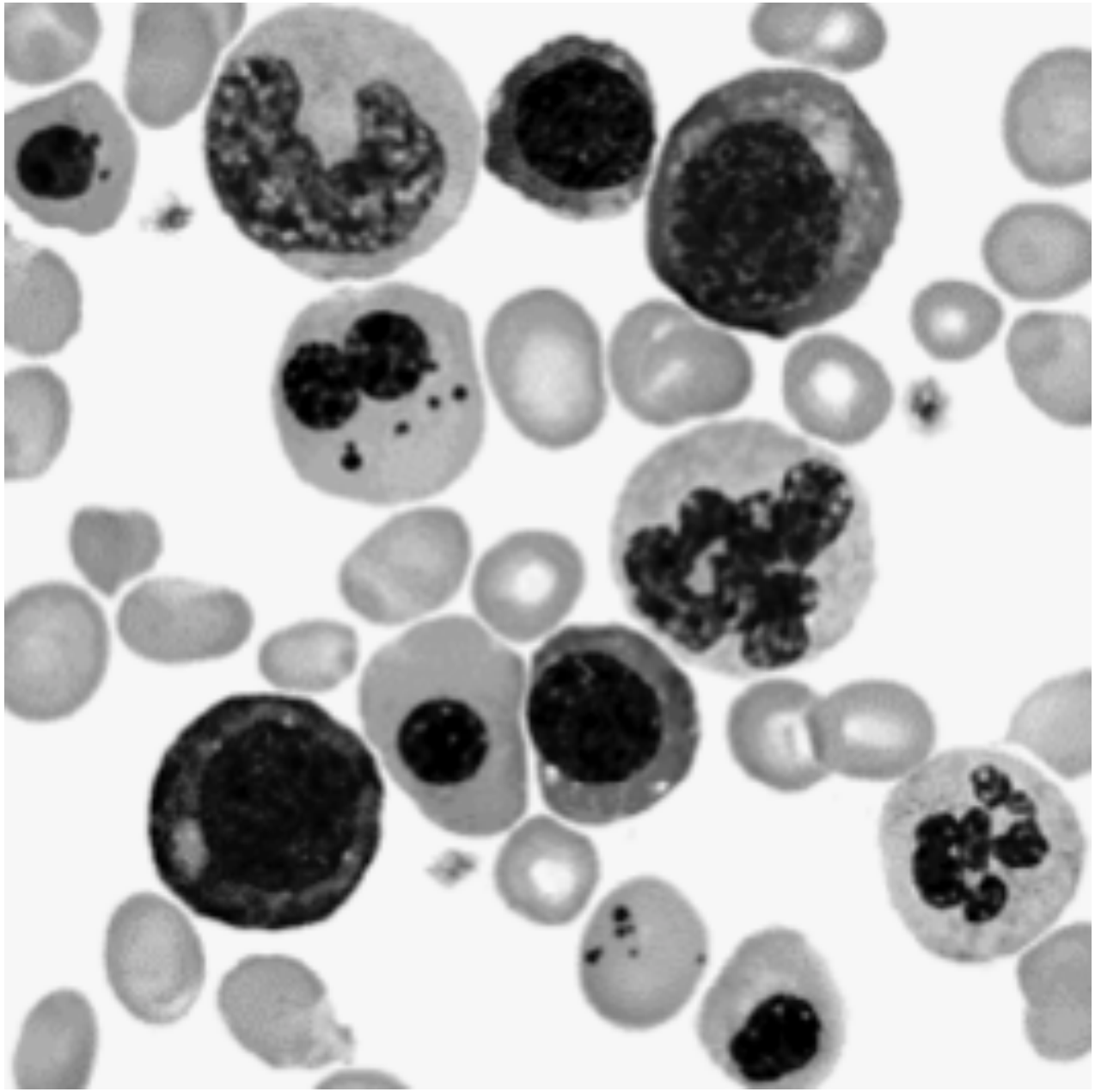
BIG cells!

immature nucleus

mature cytoplasm



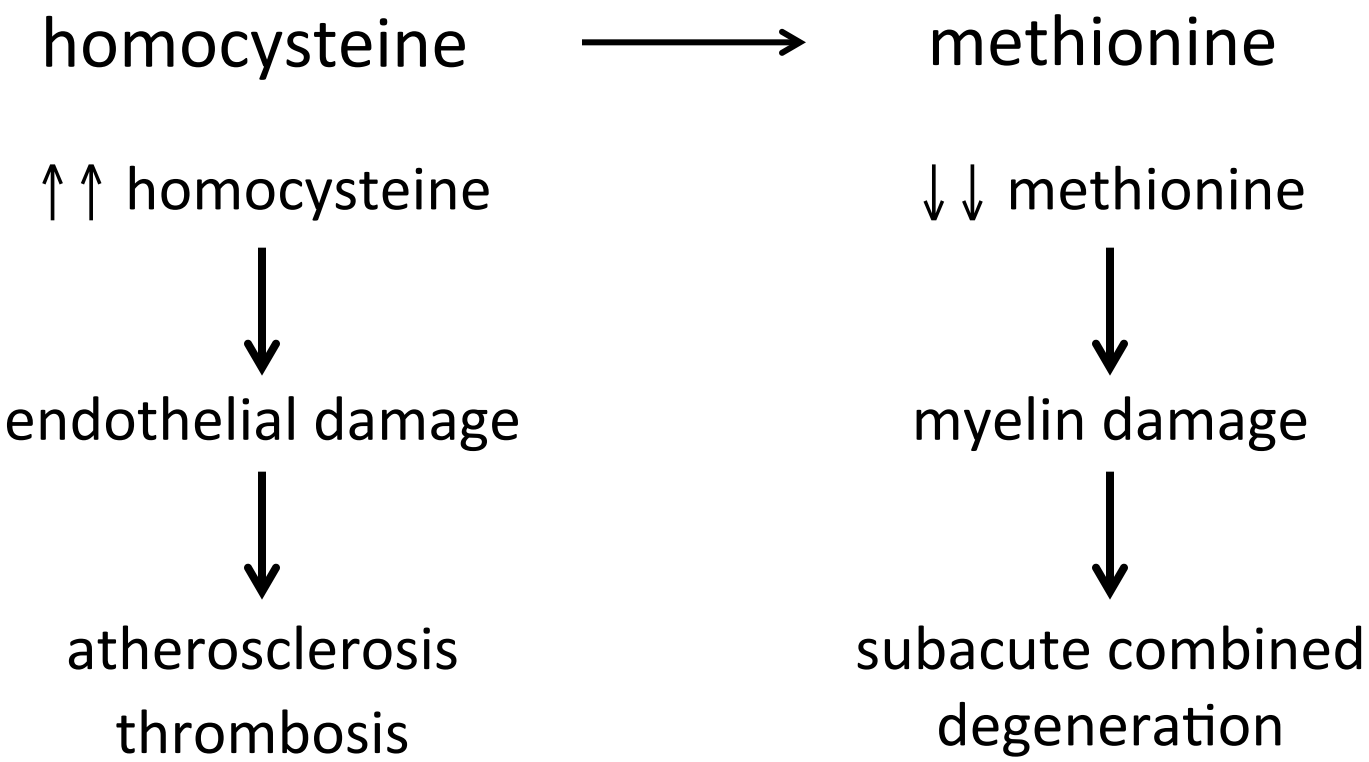
Megaloblastic anemia



Megaloblastic anemia

Atrophic glossitis in megaloblastic anemia

What else is B_{12} good for?



Three Ways to Get Anemic

Lose blood

Destroy too much blood

- Extracorpuscular reasons
- Intracorpuscular reasons

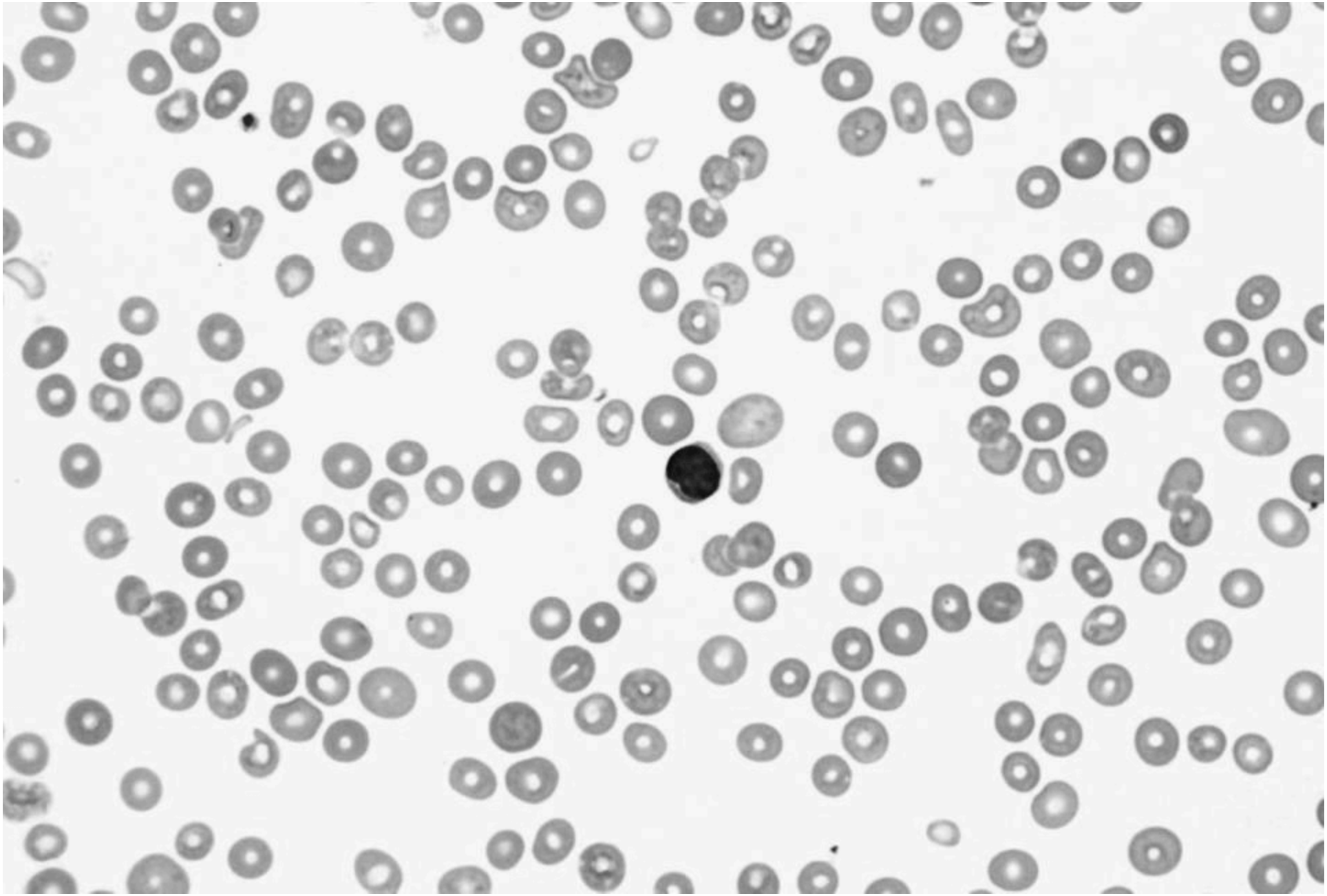
Make too little blood

- Too few building blocks
- Too few erythroblasts

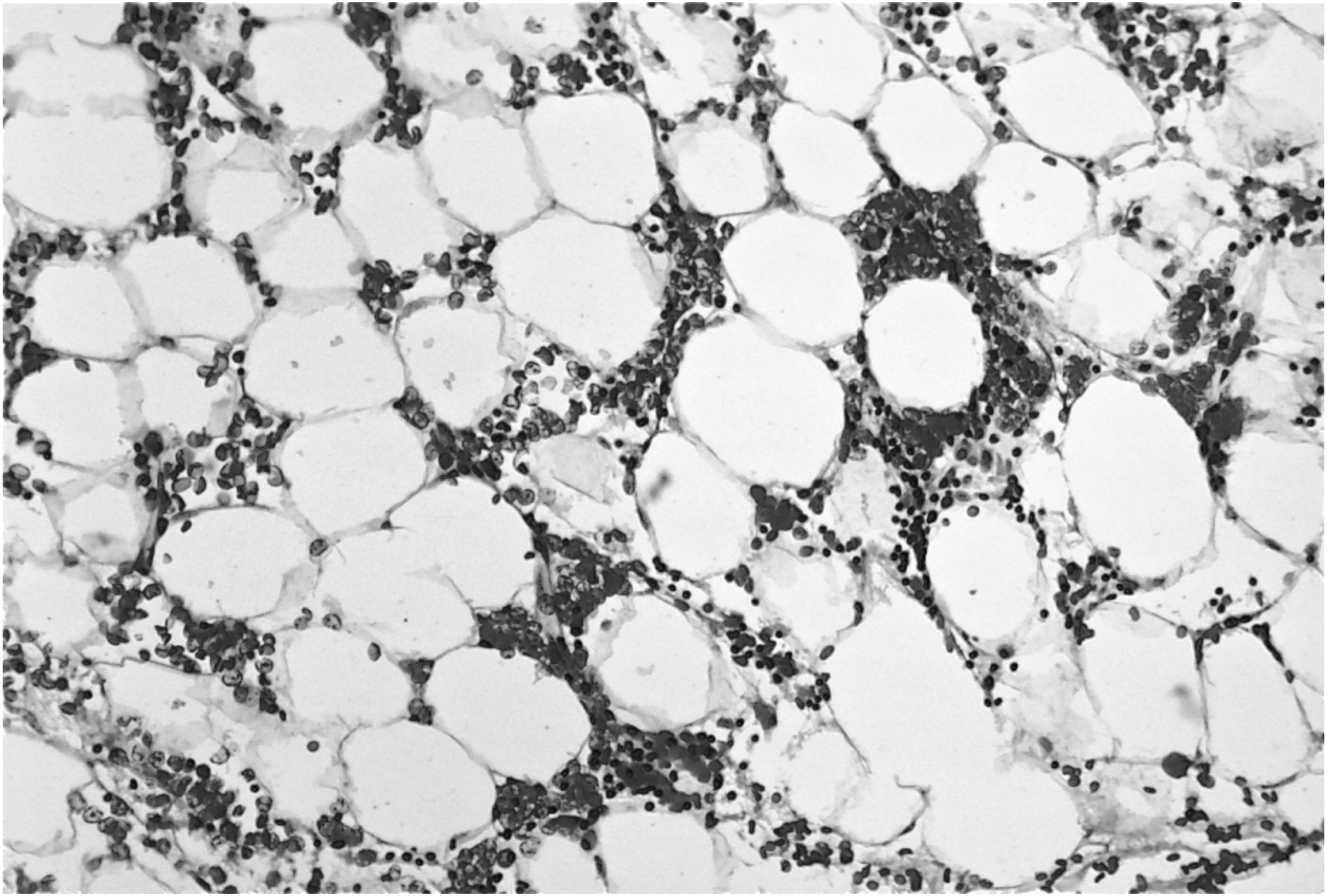
Aplastic Anemia

Things You Must Know

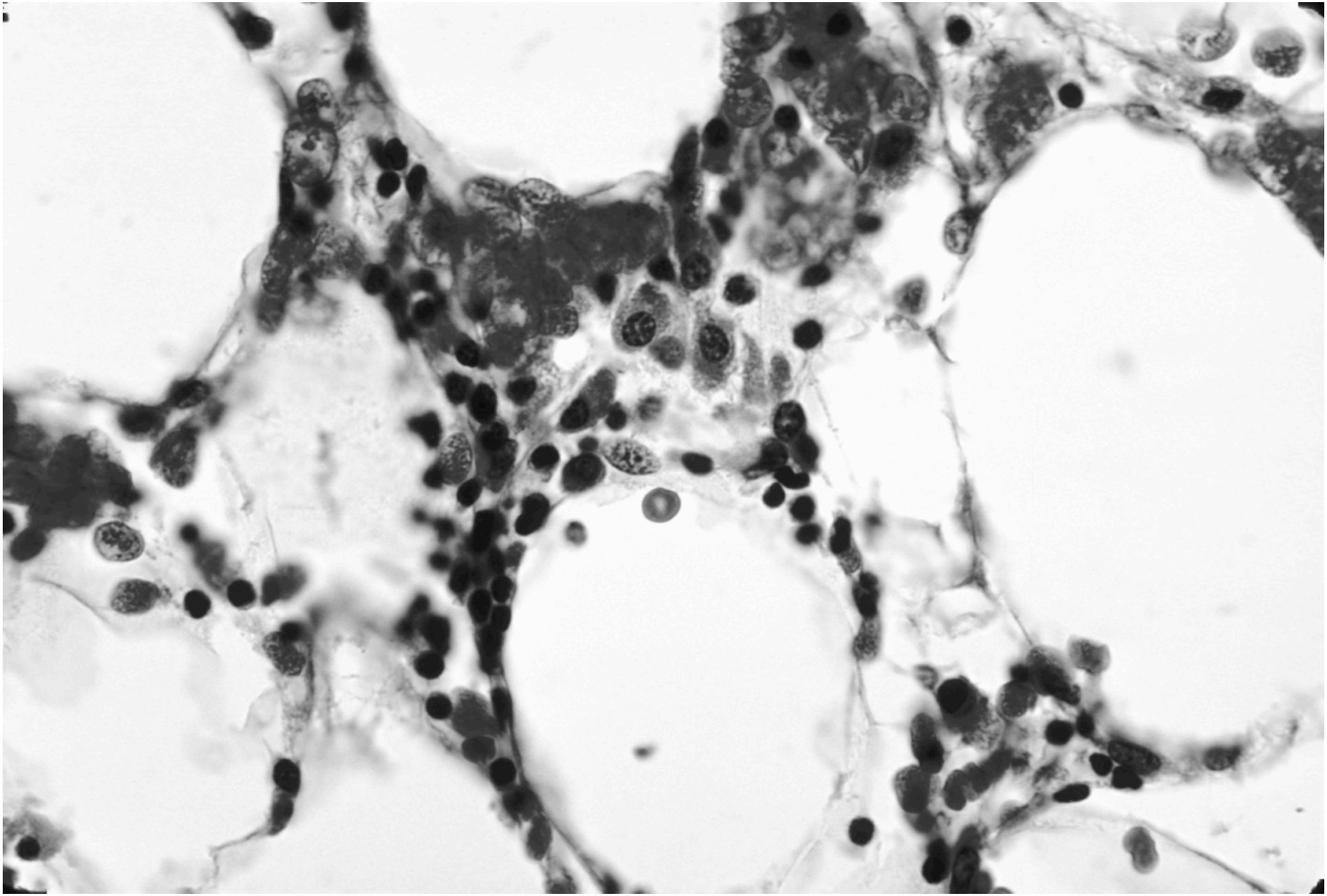
- Pancytopenia
- Empty marrow
- Most are idiopathic



Blood smear in aplastic anemia



Empty bone marrow in aplastic anemia



Empty bone marrow in aplastic anemia

Causes of Aplastic Anemia

- Idiopathic
- Drugs
- Viruses
- Pregnancy
- Fanconi anemia

Three Ways to Get Anemic

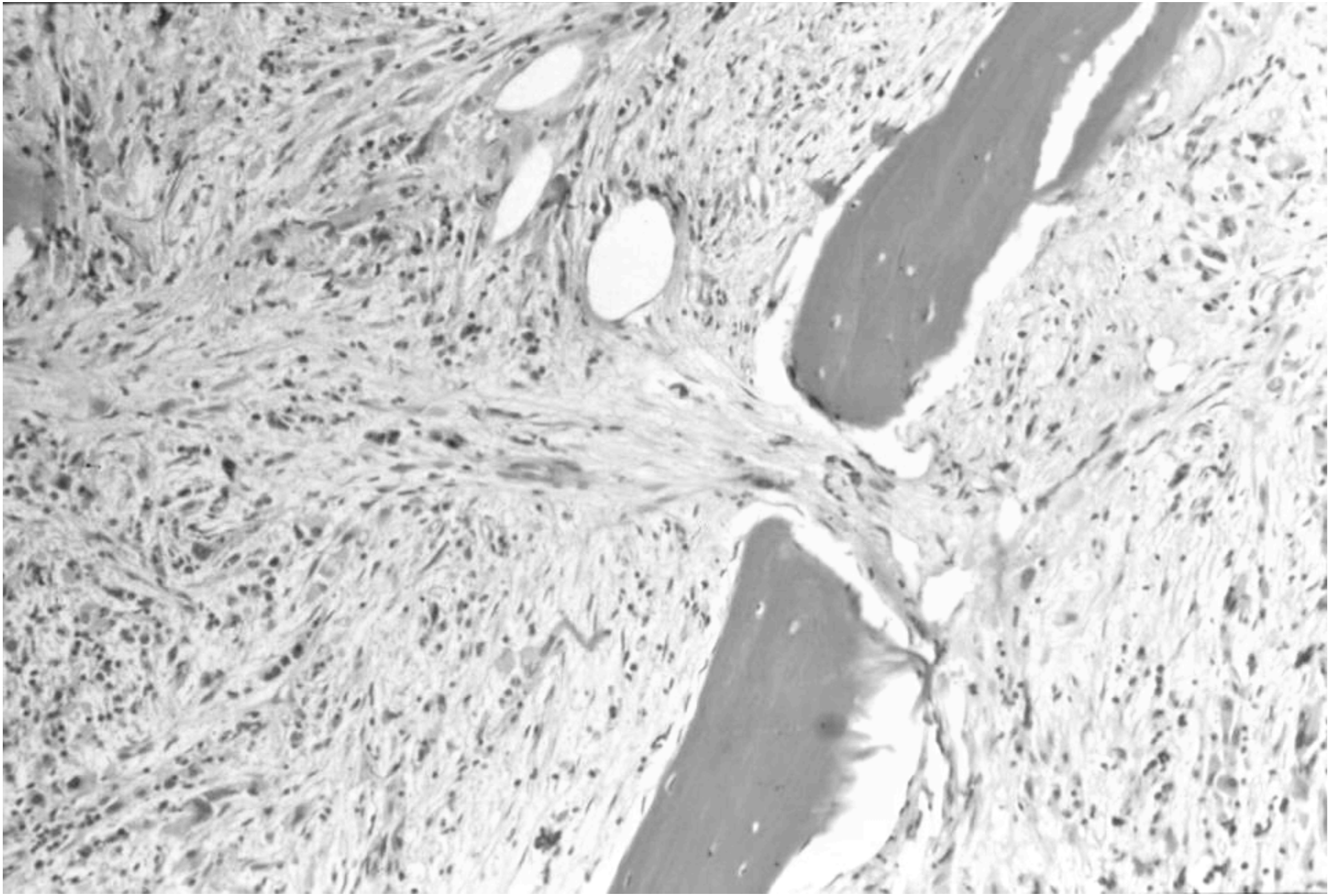
Lose blood

Destroy too much blood

- Extracorpuscular reasons
- Intracorpuscular reasons

Make too little blood

- Too few building blocks
- Too few erythroblasts
- Not enough room



Bone marrow full of fibrosis