THE BLOOD-RED CELLS. ANEMIA.

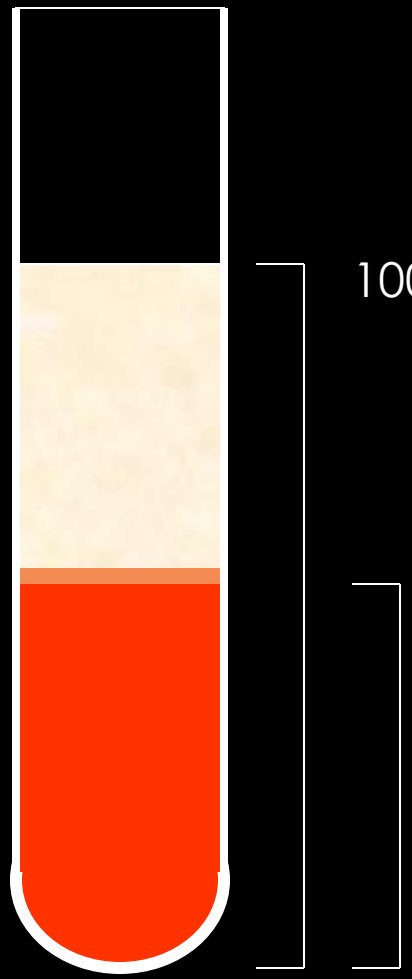
Prof. Maria Tzekova, MD, PhD, DSc

General Properties of Whole Blood

- Fraction of body weight **8%**
- Volume
  - **Female: 4-5 L**
  - **Male: 5-6 L**
- temperature **38° C (100.4° F)**
- pH **7.35 - 7.45**
- Viscosity (relative to water)
  - **Whole blood: 4.5-5.5**
  - **plasma: 2.0**
- Osmolarity **280-300 mOsm/L**
- Mean salinity (mainly NaCl) **0.85%**

Hematocrit

RBCs as percent of total blood volume



100%

- Female: **37%-48%**
- male: **45%-52%**

General Properties of Whole Blood

Hemoglobin

Female:	12-16 g/100 ml
male:	13-18 g/100 ml

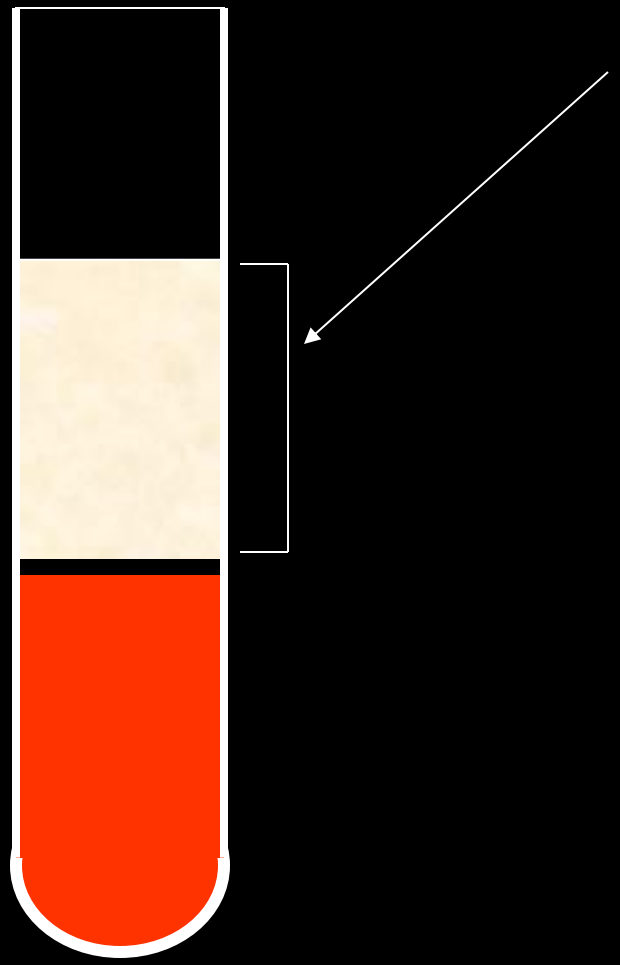
Mean RBC count

Female:	4.8 million/μl
male:	5.4 million/μl

Platelet counts 130,000-360,000/μl

Total WBC counts 4,000-11,000/μl

Plasma



Composition of Plasma

Water	92% by weight
Proteins	Total 6-9 g/100 ml
Albumin	60% of total plasma protein
Globulin	36% of total plasma protein
Fibrinogen	4% of total plasma protein
Enzymes of diagnostic value	trace
Glucose (dextrose)	70-110 mg/100 ml
Amino acid	33-51 mg/100 ml
Lactic acid	6-16 mg/100 ml

Composition of Plasma (continued)

Total lipid	450-850 mg/100 ml
Cholesterol	120-220 mg/100 ml
Fatty acids	190-420 mg/100 ml
High-density lipoprotein (HDL)	30-80 mg/100 ml
Low-density lipoprotein (LDL)	62-185 mg/100 ml
Neutral Fats (triglycerides)	40-150 mg/100 ml
Phospholipids	6-12 mg/100 ml

Composition of Plasma (continued)

Iron	50-150 μg/100 ml
Vitamins (A, B, C, D, E, K)	Trace amount

Electrolytes

Sodium	135-145 mEq/L
Potassium	3.5-5.0 mEq/L
Magnesium	1.3-2.1 mEq/L
Calcium	9.2-10.4 mEq/L
Chloride	90-106 mEq/L
Bicarbonate	23.1-26.7 mEq/L
Phosphate	1.4-2.7 mEq/L
Sulfate	0.6-1.2 mEq/L

Composition of Plasma (continued)

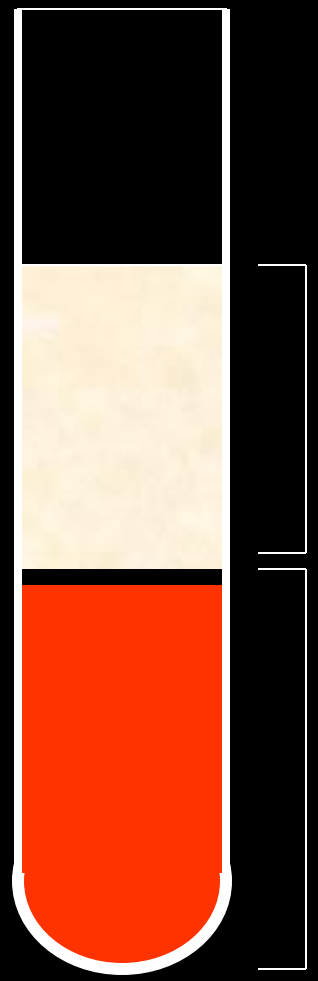
Nitrogenous Wastes

Ammonia	0.02-0.09 mg/100 ml
Urea	8-25 mg/100 ml
Creatine	0.2-0.8 mg/100 ml
Creatinine	0.6-1.5 mg/100 ml
Uric acid	1.5-8.0 mg/100 ml
Bilirubin	0-1.0 mg/100 ml

Respiratory gases (O2, CO2, and N2)


plasma
serum
clotting proteins
(fibrin)

Formed elements include:



Erythrocytes (red blood cells, RBCs)

Platelets (cellular fragments)

Leukocytes (white blood cells, WBCs)

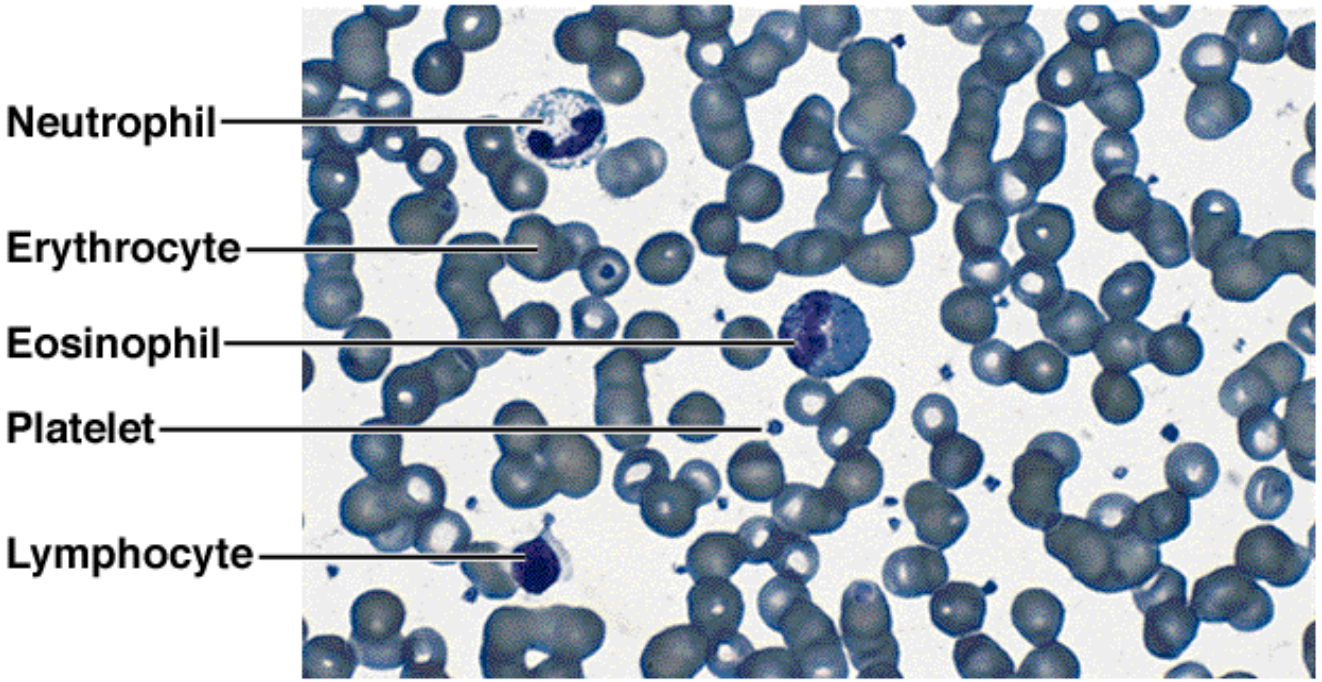
Granulocytes

- ***Neutrophils***
- ***Eosinophils***
- ***Basophils***

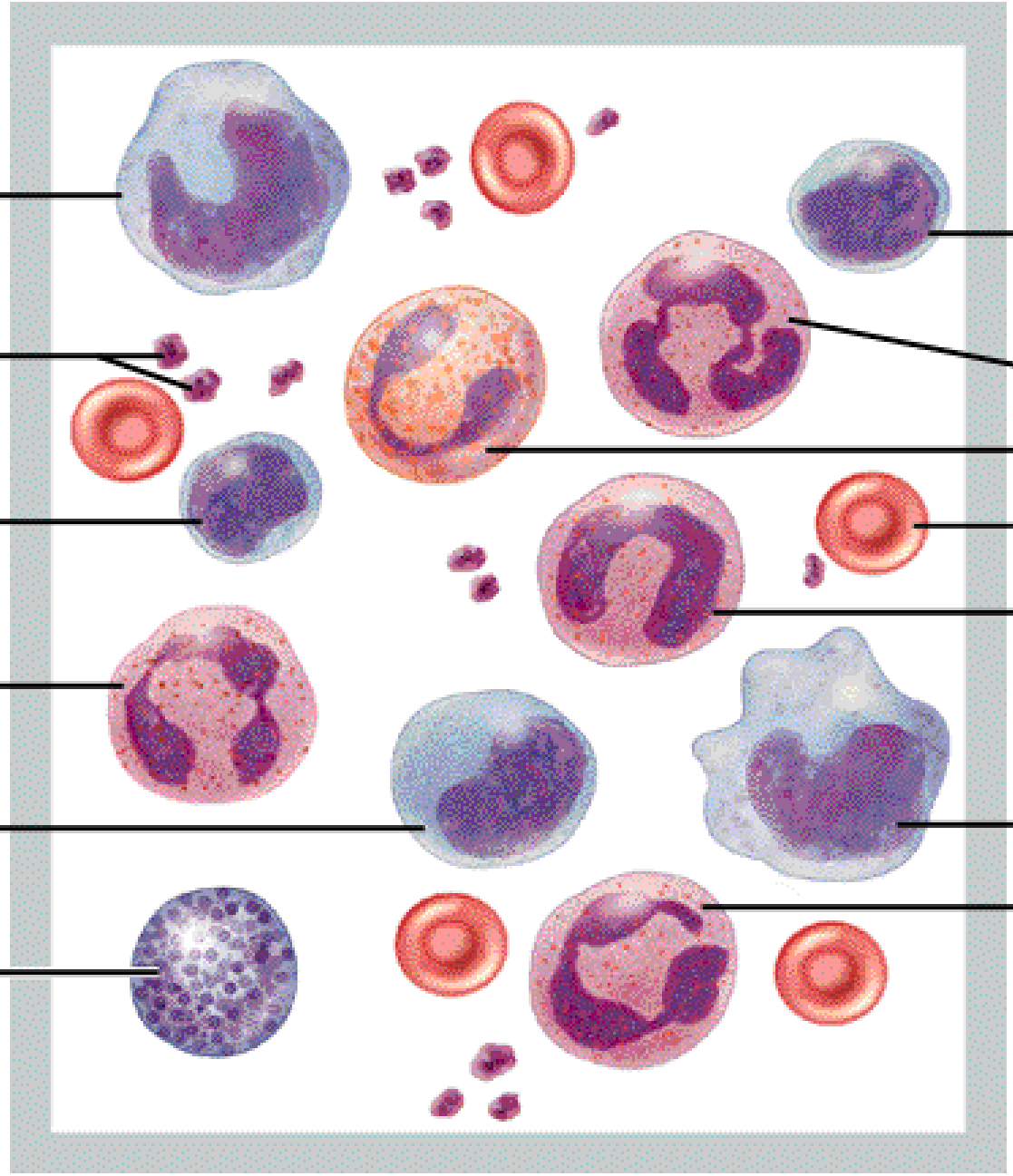
Agranulocytes

- ***Lymphocytes***
- ***Monocytes***

Normal Blood Smear

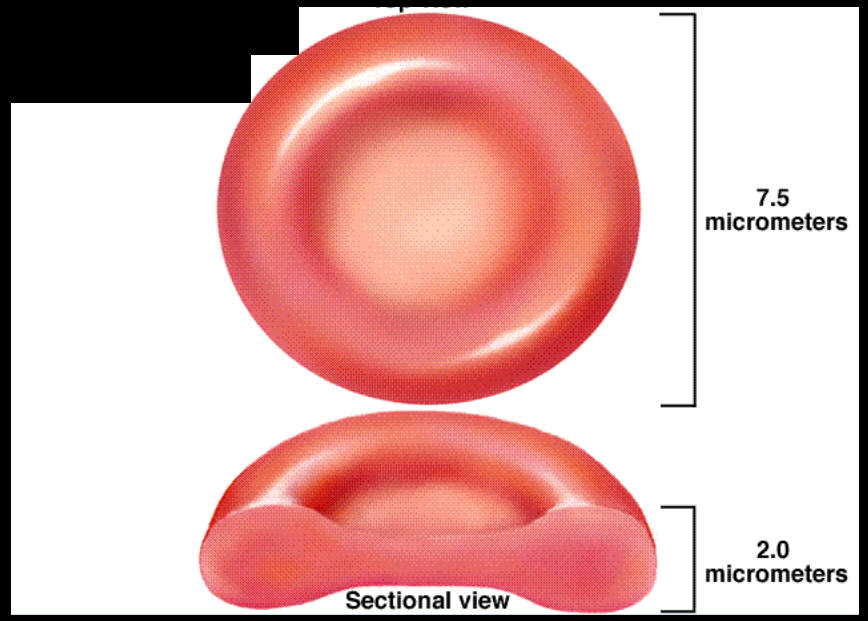


Formed Elements of Blood



Erythrocytes
(red blood cells)

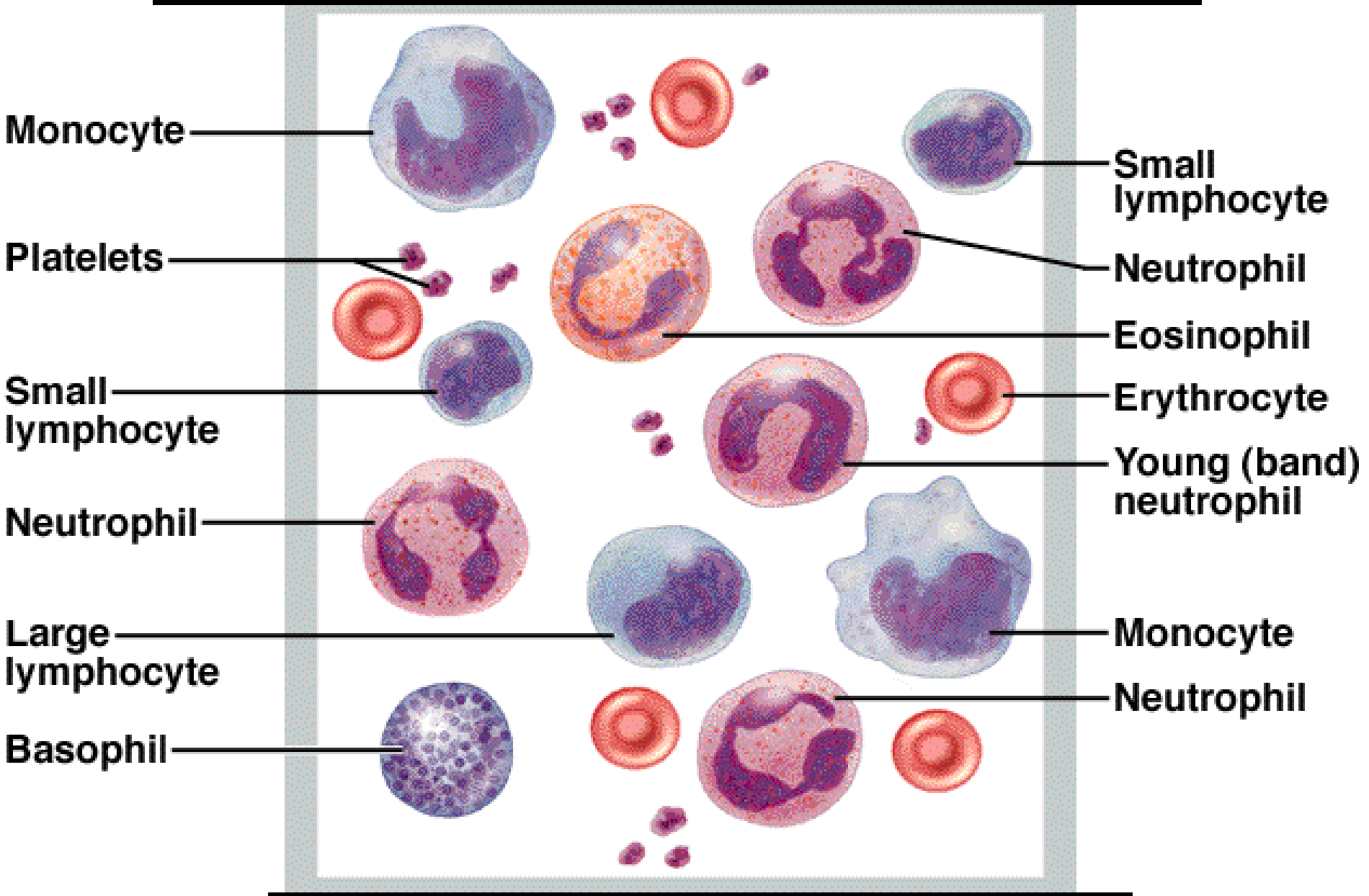
Erythrocytes (Red Blood Cells, RBCs)



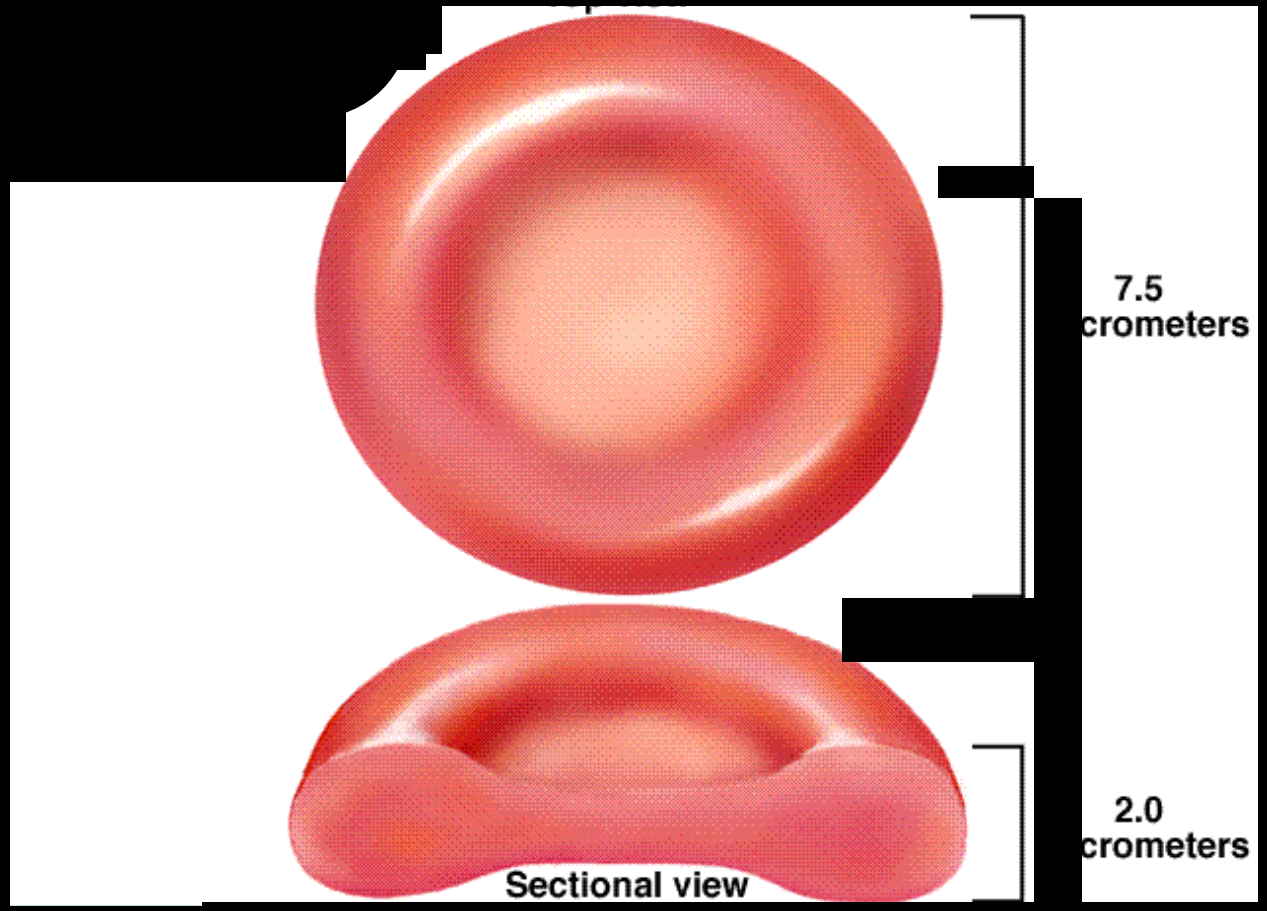
Appearance:

- ***biconcave disc*** shape, which is suited for gas exchange. The shape is flexible so that RBCs can pass though the smallest blood vessels, i.e., capillaries.

Erythrocytes are smaller than Leukocytes.



Erythrocytes (Red Blood Cells, RBCs)



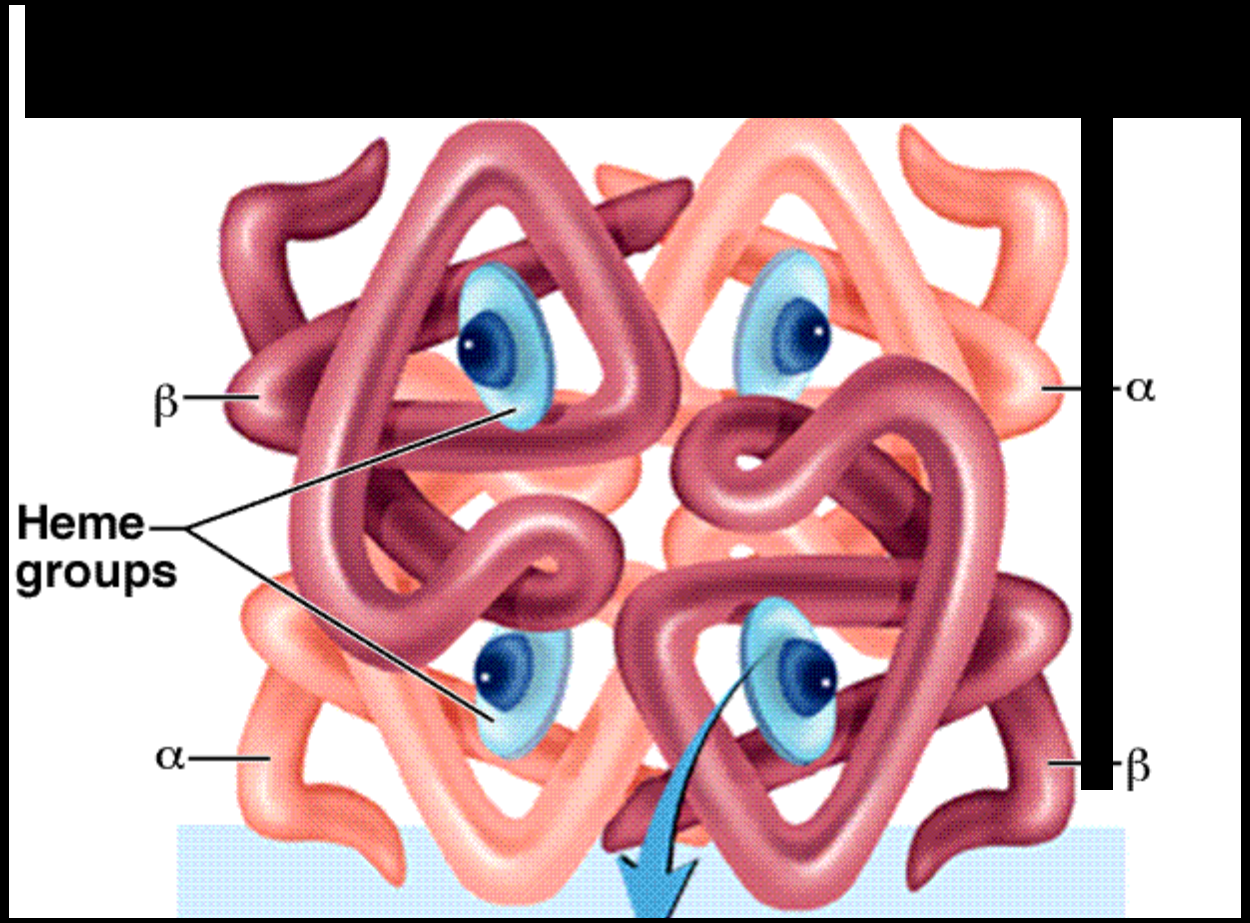
Structure:

-Primary cell content is *hemoglobin*, the protein that binds oxygen and carbon dioxide.

- no nucleus nor mitochondria

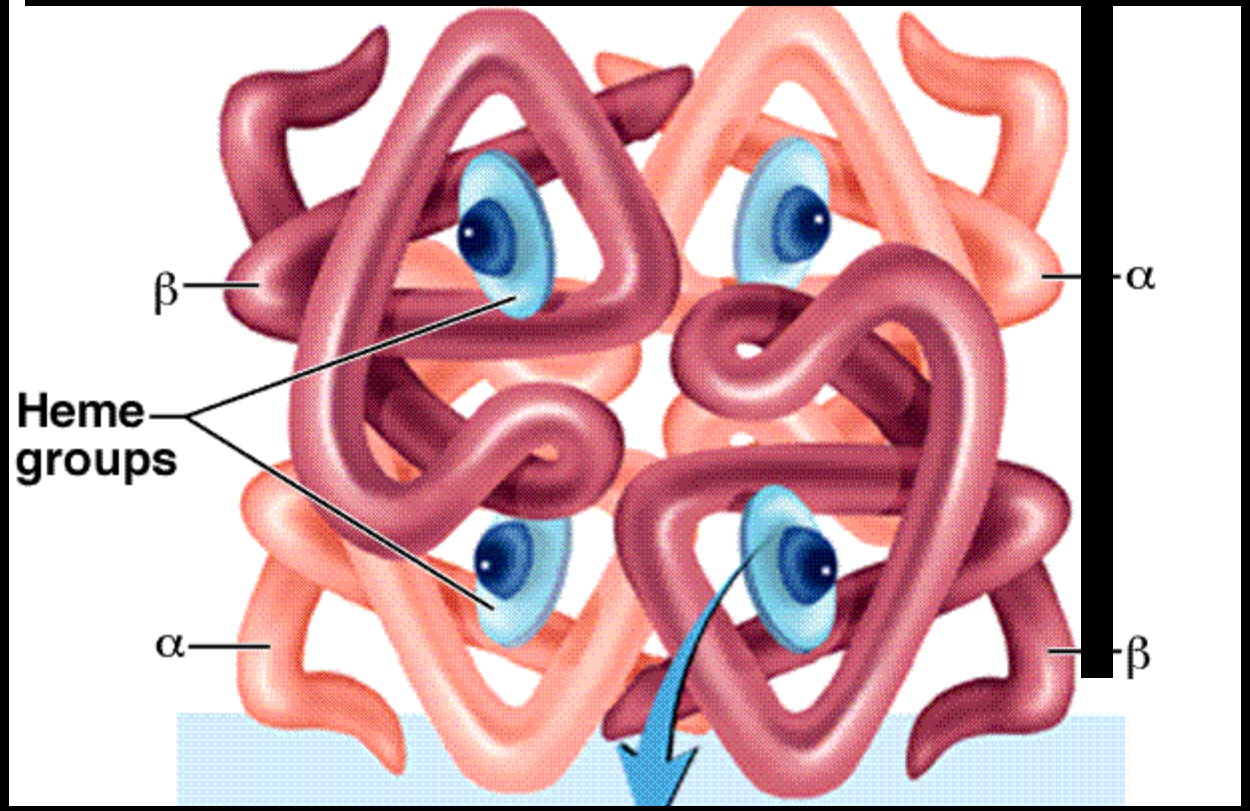
Hemoglobin consists of :

globin and *heme* pigment



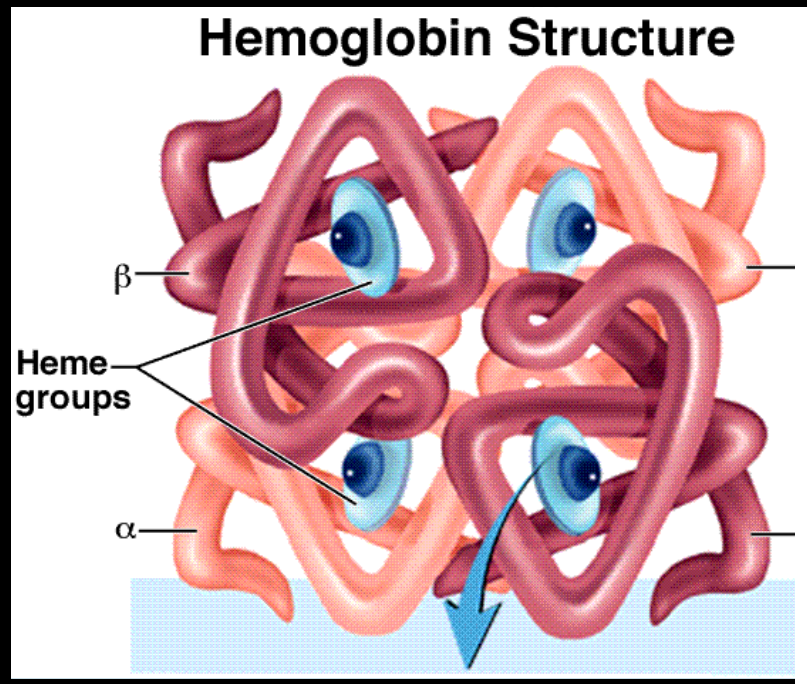
Globin

- Consists of two α and two β subunits
- Each subunit binds to a heme group



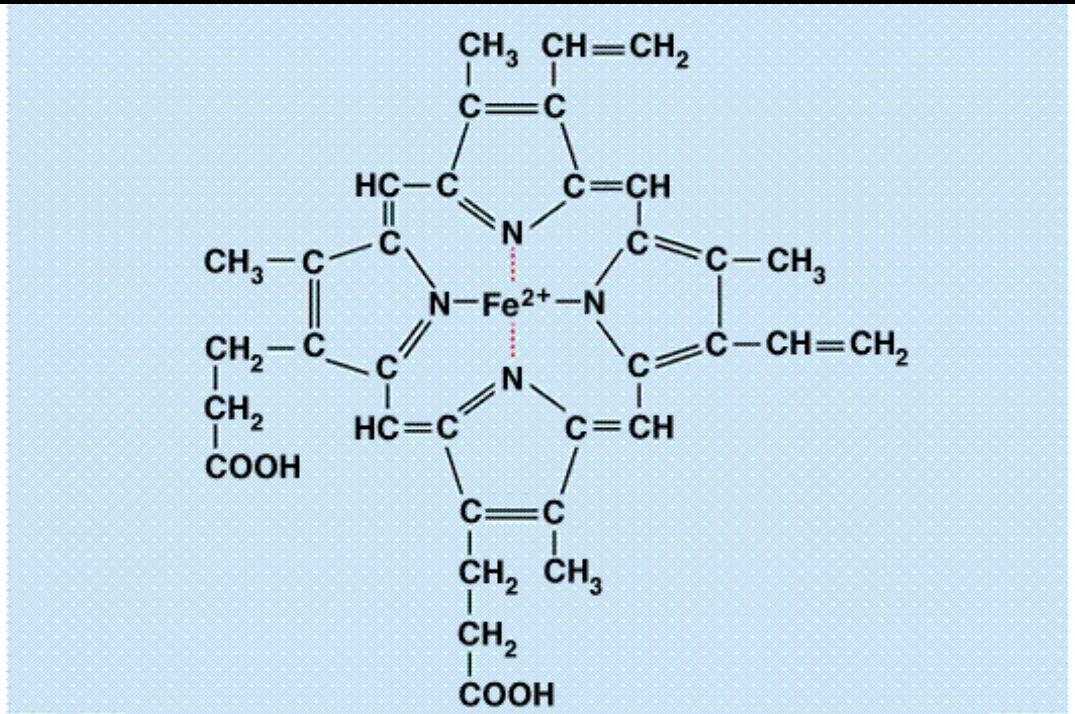
Heme Groups

Each heme group bears an atom of iron, which binds reversibly with one molecule of oxygen

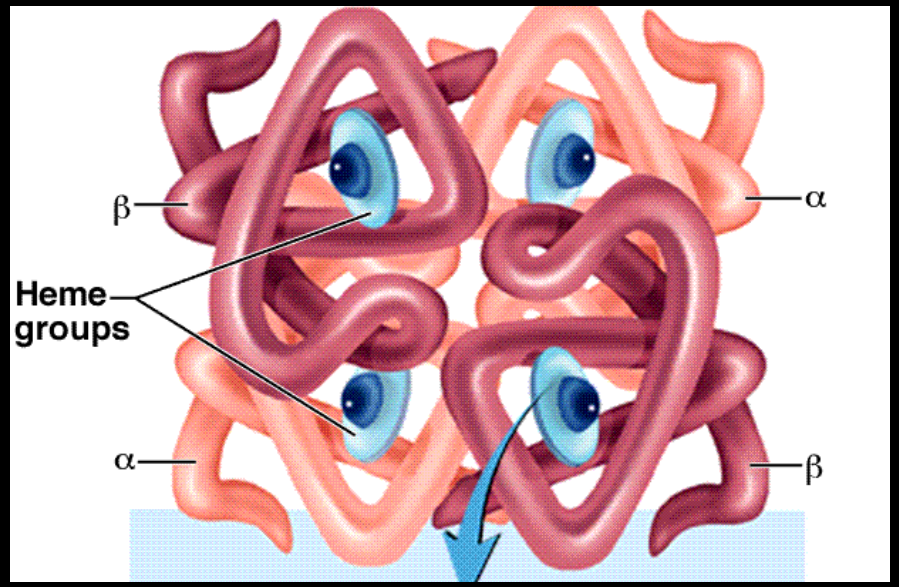


carry four molecules of oxygen

Heme Group Structure

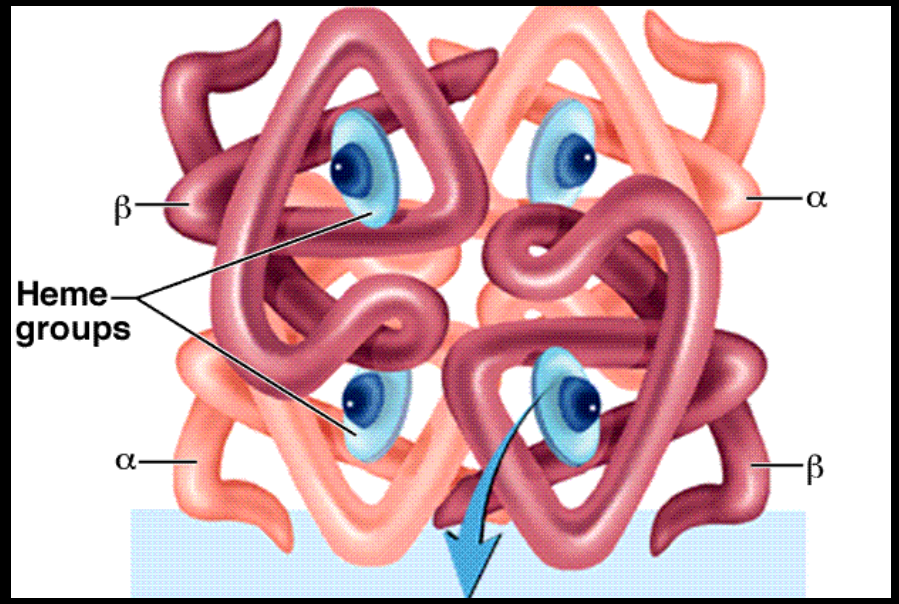


Carbon monoxide competes with oxygen for heme binding with a much higher affinity.



Problem: deoxygenate hemoglobin

Treatment: hyperbaric oxygen chamber



Oxyhemoglobin

- bound with oxygen
- red

Deoxyhemoglobin

- free of oxygen
- dark red.

Carbaminohemoglobin

20% of carbon dioxide in the blood binds to the **globin** part of hemoglobin, which is called ***carbamino-hemoglobin***.

Functions of Erythrocytes

1) Primary Function

Transport oxygen from the lung to tissue cells and carbon dioxide from tissue cells to the lung

2) Buffer blood pH

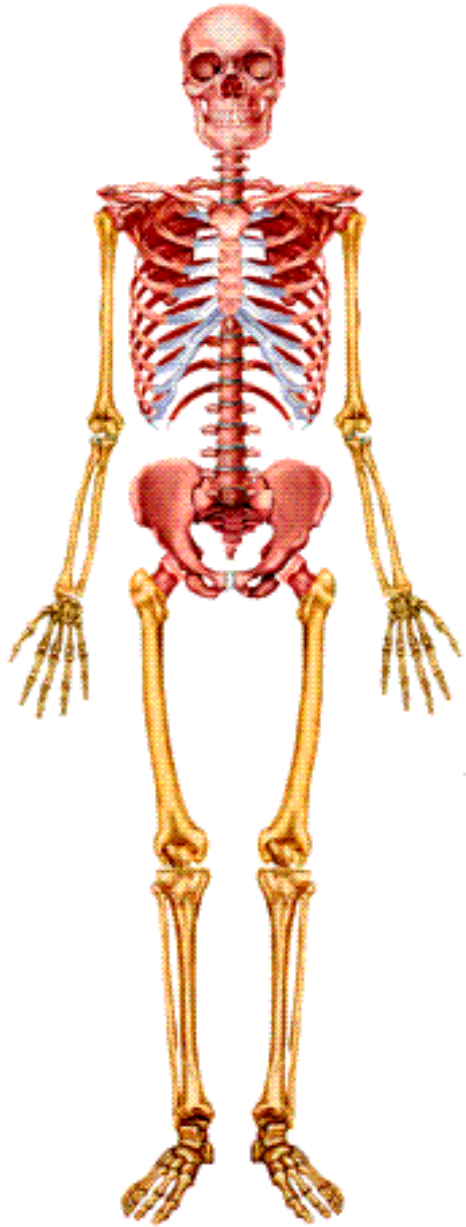
Production of Erythrocytes

Hematopoiesis
refers to whole blood cell production.

Erythropoiesis
refers specifically to red blood cell production.

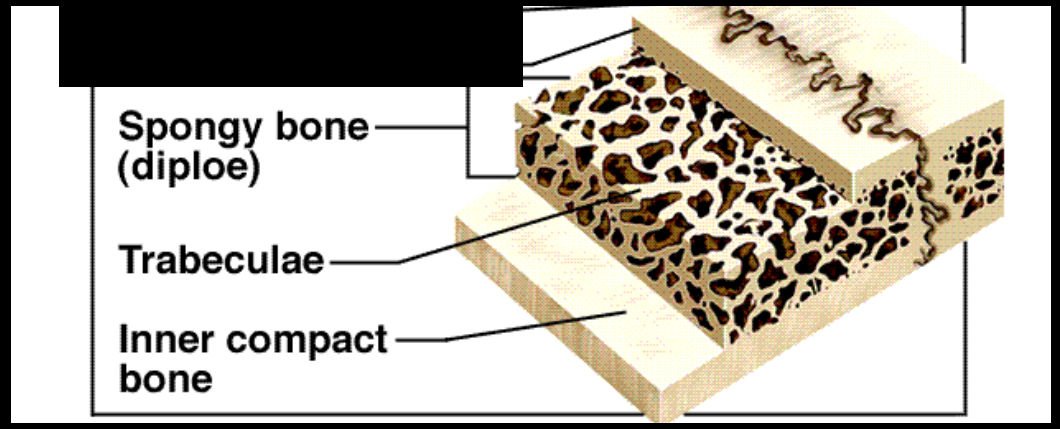
All blood cells, including red and white, are produced in ***red bone marrow***.

On average, one ounce, or 100 billion blood cells, are made each day.

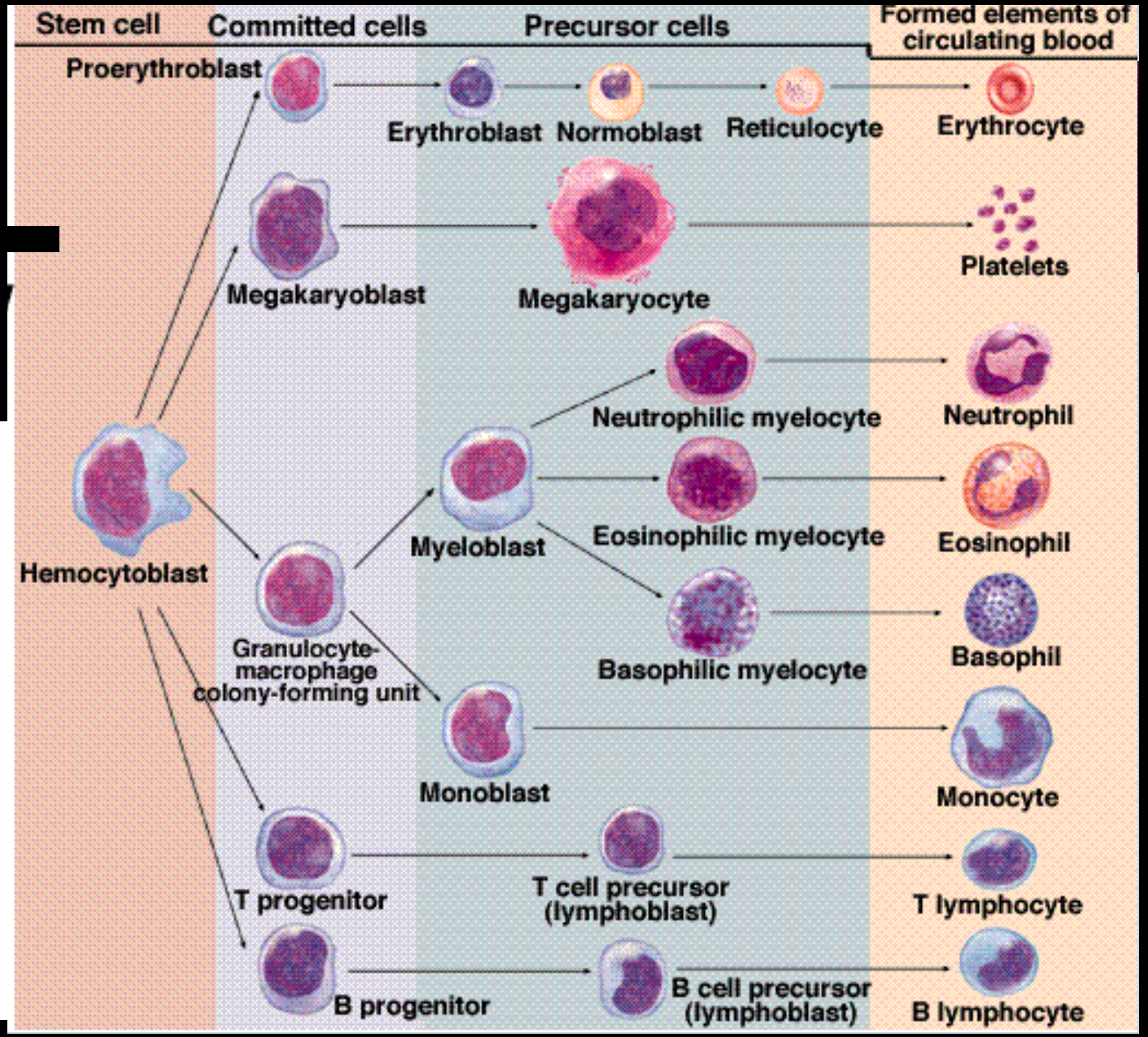


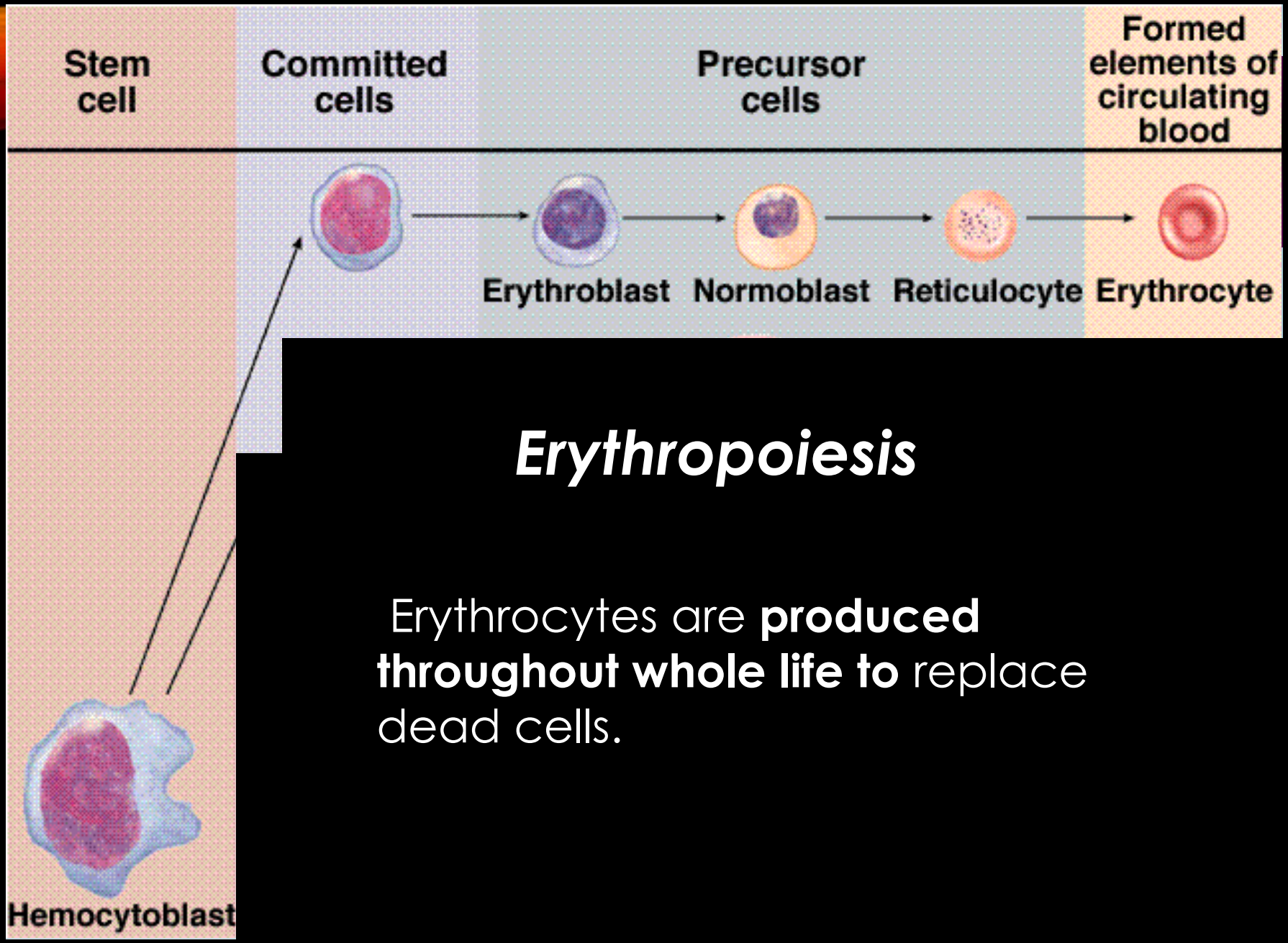
Hematopoiesis

-The **red bone marrow** is a network of reticular connective tissue that borders on wide blood capillaries called blood sinusoids. As hemocytoblasts mature, they migrate through the thin walls of the sinusoids to enter the blood.



All of blood cells including red and white arise from the same type of stem cell, the ***hematopoietic stem cell*** or ***hemocytoblast***





Erythropoiesis

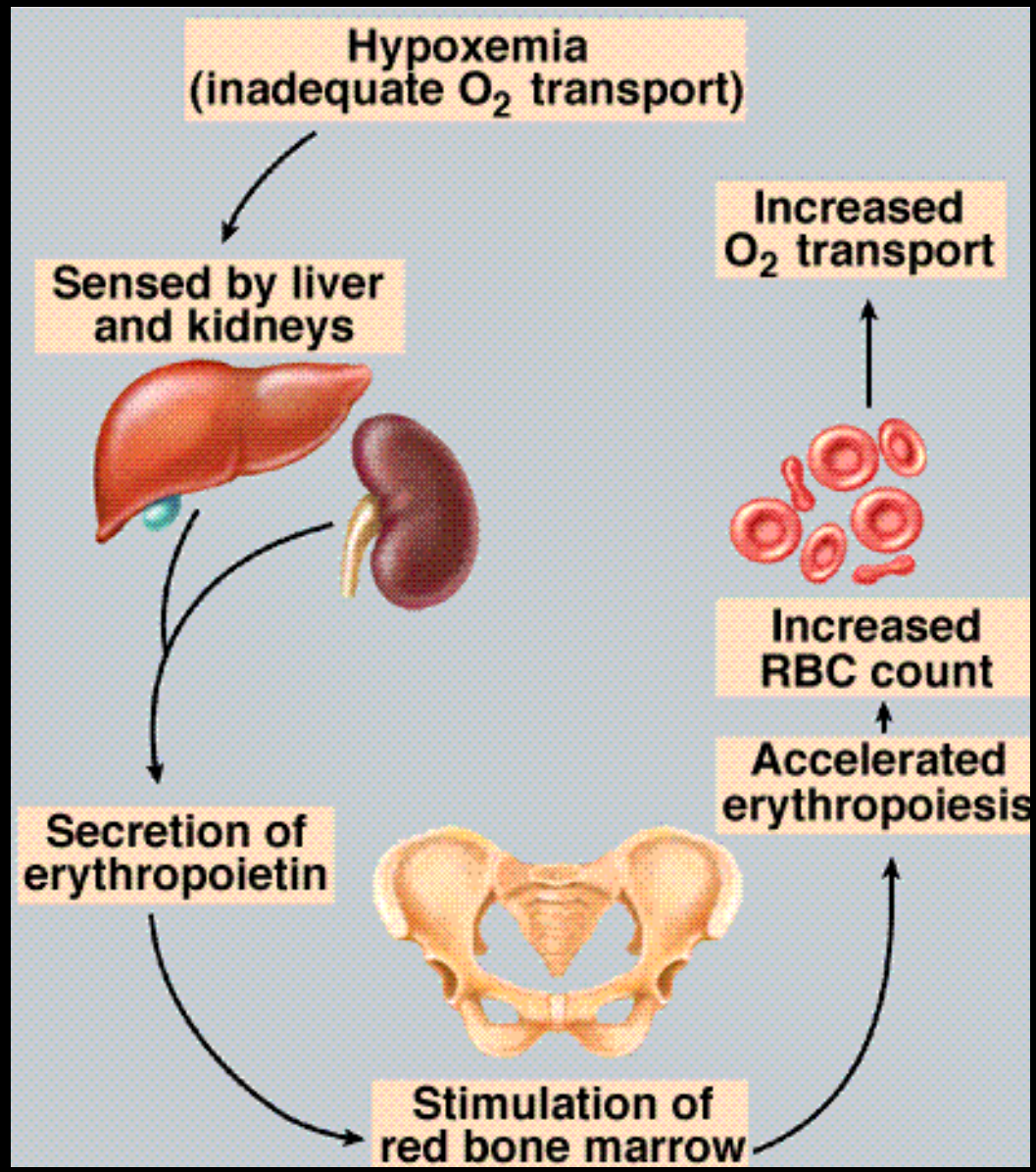
Erythrocytes are **produced throughout whole life to** replace dead cells.

Feedback Regulation of Erythropoiesis

- regulated by renal oxygen content.

- ***Erythropoietin,*** a glycoprotein hormone, is produced by renal cells in response to a decreased renal blood O2 content.

- Erythropoietin stimulates erythrocyte production in the red bone marrow.



A drop in renal blood oxygen level can result from:

1) reduced numbers of red blood cells due to hemorrhage or excess RBC destruction.

2) reduced availability of oxygen to the blood, as might occur at high altitudes or during pneumonia.

3) increased demands for oxygen (common in those who are engaged in aerobic exercise).

Ways to increase Red Blood Cell Count in Sports

Legal

raise RBC count by training athletes at high altitude

Illegal

use *erythropoietin, androgen,* or their analogs

Dietary Requirements for Erythropoiesis

Iron

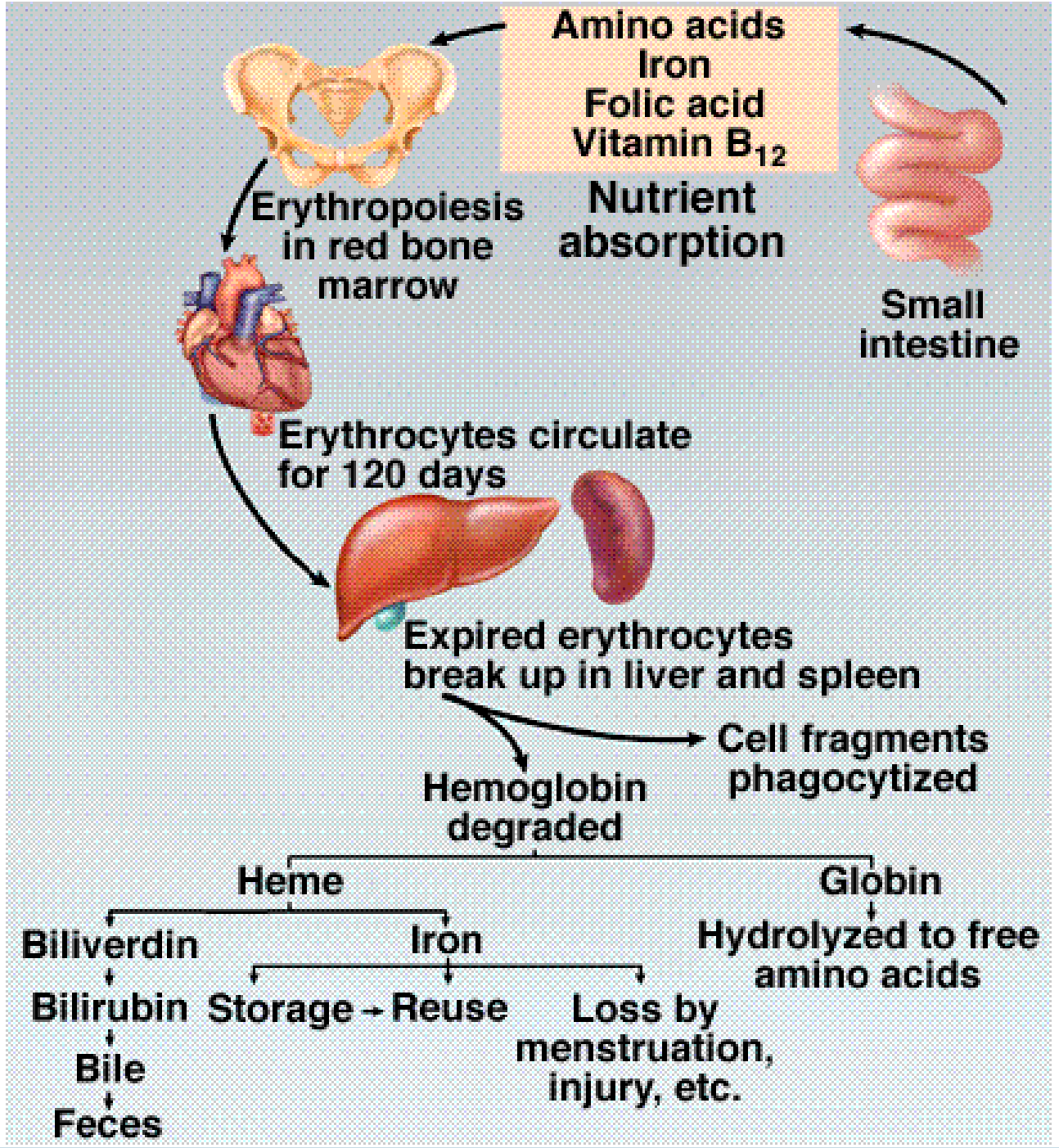
vitamin B12

folic acid

More important to women due to the loss of blood during menstruation

Erythrocyte Life Cycle

The average life span of erythrocytes is 120 days.



Erythrocyte Disorders

Anemia

is a condition in which the blood has an abnormally low oxygen-carrying capacity.

Common causes of anemia include:

1) an insufficient number of red blood cells

2) decreased hemoglobin content

3) abnormal hemoglobin

   Two such examples are ***Thalassemias*** and ***Sickle-cell anemia***, which are caused by genetic defects.

Erythrocyte Disorders - 2

Polycythemia

is an abnormal excess of erythrocytes that increases the viscosity of the blood, causing it to sludge or flow sluggishly.

Common causes of polycythemia include:

1) Bone marrow cancer
2) A response to reduced availability of oxygen as at high altitudes

DEFINITION OF ANEMIA

- Anemia: A reduction in
  - red cell mass
  - O2-carrying capacity

- It is expressed in terms of reduction in the concentration of **Hb (or RBC or Hct%)** compared to values obtained from a reference population.

CLASSIFICATION OF ANEMIA (ADULTS)

REFERENCE VALUES (I)

Parameter	Female	Male
RBC ($x10^{12}$/L)	4.8±0.6	5.4±0.9
Hb (g/dL)	14±2	16±2
Htc (%)	42±5	47±5

REFERENCE VALUES (II)

- **Ret (% / n)** 0.5-2.5 / 50-100x10^9/L
- **MCV (fl)** 90±7
- **MCH (pg)** 29±2
- **MCHc (g/dL)** 34±2
- **RDW (%)** 11.5-14.5

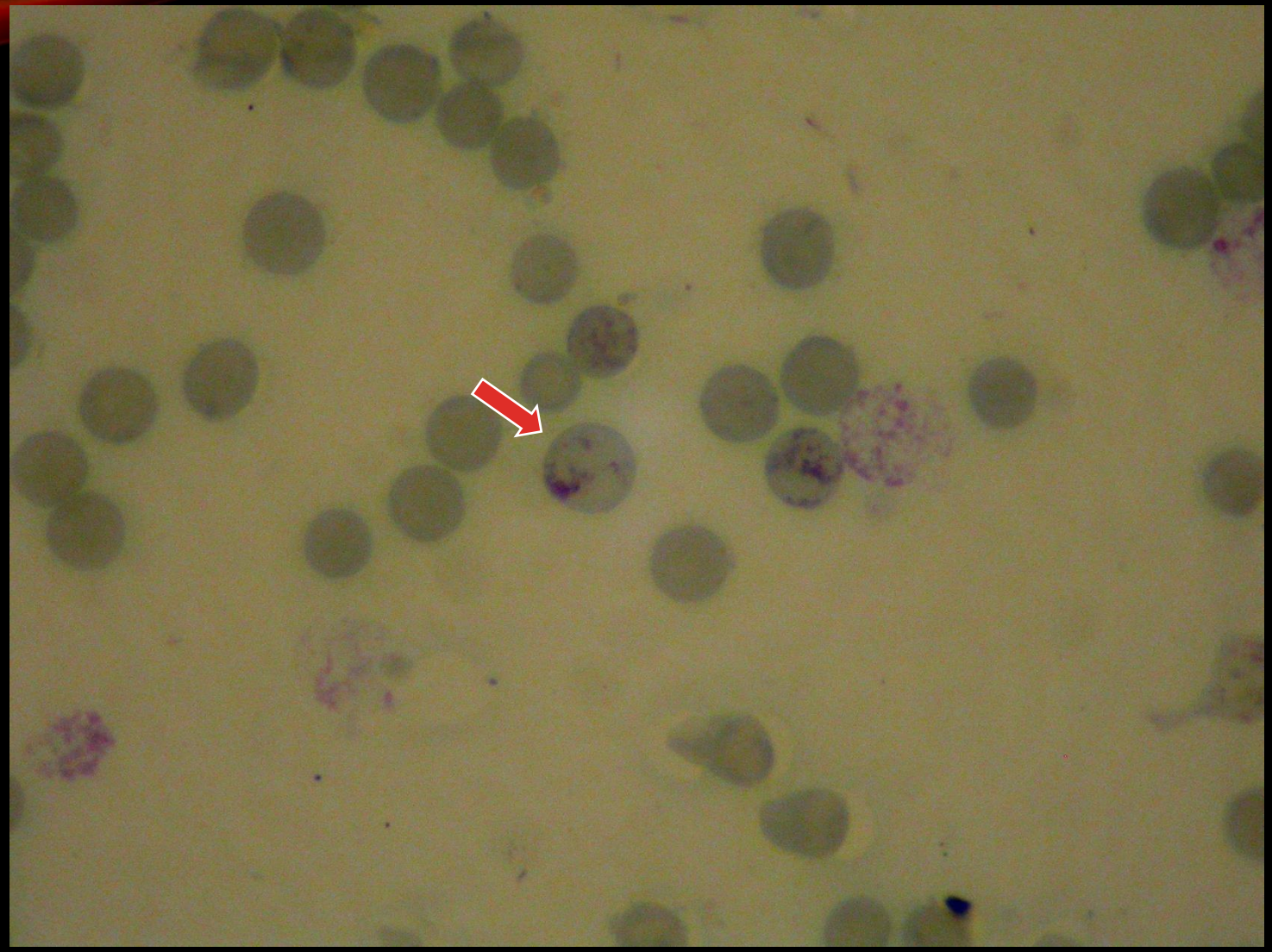
RETICULOCYTE

Normal Ranges

- Male: % 0.8 - 2.5
- Female: % 0.8 - 4.1

Corrected Rtc: Patient Hb/Normal Hb x Rtc %

Reticulocytosis: > 100.000 /mm^3



DEFINITION OF ANEMIA

- Hb level of a patient which is below the normal ranges of that age and sex.

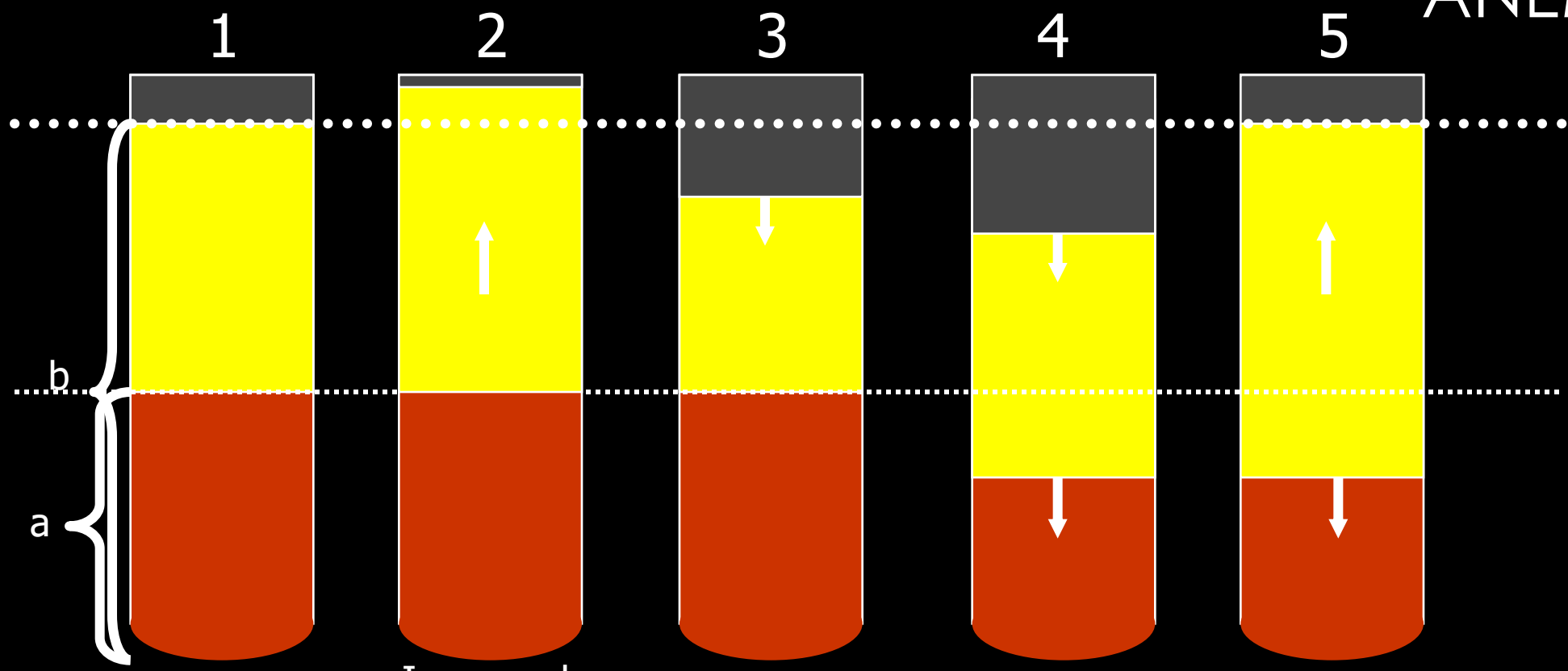
  For adults:

- WHO criteria define anemia as hemoglobin level lower than 12 g/dL in women and 13 g/dL in men
- But: **The reference values for red cells ,Hb or Hct may difer according to**
  - sex/age
  - Race
  - Altitude
  - Socioeconomical changes
  - Study/reference etc

!!!!!

- Plasma volume changes have to be considered before determining a diagnosis of anemia .
  - Volume contraction: Underestimation of anemia
  - Volume overload: Underestimation of Hb level

VOLUME CHANGES/ACUTE BLEEDING AND ANEMIA



!!!!!

- A normal Hb in a patient in whom an elevated Hb level is expected may represent anemia .(eg:COPD + Hb:N)

!!!!!!

- Different red cell measures of the same patient may give discordant values in special conditions. (eg:Thalassemia trait)

Eg: Low Hb, high RBC, low MCV

Hb: 10 g/dL (anemia)

RBC: 6.5 million/mm3 (erythrocytosis)

MVC : 70 fL

!!!!

- Anemia is rarely a disease by itself,
- It is mostly a manifestation or consequence of an underlying (genetic or acquired) disease.
- The finding of anemia has to start attempts to disclose an underlying disease .
  - What is the cause of anemia ?

ANEMIA LEADS TO TWO SYMPTOM COMPLEXES;

- Tissue hypoxia
  - Fatigue,dyspnea on exertion etc
- Compensatory attempts
  - Tachycardia,hyperventilation etc

- The amount of O2 necessary to support life is : 250 ml/min
- O2 carrying capacity of normal blood:1.34 ml/g-Hb (200 ml/L-blood)
- Cardiac output: 5000 ml/min
- O2 delivery to tissues : 1000 ml/min

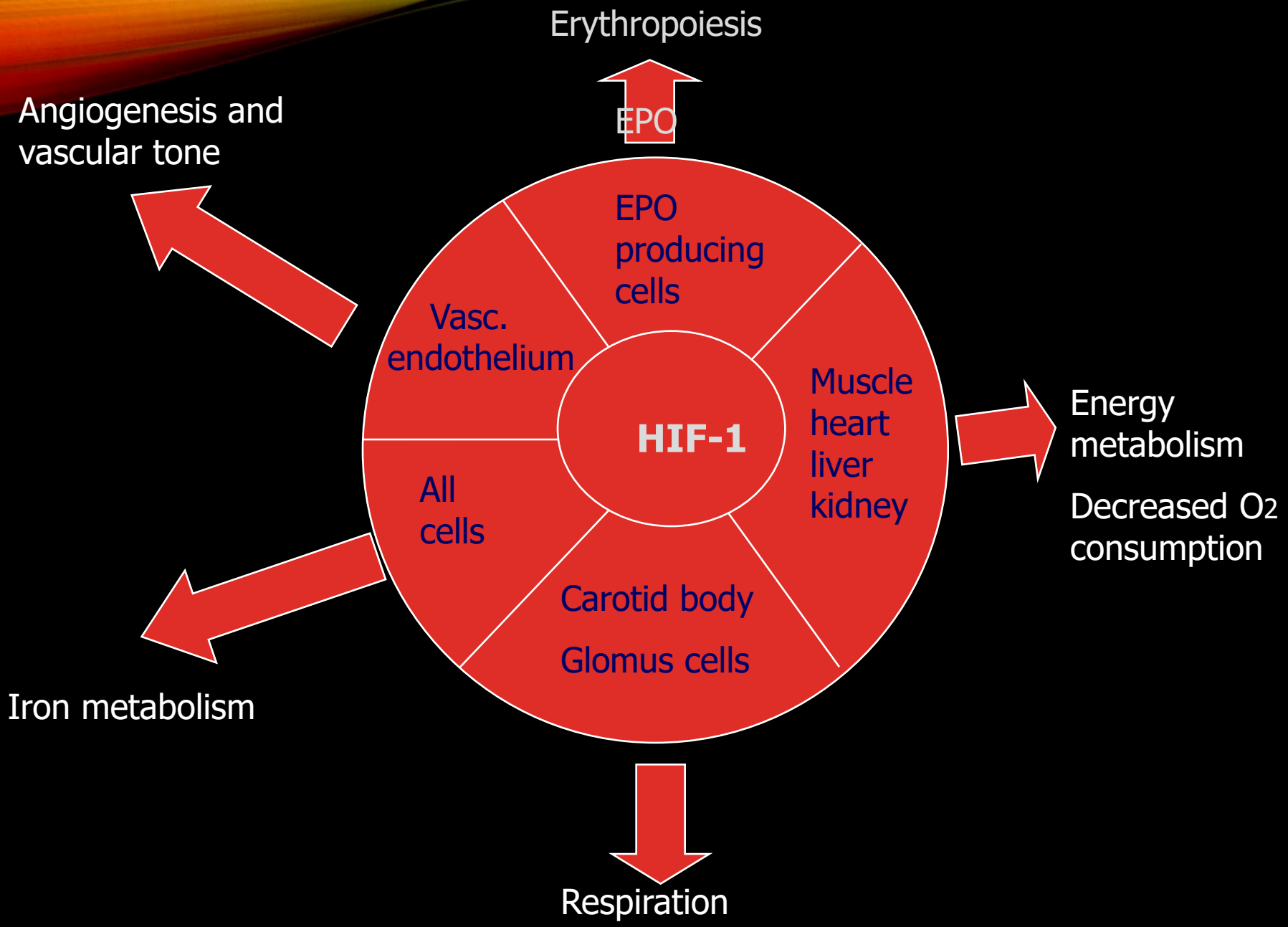
- Reduced levels of Hb results with reduced oxygen delivery to tissues , leading to tissue hypoxia.
- The symptoms and findings of anemia concern many different systems/organs due to the widespread nature of hypoxia.

- The most pronounced effects and symptoms derive from
  - skeletal muscles, heart,and central nervous system

    (due to their greater oxygen demand and compensatory actions).
- What is the mechanism underlying compensatory mechanisms ?

HYPOXIA-INDUCIBLE TRANSCRIPTION FACTOR 1

- A DNA binding protein
- Regulated by the O2 tension
- Regulates genes that promote cell survival under hypoxic conditions
    - Up-reg. EPO gene
    - Up-reg.Glycolytic enzyme genes
    - Up-reg. Angiogenesis
    - Respiratory control
    - Energy metabolism


Erythropoiesis
EPO
Angiogenesis and vascular tone
EPO producing cells
Vasc. endothelium
HIF-1
Muscle heart liver kidney
All cells
Carotid body
Glomus cells
Energy metabolism
Decreased O2 consumption
Iron metabolism
Respiration

Compensating mechanisms in anemia

- The rate of blood circulation and cardiac output increases.
- An increase in plasma volume maintains total blood volume in normal or near normal ranges.
- Redistribution of blood flow.

CLINICAL SYMPTOMS AND FINDINGS OF ANEMIA

- Different patients may have different severity of symptoms even for the same level of Hb.
- The severity of the symptoms of anemia are related to;
  - The severity of anemia
  - The age,CVS,pulmonary status etc of the patient
  - The rate of the development of anemia
    - Gradual or
    - Rapid onset

CLINICAL SYMPTOMS AND FINDINGS OF ANEMIA

- The symptoms and findings are related to:

- anemia itself

or

- to the underlying disease that causes anemia .

CLINICAL SYMPTOMS AND FINDINGS OF ANEMIA (2)

- Fatigue, weakness
  - Tiredness, lassitude, reduced exercise tolerence
  - Generalized muscular weakness

- Pallor /skin or mucous membranes
  - Skin color may change due to other reasons;
    eg :Blood flow of skin, subcutaneous fluid , pigment changes

CLINICAL SYMPTOMS AND FINDINGS OF ANEMIA

Pallor (paleness):

- Look at
  - Mucous membranes of mouth and pharynx
  - Conjunctivae,lips, nail beds,palms
    - Creases of the palms lose their pink colour when the Hb < 7g/dL
- In pernicious anemia there is a lemon yellow pallor.
- Pallor + mild scleral icterus suggests hemolytic anemia.
- Pallor+ petechiae suggests severe bone marrow failure

CLINICAL SYMPTOMS AND FINDINGS OF ANEMIA

- Some other skin/mucosal changes
  - Premature graying of hair:pern.anemia
  - Hair loss and fragility + spooning of the nails:iron deficiency
  - Chronic leg ulcers:Sickle cell or other hemolytic anemia
  - Glossitis/burning sense :Pern. anemia, iron deficiency(rare)
  - Chelitis(angular stomatitis):iron def.
  - Siideropenic dysphagia: iron def.
  - Painful ulcerative mouth lesions: aplastic anemia/leukemia

CLINICAL SYMPTOMS AND FINDINGS OF ANEMIA
CARDIOVASCULAR SYSTEM (1)

- Palpitation and dyspnea (during activity)
- Angina pectoris
- Claudicatio intermittans
- ***Murmurs:*** Mid systolic (rarely diastolic) , mainly pulmonary valvular or apical or over major peripheral arteries or jugulary veins

Clinical symptoms and findings of anemia

Cardiovascular System(2)

- High output state: Collapsing pulse, high pulse pressure
- Cardiomegaly
- Congestive failure
- Ischemic ECG changes

CLINICAL SYMPTOMS AND FINDINGS OF ANEMIA

CENTRAL NERVOUS SYSTEM

- Headache
- Faintness
- Giddiness
- Tinnitus
- Decreased concentration ability
- Drowsiness,decreased muscle strength
- Clouding of consciousness
- Symptoms are more prominent in older patients
- Paresthesias:Vitamin B12 deficiency (or other).

CLINICAL SYMPTOMS AND FINDINGS OF ANEMIA

Reproductive system

- Menstrual changes:
  - Amenorrhea ,
  - Menorrhagia(mostly a cause of anemia)
- Loss of libido

Clinical symptoms and findings of anemia

Gastrointestinal system

(these symptoms may indicate underlying disorder that might indeed be a cause of anemia)

- Anorexia
- Flatulence
- Nausea
- Constipation
- Weight loss

These should remind GIS disease as a cause of anemia

(eg:a bleeding lesion-ulcer/malignancy etc)

CLINICAL SYMPTOMS AND FINDINGS OF ANEMIA

- Ocular Fundi:
  - Pale and sometimes
  - Hemorrhages
  - Papillaedema

Clinical symptoms and findings of anemia

- Renal Changes
  - Slight proteinuria
  - Concentrating defects
  - Further reduction of renal function in patients with previous renal impairment

  (Renal failure itself is a cause of anemia!)

- Pyrexia: Due to a hypermetabolic state or other underlying disease (which may be a cause of anemia)

SOME OTHER EXAMPLES FOR HISTORY AND PHYSICAL EXAMINATION

- The duration of symptoms (acute/insidious)
- Bleeding ? Nose/skin/urine/mens/stool etc
- Family history
  - Anemia, gall stones and splenectomy
  - Bleeding disorder
- Occupation, hobbies,dietary history,alcohol or drug use,travel history etc (toxic/infectious contacts)
- Ask for skin and hair/nail changes

SOME OTHER EXAMPLES FOR HISTORY AND PHYSICAL EXAMINATION

- Pain / mass / fever/systemic overview for an underlying disease
  - Renal/endocrine/liver disease or
  - Chronic infection/malignancy/imflamatory condition
- Parasitis
- Pregnancies
- Paresthesias ,walking difficulty
- Sternal or other bone tenderness
- Splenomegaly, hepatomegaly
- Lymphadenomegaly

DIAGNOSIS AND INVESTIGATION:

- Is the patient anemic?
- What is the type of anemia?
- What is the cause of anemia?

CLASSIFICATION OF ANEMIA

- **Morphologic**
  - Normocytic: MCV= 80-100fL
  - Macrocytic: MCV > 100 fL
  - Microcytic : MCV < 80 fL

- **Pathogenic (underlying mechanism)**
  - Blood loss (bleeding)
  - Decreased RBC production
  - Increased RBC destruction/pooling

NORMOCYTIC ANEMIAS

- Acute post-hemorrhagic anemia
- Hemolytic anemia (except thalassemia and some other Hb disorders)
- Aplastic anemia
- Pure red cell aplasia
- Bone marrow infiltration
- Endocrin diseases
- Renal failure
- Liver disease
- Chronic disease anemia
- Protein malnutrition
- Hypovitaminosis C

MICROCYTIC ANEMIAS

- Iron deficiency anemia
- Thalassemia
- Sideroblastic anemia
- Lead poisoning
- Anemia of chronic diseases (some cases)

MACROCYTIC ANEMIAS

- **Megaloblastic**
- **Non-megaloblastic**

MEGALOBLASTIC MACROCYTIC ANEMIAS

- Vit B12 deficiency
- Folic acid deficiency
- Other.

NON-MEGALOBLASTIC MACROCYTIC ANEMIAS

- Anemia of acute bleeding
- Hemolytic anemias
- Leukemias

(esp: acute)

- Myelodysplastic syndromes
- Liver disease
- Aplastic anemia
- Diseases infiltrative to the bone marrow
- Alcoholism
- Hypothyroidism
- Scurvy

PATHOGENIC CLASSIFICATION (CAUSES OF ANEMIA)

- Relative (increased plasma volume)
- Decreased RBC production
- Blood loss
  - Anemia due to acute bleeding
- Increased RBC destruction

Pathogenic classification (Causes of anemia)

- Decreased RBC production
  - Decreased Hb production
  - Defective DNA synthesis
  - Stem cell defects
    - Pluripotent stem cell
    - Erythroid stem cell(progenitors)
  - Other less defined reasons
- Blood loss
  - Anemia due to acute bleeding
- Increased RBC destruction
- Relative(increased plasma volume)

DECREASED HB PRODUCTION

- Iron deficiency anemia
- Thalassemia
- Sideroblastic anemia
- Lead poisoning

DEFECTIVE DNA SYNTHESIS

- Vit B12 deficiency
- Folic acid deficiency
- Other.

PLURIPOTENT STEM CELL DEFECTS

- Aplastic anemia
- Leukemia or myelodysplastic syndromes

Defective erythroid stem cell

- Pure red cell aplasia
- Anemia of chronic renal failure
- Endocrin disease anemia
- Congenital dyserythropoetic anemias

DECREASED RBC PRODUCTION DUE TO MULTIPL OR UNDEFINED MECHANISMS

- Anemia of chronic diseases
- Bone marrow infiltration
- Anemia due to nutritional defects

ANEMIAS CAUSED BY INCREASED RBC DESTRUCTION (HEMOLYTIC ANEMIAS)

Can be classified as;

- Hemolysis due to intracorpuscular defects
- Hemolysis due to extracorpuscular defects

Or

- Hereditary hemolytic diseases
- Acquired hem. diseases

Or

- Intravascular hemolysis
- Extravascular hemolysis etc.

A Very Simple Classification of Hemolytic Anemias

Intracorpuscular

1- Abnormalities of RBC interior

- **a. Enzyme defects**
- **b. Hemoglobinopathies & Thalassemia M**

2-RBC membrane abnormalities

- **a. Hereditary spherocytosis, elliptocytosis etc**
- **b. Paroxysmal nocturnal hemoglobinuria**

Extracorpuscular

- **c. Spur cell anemia**

3- Extrinsic factors

- **a. Hypersplenism**
- **b. Antibody : immune hemolysis**
- **c. Traumatic & Microangiopathic hemolysis**
- **d. Infections , toxins , etc**

Hereditary

Acquired

IS THE PATIENT ANEMIC ?

- RBC count
- HB level
- Hct level
- Volume status

WHAT IS THE TYPE OF ANEMIA?

- History and physical exam.
- RBC,HB,Hct ,
- MCV, MCH,RDW
- Red cell morphology (peripheral smear)
- Reticulocyte count
  - Incresed ?
- Other Lab. investigations

LAB. INVESTIGATION OF ANEMIA(1)

- WBC count and differential
- Platelet count and morphology
- ESR
- Biochemistry, special tests and others
- Bone marrow exam.(only when indicated)

LAB. INVESTIGATION OF ANEMIA(2)

- Serum values of
  - Iron
  - TIBC
  - Ferritin
  - Bilirubins
  - Proteins / electrophoresis
  - LDH
  - Vit B12 and /or Folic acid

  (*None of these tests are routine screening tests*)

LAB. INVESTIGATION OF ANEMIA(3)

- Red cell enzymes
- Hb F,A2,Hb electrophoresis
- Coombs tests
- Liver, renal, endocrin functional tests
- Urinalysis
  - Hemosiderin
- Occult GIS bleeding / parasites etc

(*tests should be chosen individually-do not order routinly*)

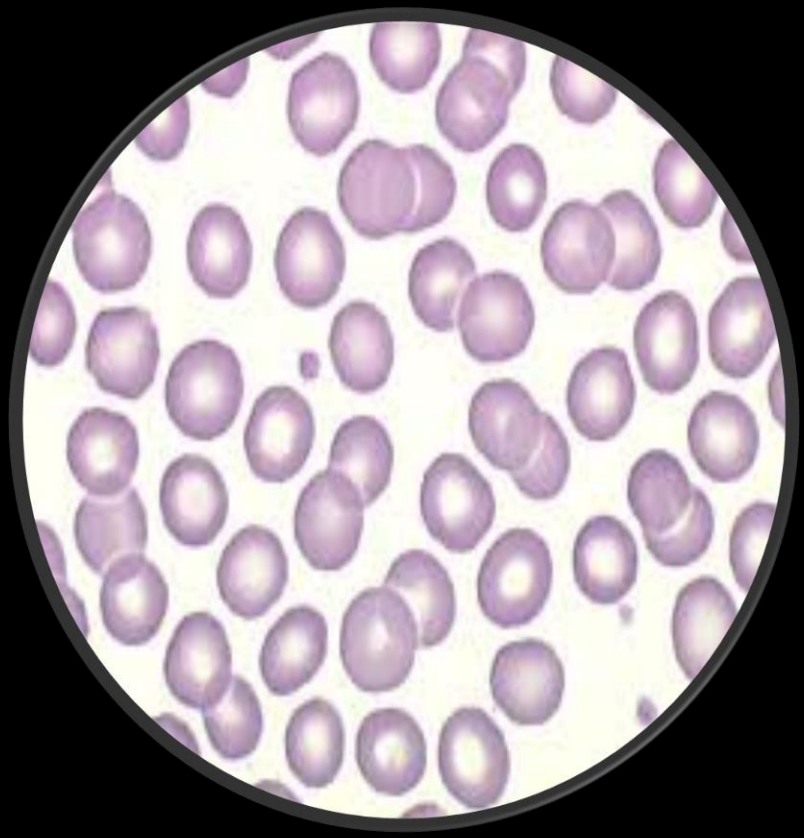
RED BLOOD CELL MORPHOLOGY

- NORMAL RED BLOOD CELLS

II. Variation In Erythrocyte Size (Anisocytosis)

Anisocytosis

Variations in size (Microcyte and Macrocyte)



Normocytic RBC's

Normal size of RBC (8 μm) with a range of 7 to 9 μm.

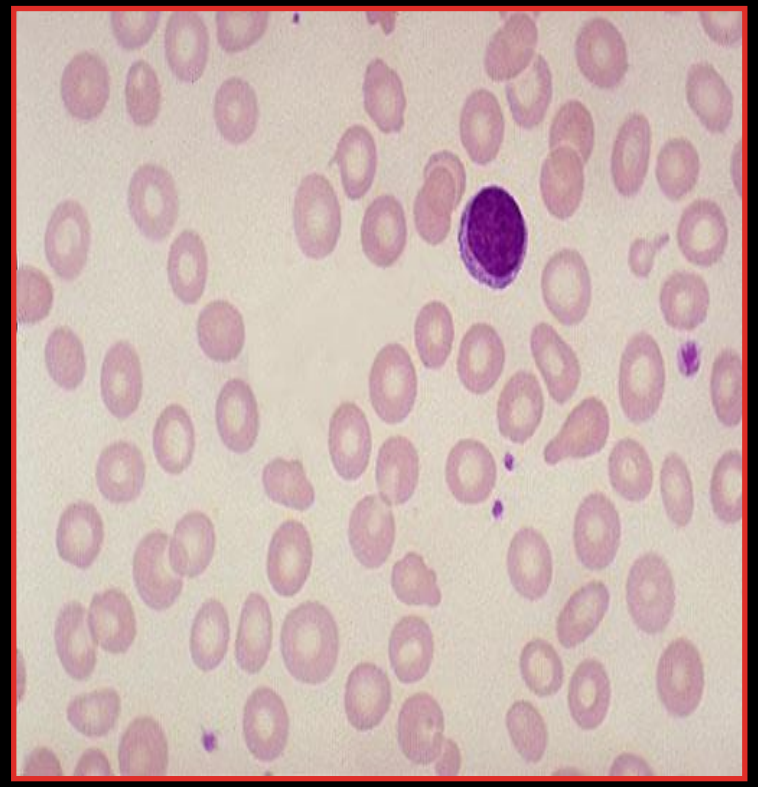
The nucleus of a small lymphocyte (± 8 μm) is a useful guide to the size of a red blood cell).

Microcytic

RBC cell smaller than the normal RBC (<7 μm), and is associated with a decrease in hemoglobin synthesis

Found in

- Iron deficiency anemia.
- Thalassaemia.
- Sideroblastic anemia.
- Lead poisoning.
- Anemia of chronic disease.

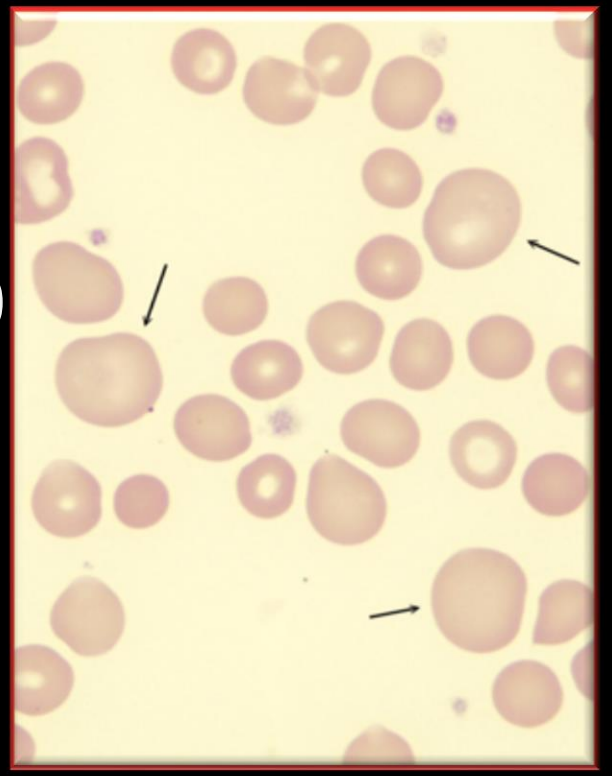


Macrocyte

RBC larger than the normal (>9 μm) and is the result of a defect in nuclear maturation or stimulated erythropoiesis. May be round or oval in shape, the diagnostic significance being different.

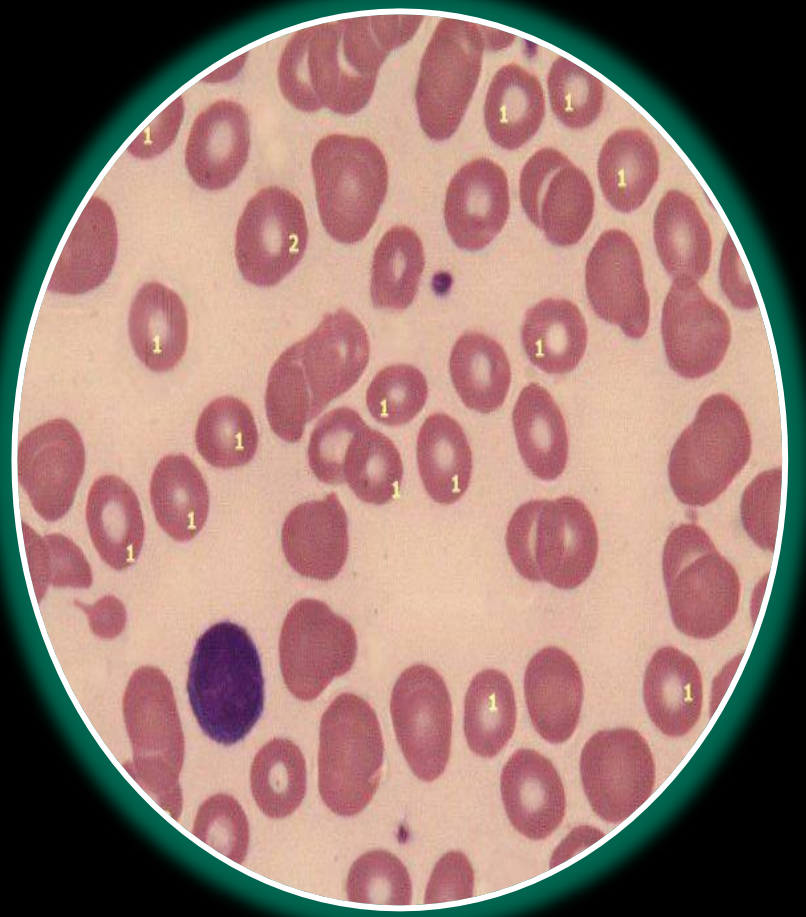
Found in

- Folate and B12 deficiencies (oval)
- Ethanol (round)
- Liver disease (round)
- Reticulocytosis (round)



Example :

Most erythrocytes presented in the picture are microcytes (compare with the small lymphocyte). The degree of hemoglobinization is sufficient. Normal platelets and single ovalocytes are present.



1. Microcyte
2. Normocyte

Variation In Erythrocyte Color

- A normal erythrocyte has a pinkish-red color with a slightly lighter-colored center (central pallor) when stained with a blood stain, such as Wright.
- The color of the erythrocyte is representative of hemoglobin concentration in the cell.
- Under normal conditions, when the color, central pallor, and hemoglobin are proportional, the erythrocyte is referred to as Normochromic.

Hypochromia

- Increased central pallor and decreased hemoglobin concentration, the central pallor occupies more than the normal third of the red cell diameter.

Found in

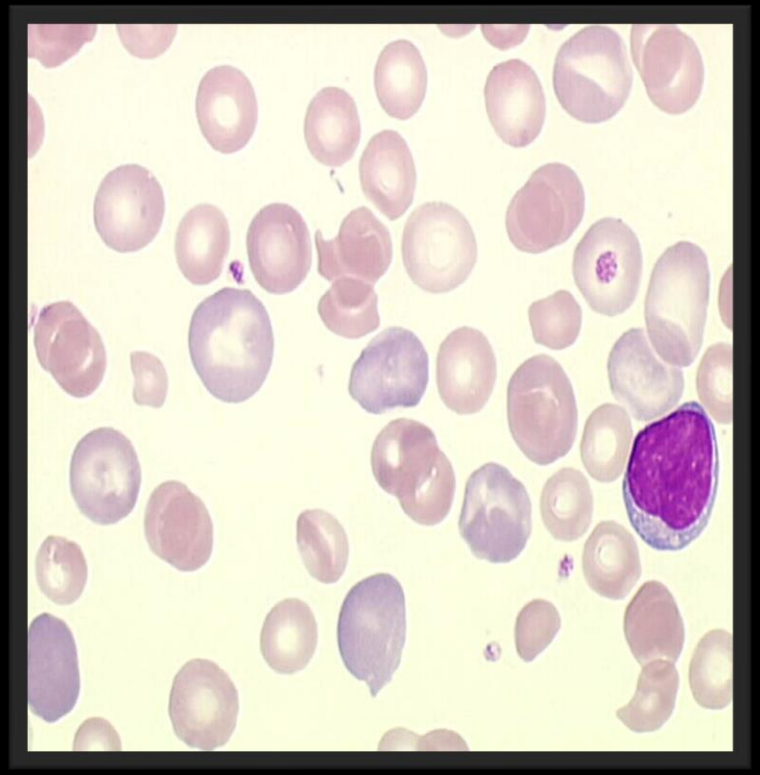
- Iron deficiency
- Thalassaemia
- any of the conditions leading to Microcytosis

Polychromasia

- Red cells stain shades of blue-gray as a consequence of uptake of both eosin (by hemoglobin) and basic dyes (by residual ribosomal RNA). Often slightly larger than normal red cells and round in shape - round macrocytosis.

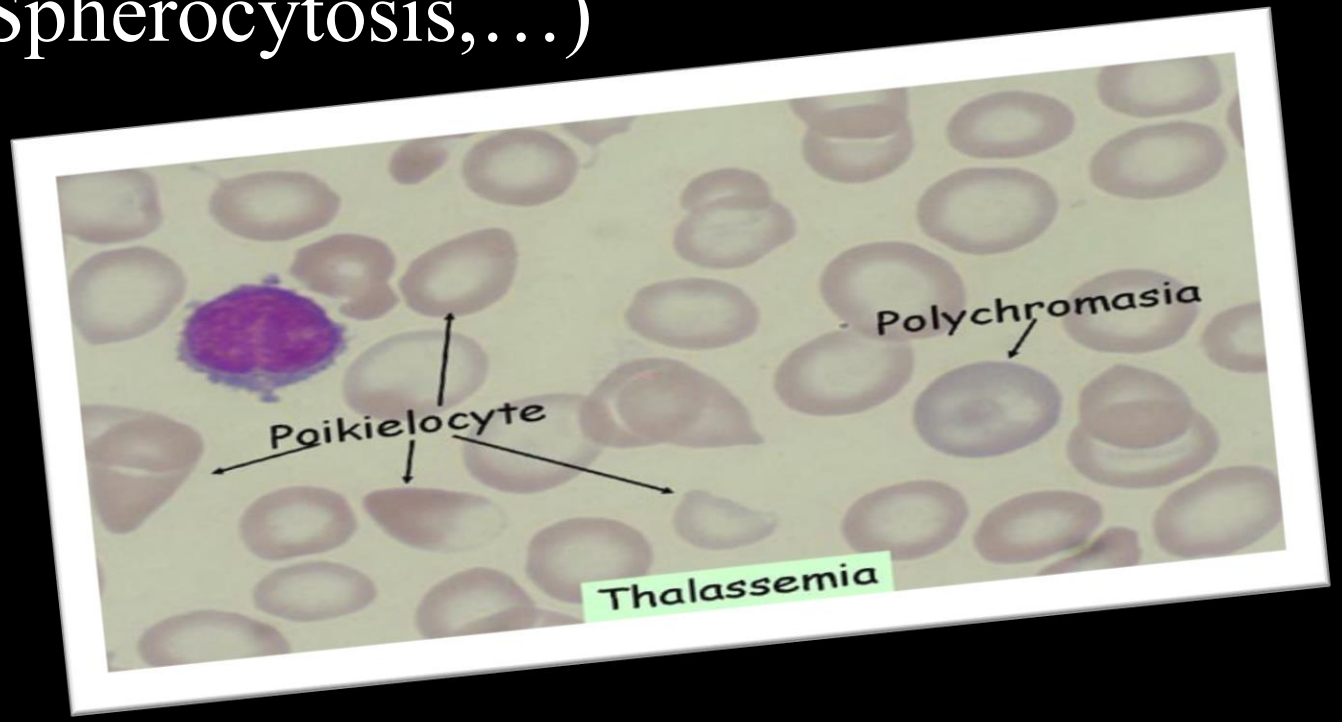
Found in

Any situation with reticulocytosis – for example bleeding, hemolysis or response to heamatinic factor replacement.



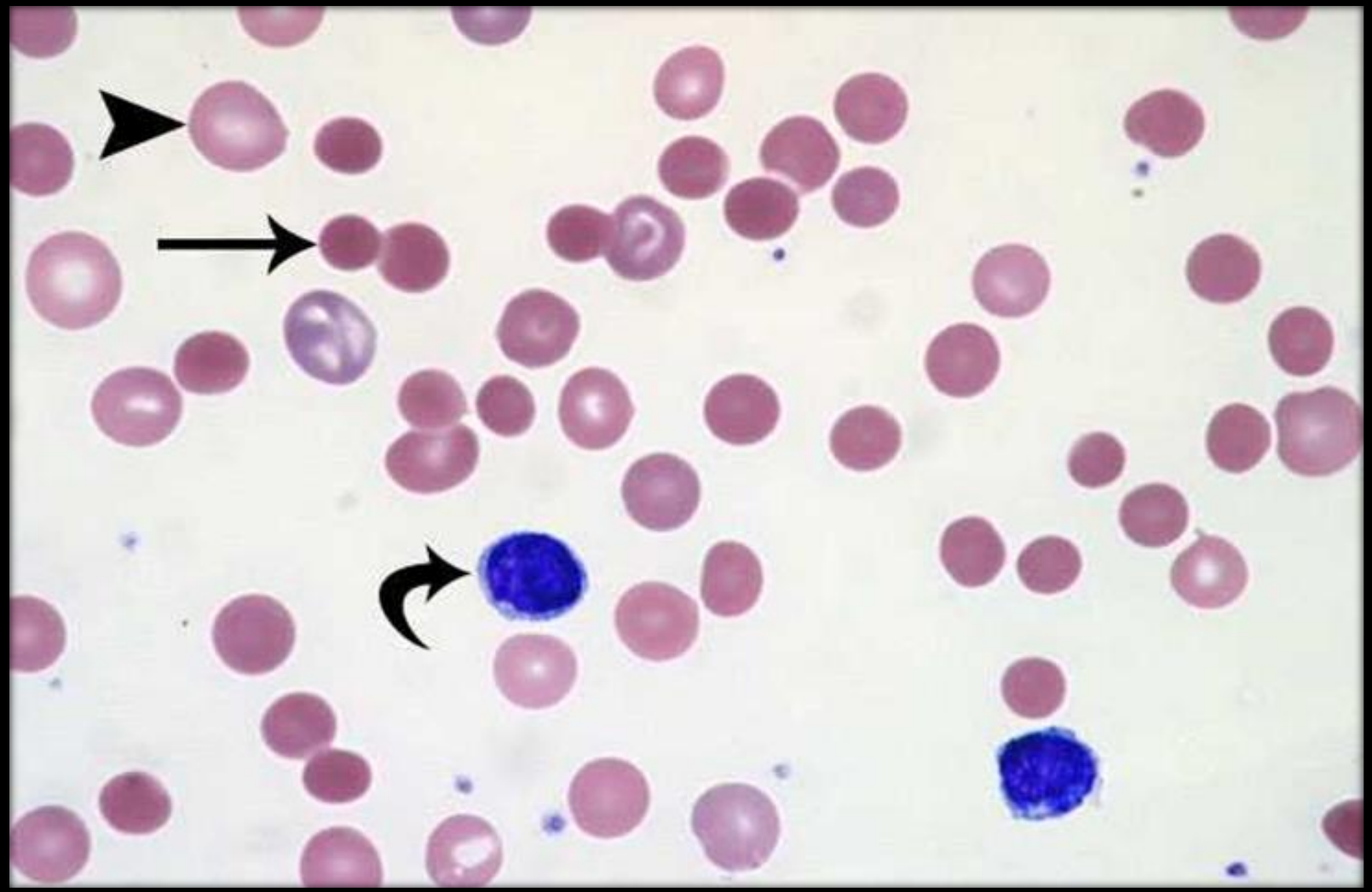
IV. Shape Abnormalities of Erythrocytes

- Poikilocytosis is the general term for mature erythrocytes that have a shape other than the round, biconcave disk.
- Poikilocytes can be seen in many shapes.(e.g. Acanthocyte, Spherocytosis,…)



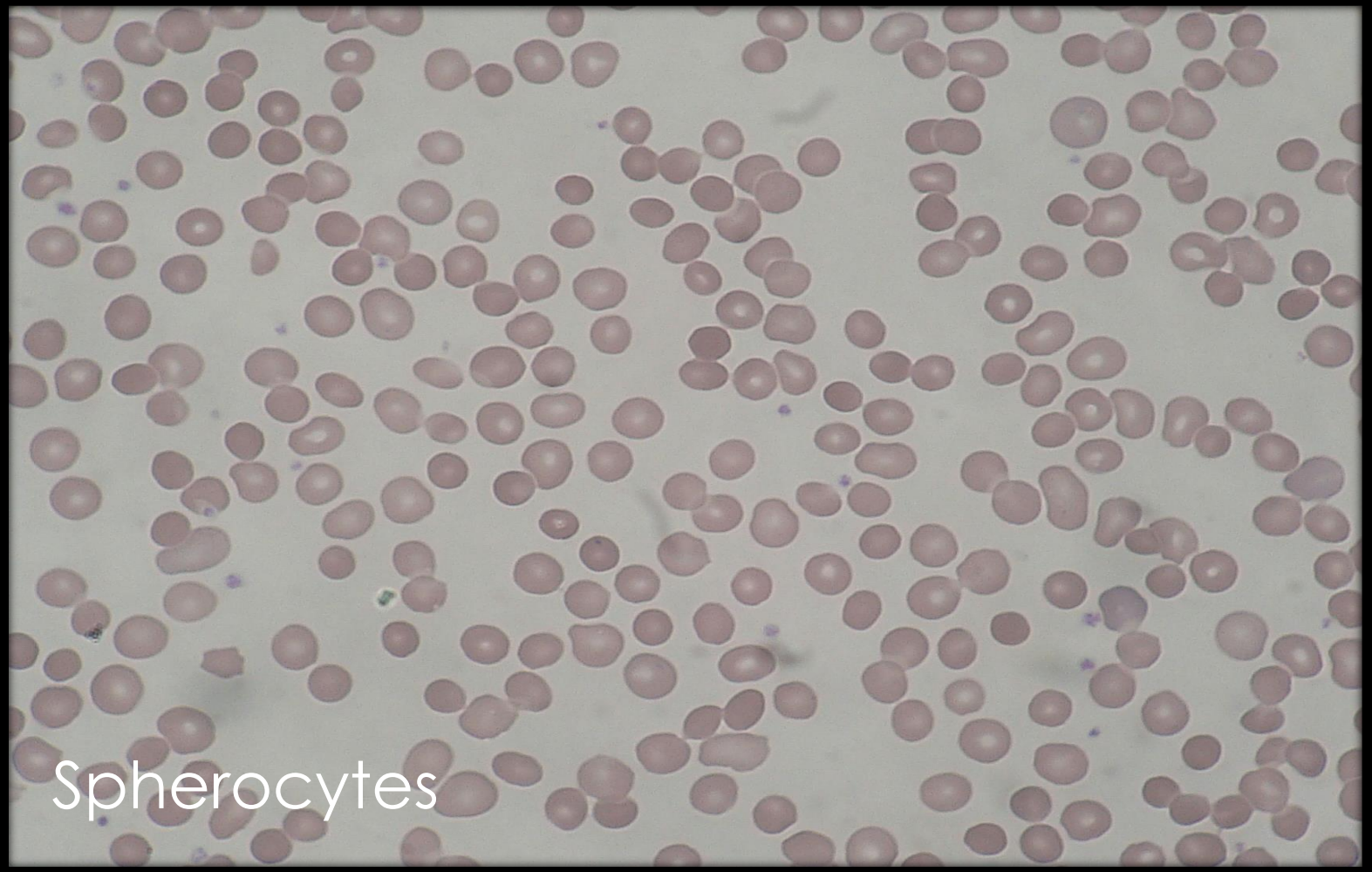
Normal Peripheral Smear

Autoimmune Hemolytic Anemia



Sphero cytes

Hereditary Spherocytosis

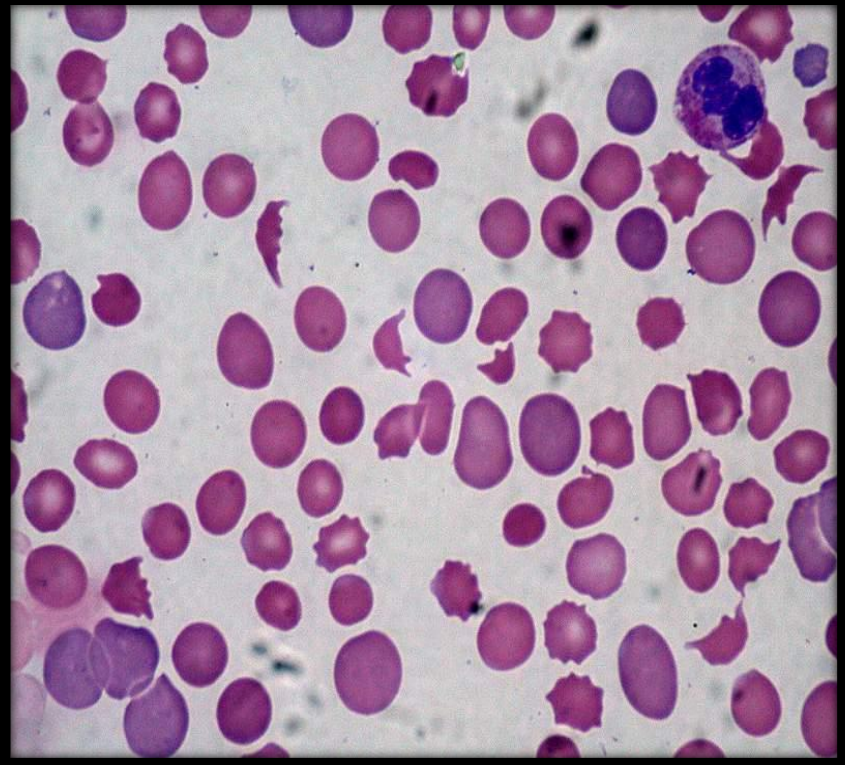


Spherocytes

Microangiopathic Hemolytic Anemia

microangiopathic hemolytic anemia (MAHA) is a microangiopathic subgroup of hemolytic anemia (loss of red blood cells through destruction)

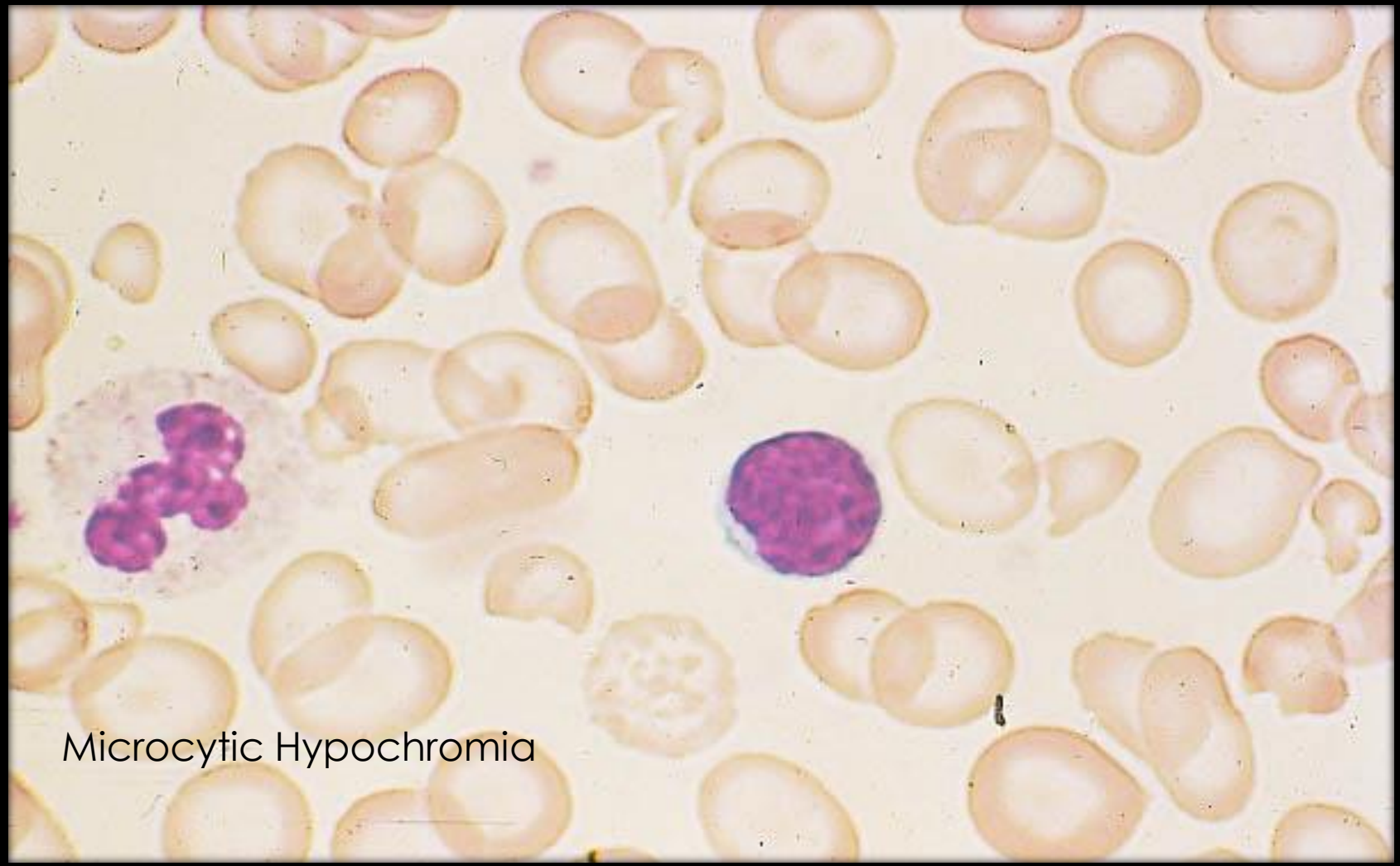
- caused by factors in the small blood vessels.
- identified by the finding of anemia and schistocytes on microscopy of the blood film.



Schistocytes

Iron Deficiency Anemia

Alpha Thalassaemia (a-/--)



SICKLE CELL ANEMIA

RED
BLOOD
CELL
MORPHOLOGY

RED BLOOD CELL MORPHOLOGY

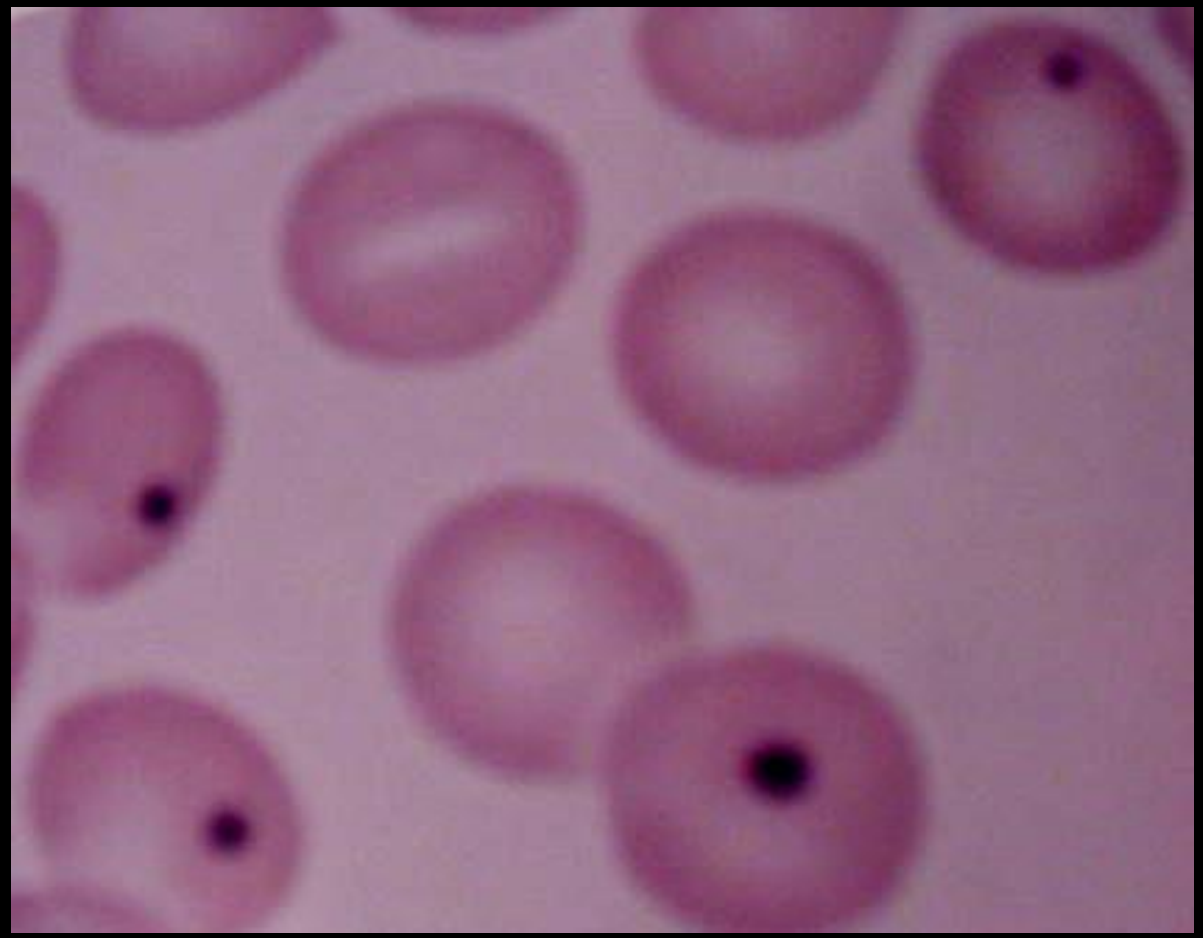
- You will see the following types of cells in a patient with sickle cell anemia, Hemoglobin SS.

RED BLOOD CELL MORPHOLOGY

- Target cells are also known as codocytes. They resemble a bull's eye. These cells are indicative of an anemia state.

RED BLOOD CELL MORPHOLOGY

- Howell-Jolly bodies may be seen in sickle cell anemia. These bodies are DNA that stain dark purple within the red blood cell.

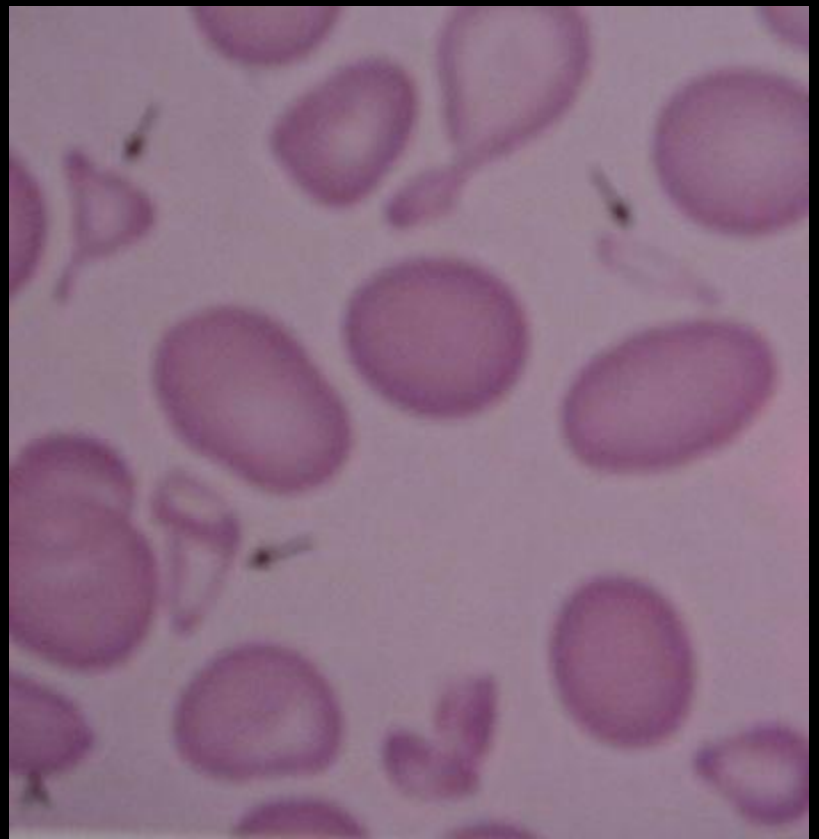


RED BLOOD CELL MORPHOLOGY

- Basophilic stippling is granules of RNA seen within the red blood cell. The granules stain blue to purple.

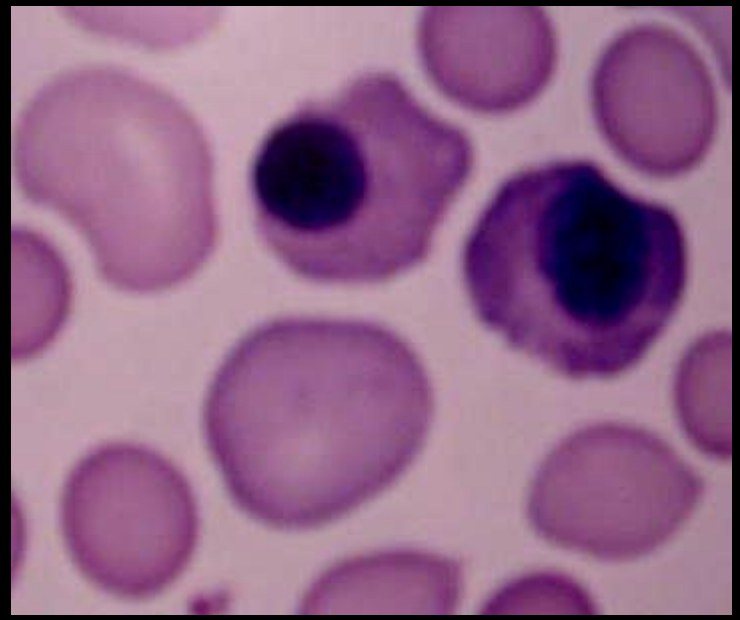
RED BLOOD CELL MORPHOLOGY

- Schizocytes are fragmented red blood cells present on the peripheral smear of sickle cell anemia.
- They are many shapes and sizes and may have pointed extremities.



RED BLOOD CELL MORPHOLOGY

Nucleated red blood cells. These red blood cells are released from the bone marrow early into the blood stream, due to the need for oxygen. Normal red blood cells do not contain a nucleus on a peripheral smear.



RED BLOOD CELL MORPHOLOGY

- Sickle cell anemia. Note the sickle shaped red blood cell.

RED BLOOD CELL MORPHOLOGY

- Sickle cell crisis.