Erythropoiesis

TEXTBOOK OF MEDICAL PHYSIOLOGY

GUYTON & HALL 11TH EDITION

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The process of
formation of RBCs is
called Erythropoiesis

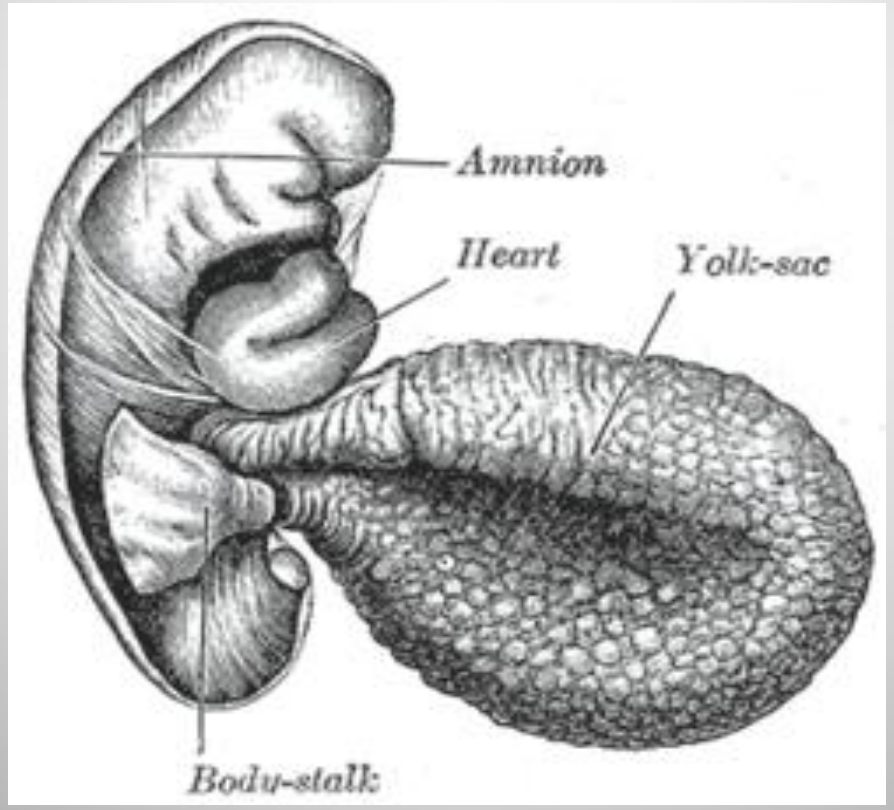
Learning Objectives of Today's Lecture

At the end of this lecture student should be able to recognize:

- Sites of **Erythropoiesis**
- Main features of **different stages** of Erythropoiesis
- Features of **mature RBCs**
- The regulation of RBC production and erythropoietin hormone secretion in response to hypoxia

Site of RBC Production

- **Early weeks of embryonic life:**
  - Nucleated RBCs - Yolk sac



Site of RBC Production, Cont.

- **Middle trimester of gestation:**
  - **Liver** form blood cells (mainly)

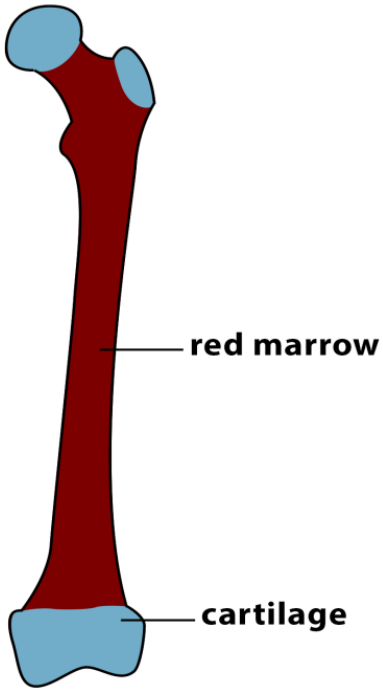
  Spleen + lymph nodes form blood cells
- **Last month of gestation and after birth:**

  - **Red bone marrow** (exclusively)

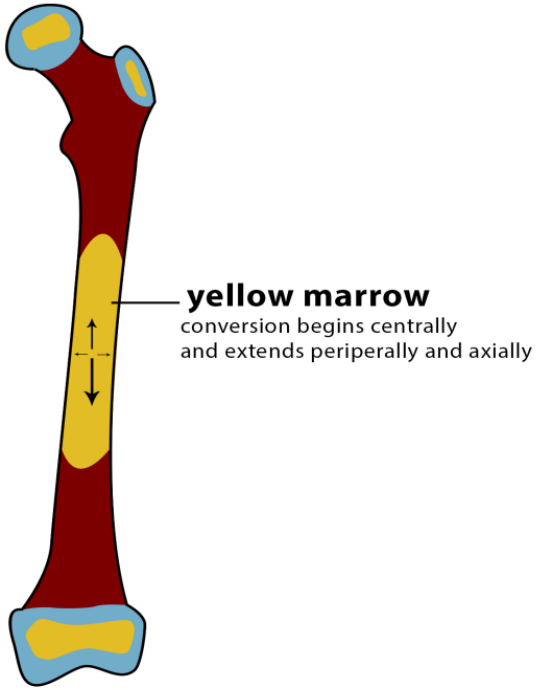
RBC Production after birth

- The bone marrow of **all bones** - **5** years
- Marrow of the **long bones** (**except for the proximal humerus and tibia**)
  - **No more red blood cells are produced after the age of 20 years.**
- **Most RBCs continue to be produced** in the marrow of the **membranous bones**, such as
  - **Vertebrae, Sternum, Ribs, and Ilia**

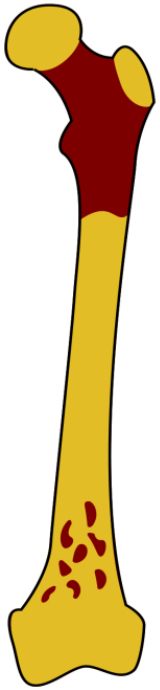
Normal bone marrow conversion



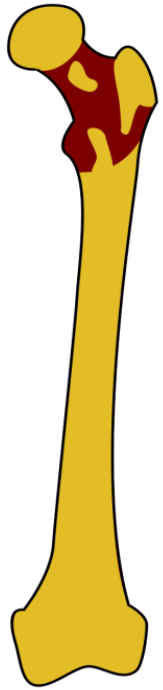
Infant
<1 year



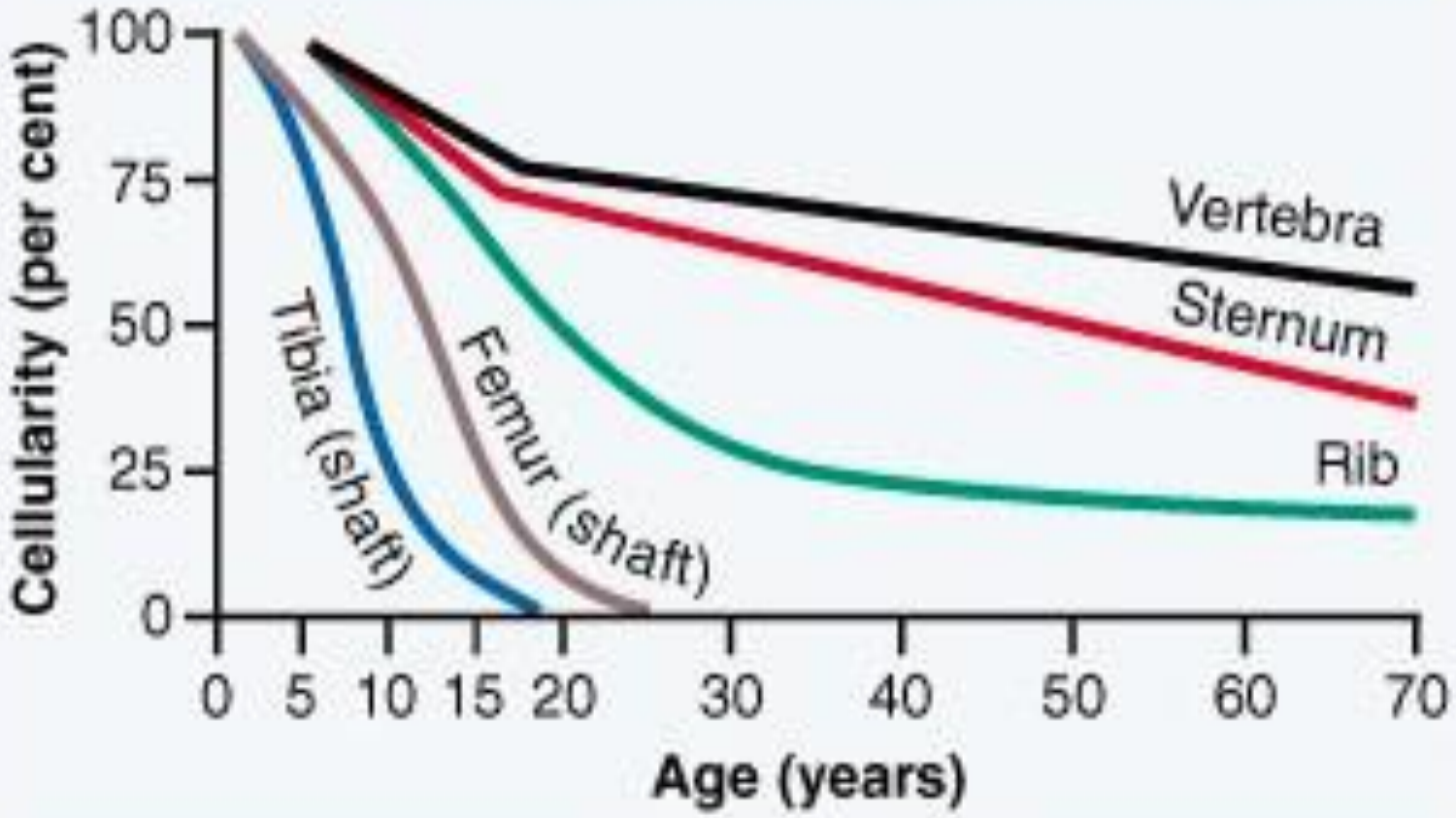
Childhood
1-10 years



Adolescent
10-20 years

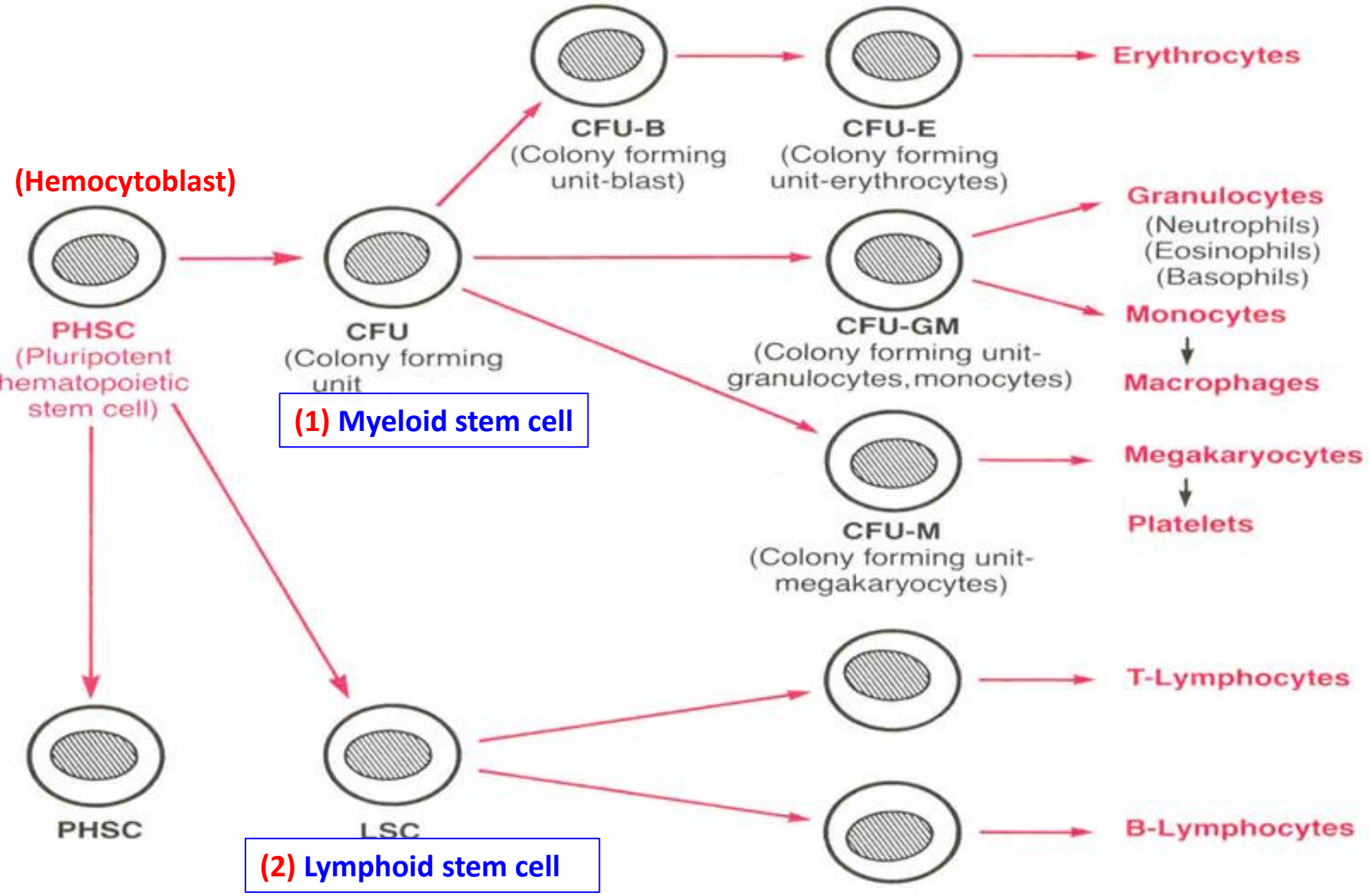


Adult
>25 years



Relative **rates of red blood cell production** in the bone marrow of different bones at different ages.

Genesis of RBC



Genesis (Production) of RBC

- ***Pluripotential hematopoietic stem cell*** ***(PHSC).***
- Committed stem cell that produces **erythrocytes** is called ***Colony-forming unit–erythrocyte*****, CFU-E**

Factors:

- *Growth inducers, such as interleukin-3*
- *Differentiation inducers.*

Stages of Erythropoiesis

PHSC

↓

Comittes stem cell, CFU-E

Proerythroblast

Basophil erythroblast

Polychromatophil erythroblast

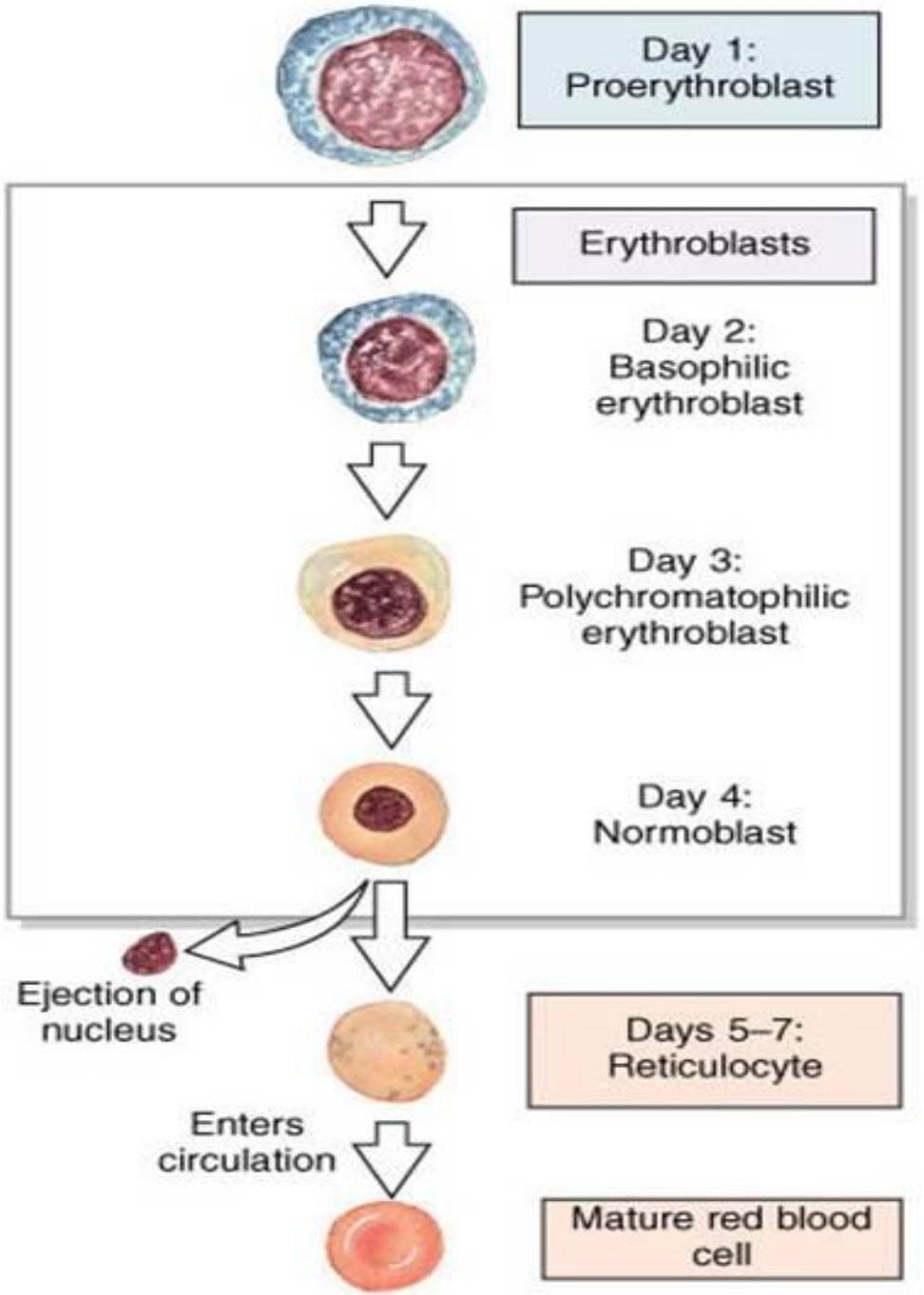
Orthochromatophil erythroblast

↓

Reticulocyte

↓

Erythrocyte



Maturation Times

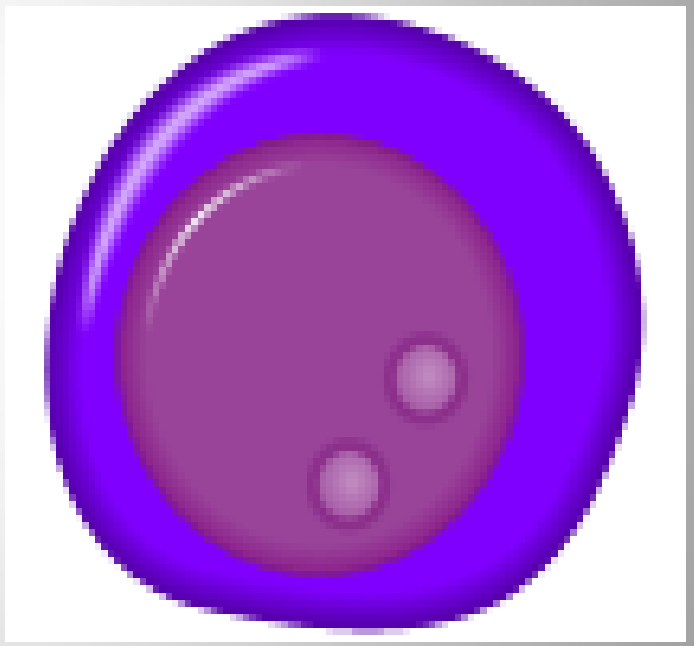
Erythroblasts actively synthesize Hb. They are categorized on the basis of total size, the amount of Hb present, and the size of nucleus.

Erythropoiesis

- RBC development is characterized by:
  - A decrease in cell size
  - A disappearance of nucleus
  - An appearance of hemoglobin

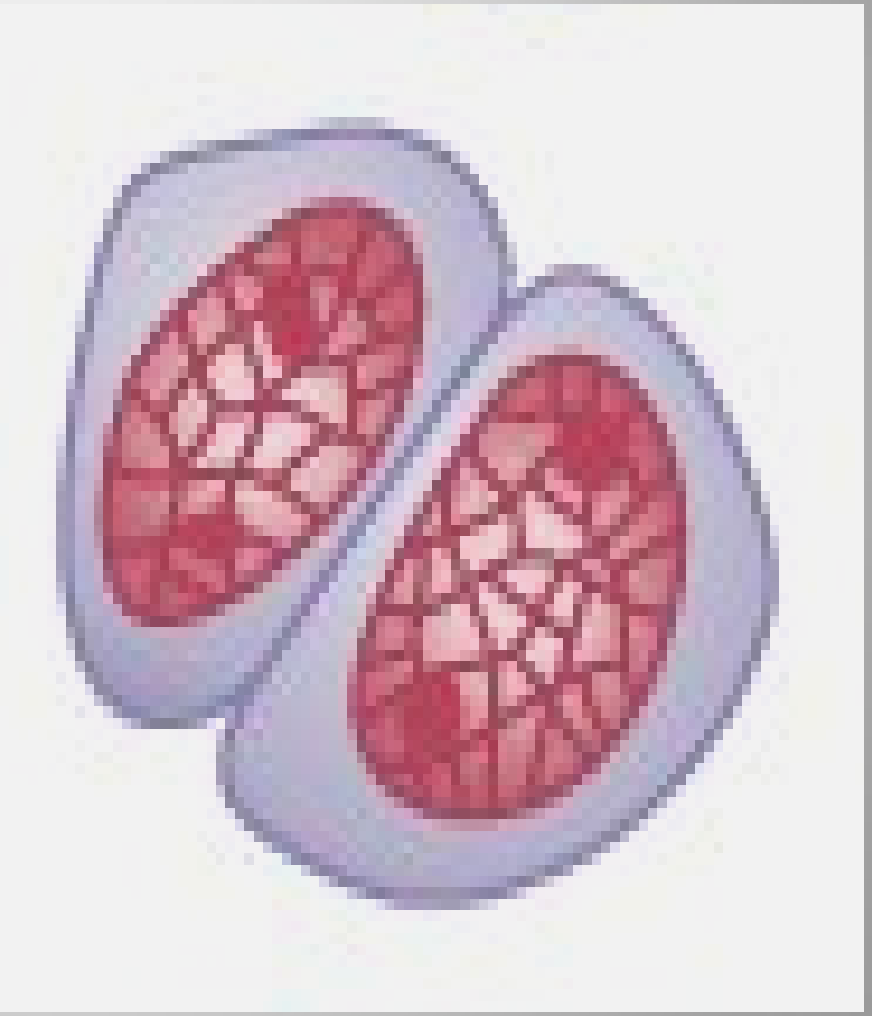
Proerythroblast

- No hemoglobin
- Nucleus 12 um
- **Contain nucleoli**



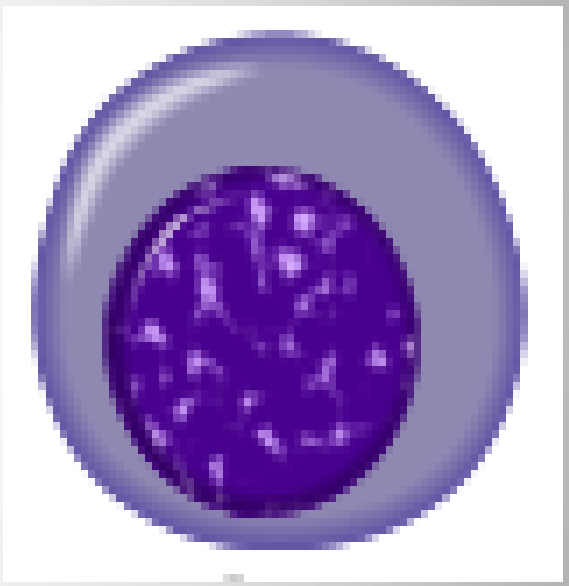
Basophil erythroblast

- Early Normoblast
- **Nucleoli disappear**
- Show **mitosis**
- Cytoplasm deep blue
  - Increase in **RNA**
- **Hemoglobin starts appearing – Little Hb**



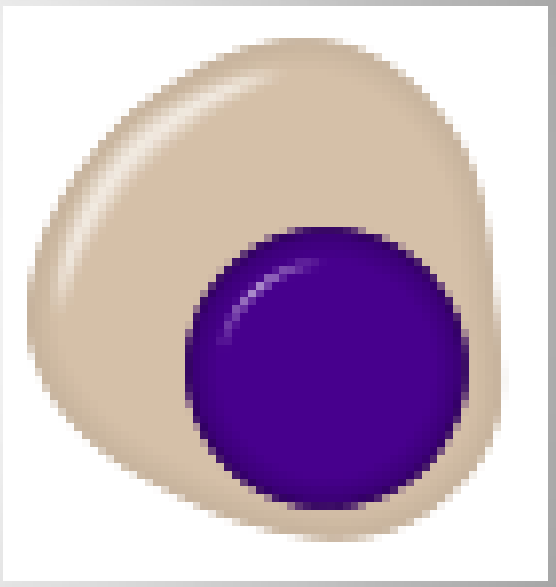
Polychromatophil erythroblast

- Late Normoblast
- **Nucleus smaller**
- **Coarse Chromatin**
- **Hemoglobin** increases



Orthochromatic Erythroblast

- **Normoblast**
- Contains a small dense **nucleus**
- **Nuclear lysis and**
- **Nuclear extrusion**



Reticulocyte

- **Reticulum**
- Remnant of **ER** & GA
- Contains RNA in the cytoplasm to:
  - **Synthesize Hb**
  - **synthesize other proteins**
- **Few Mitochondria**
- **Young RBCs (80% Hb)**
- **< 1 %** of RBCs

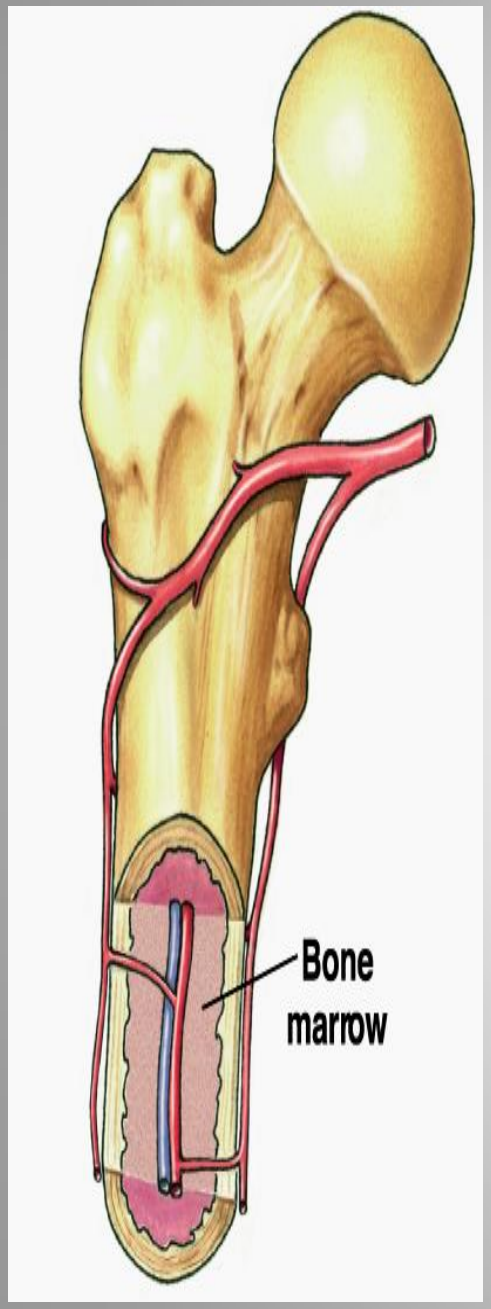
Transfer of RBC to Circulation

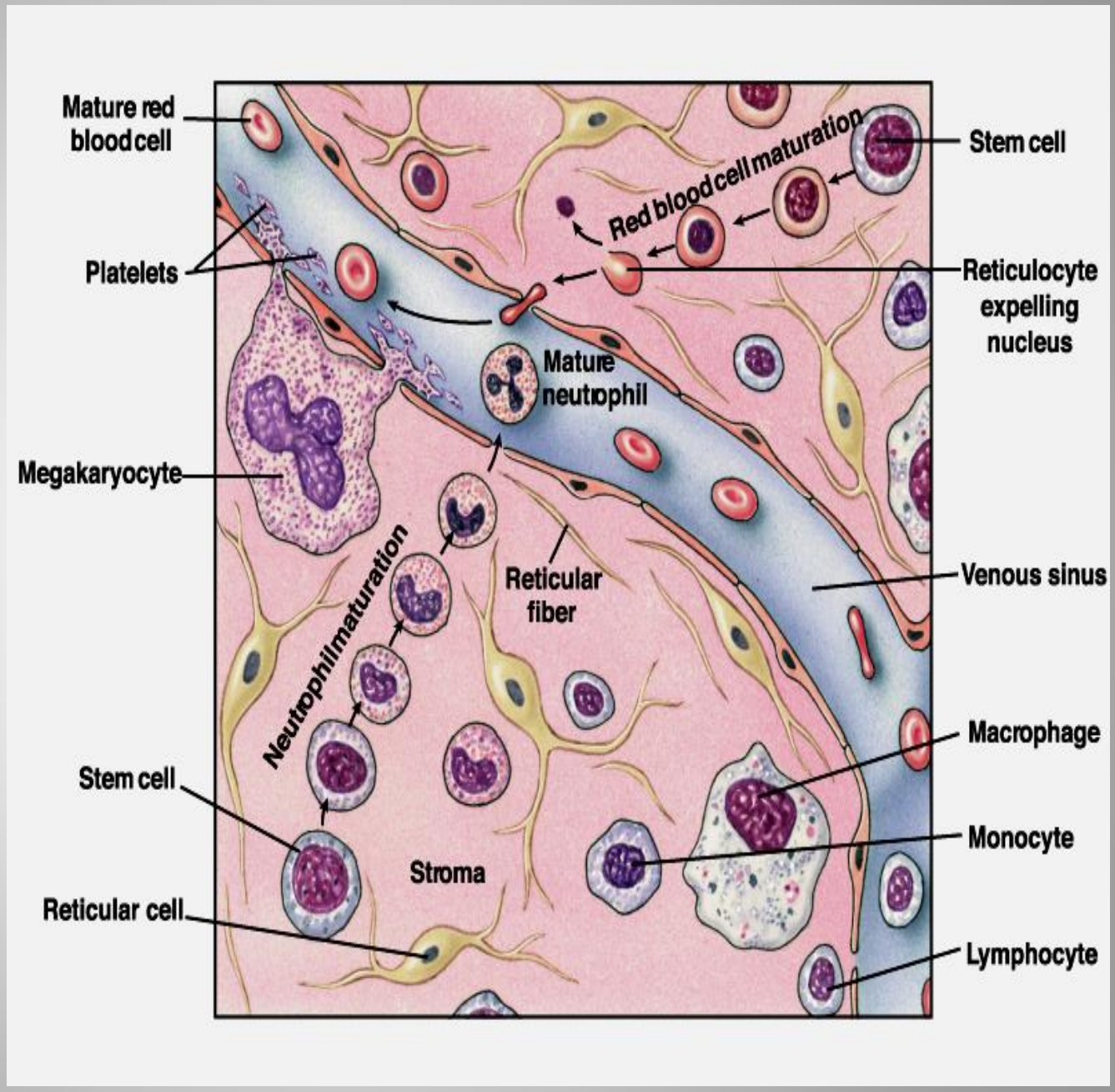
RBC pass **from the bone marrow** into the **blood capillaries**

By

Diapedesis

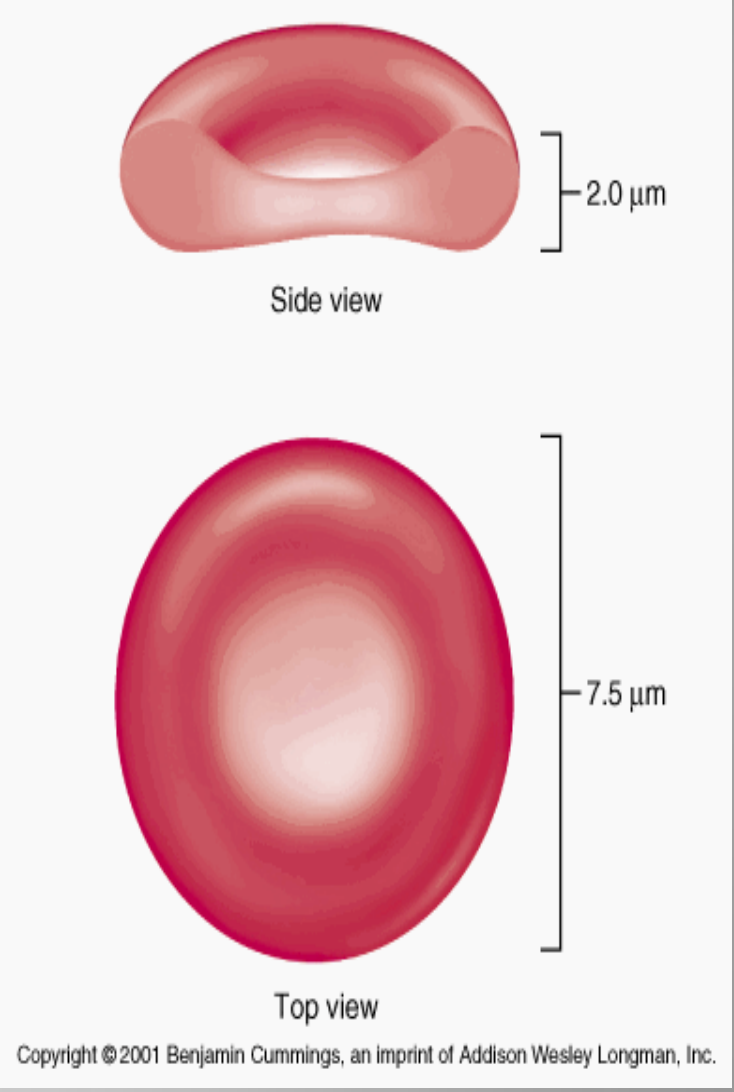
(squeezing through the pores of the capillary membrane).


Bone
marrow


Mature red blood cell
Platelets
Megakaryocyte
Stem cell
Reticular cell
Neutrophil maturation
Reticular fiber
Stroma
Red blood cell maturation
Stem cell
Reticulocyte expelling nucleus
Mature neutrophil
Venous sinus
Macrophage
Monocyte
Lymphocyte

Erythrocytes

- **Round, biconcave, disc shaped.**
- **Smooth contours**
- **Diameter 7- 8 um.**
- Normally no variation in size and shape.
- **Can deform easily**
- **Hb =34g/dl of cells**
- **Hb= 14-16 g/dl in the blood**



STRUCTURE OF RBC

- **Negative surface charge**
- **Bag of fluid** with dissolved substances and hemoglobin
- **Membrane –**
  - **Outer** glycoprotein coat
  - Lipid bilayer (PL 55%,Cholesterol 45%)
  - **Inner** protein molecules **cytoskeleton**
  - **Spectrin, Actin, Ankyrin etc.**

ENERGY METABOLISM

- **Less energy required**
- **Utilize Glucose for energy by:**
  - **Anaerobic glycolysis**
  - **Pentose phosphate pathway**

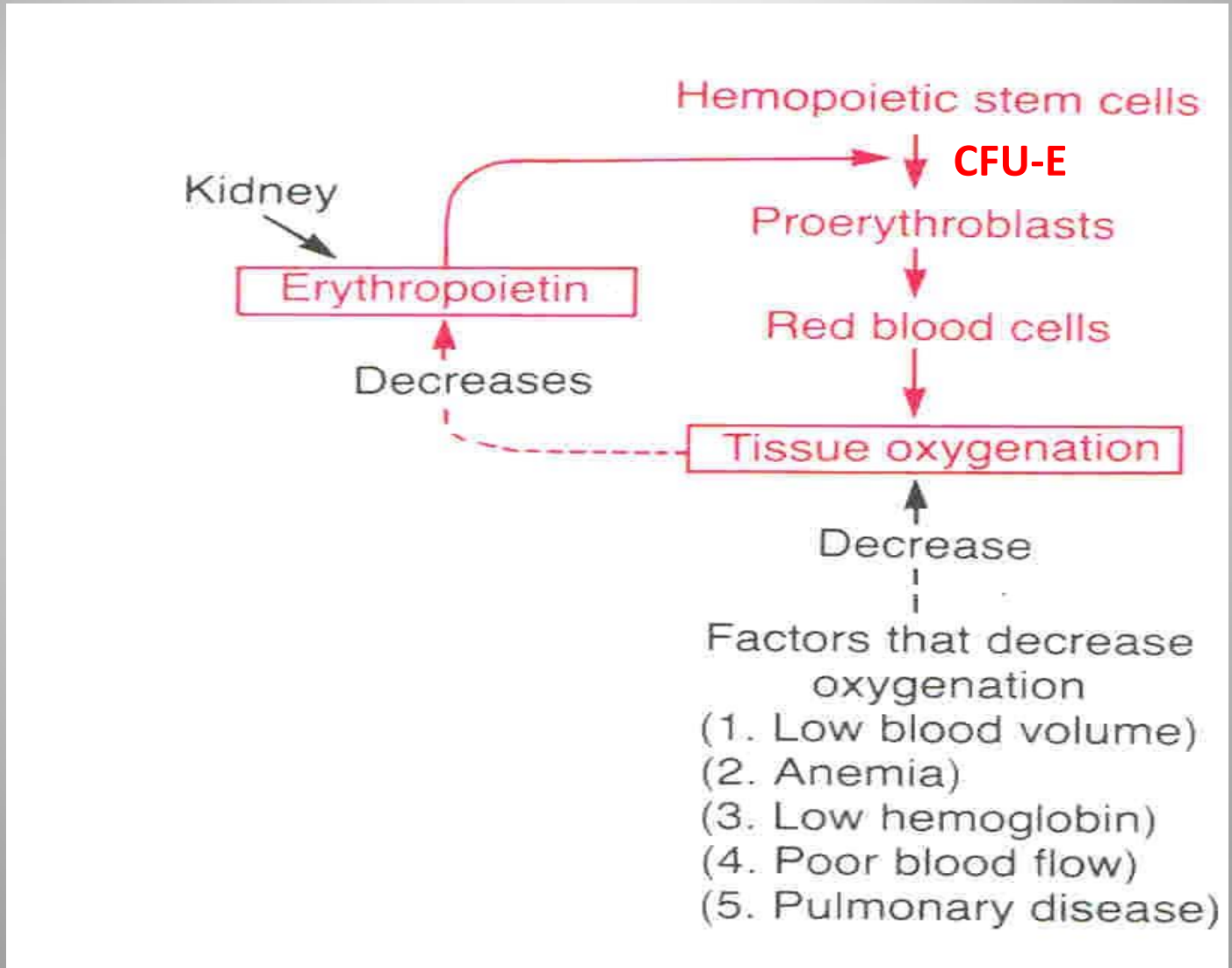
RBC Count

- *MALE :*
  - **5,200,000 ± 300000 per mm^3 (uL).**
- *FEMALE :*
  - **4,700,000 ± 300000 per mm^3 (uL).**
- **LIFE SPAN**: 120 Days.

Regulation of RBC production

- Erythropoiesis is stimulated by erythropoietin (EPO) hormone produced by the kidney in response to hypoxia (low oxygen in the blood)
- Hypoxia caused by:
  - Low RBC count (Anaemia)
  - Hemorrhage
  - High altitude
  - Prolong heart failure
  - Lung disease

Tissue oxygenation and RBC formation

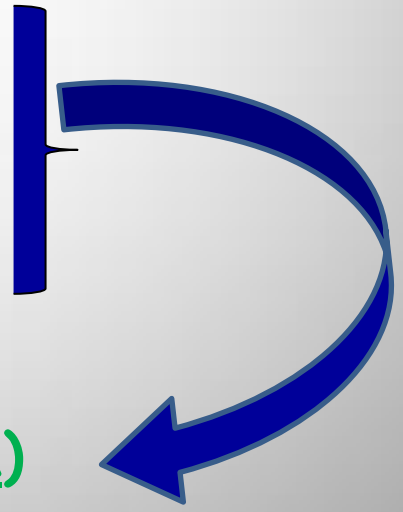


Erythropoietin (EPO)

- Glycoprotein
- 90% of EPO is produced from peritubular fibroblasts in the renal cortex and 10% from the liver
- Renal failure or Chemotherapy)? → Low levels of EPO

Erythropoietin (EPO)

- Glycoprotein
- 90% of EPO is produced from peritubular fibroblasts in the renal cortex and 10% from the liver
- Renal failure?
- Stimulate the growth of early stem cells
- Can be measured in plasma & urine
- High levels of erythropoietin
  - Anemia, hemorrhage
  - High altitude
  - Heart failure
  - Lung Disease



(Result in polycythemia)

Role of EPO

- EPO stimulates increased cell division rates in erythroblasts and stem cells that produce erythroblasts.
- EPO speeds up the maturation of RBCs by accelerating the rate of Hb synthesis.
- Under maximum EPO stimulation, bone marrow can increase the rate of RBC production tenfold.
- Blood doping?

Main Features - Stages of Erythropoiesis

- Proerythroblast
- Basophilic Erythroblast
- Polychromatophil Erythroblast
- Orthochromatic erythroblast
- Reticulocyte
- Erythrocyte