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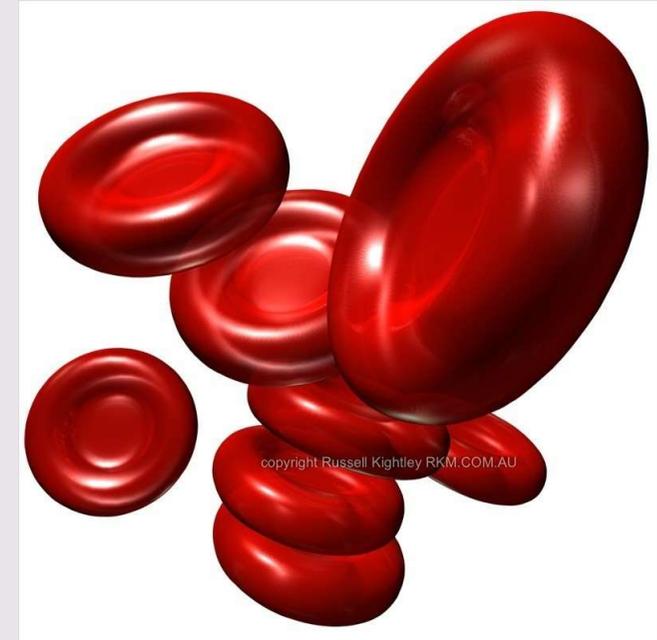
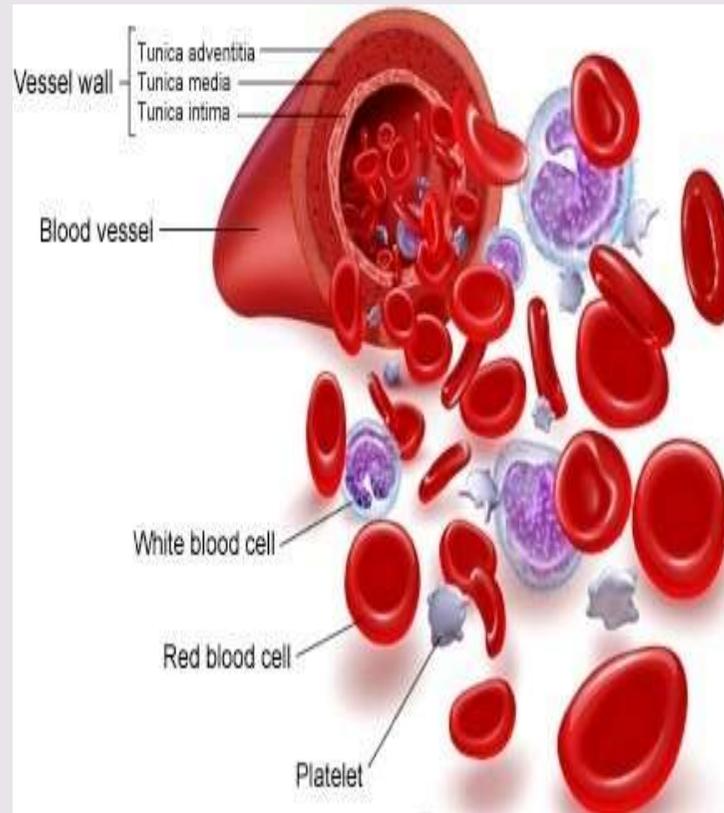
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# ERYTHROPOIESIS



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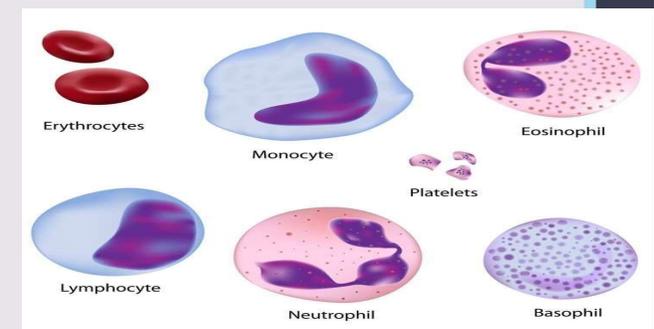


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# Hemopoiesis

- v Hemo: Referring to blood cells
- v Poiesis: “The development or production of”
- v The word Hemopoiesis refers to the production & development of all the blood cells:
  - θ Erythrocytes: **Erythropoiesis**
  - θ Leucocytes: Leucopoiesis
  - θ Thrombocytes: Thrombopoiesis.



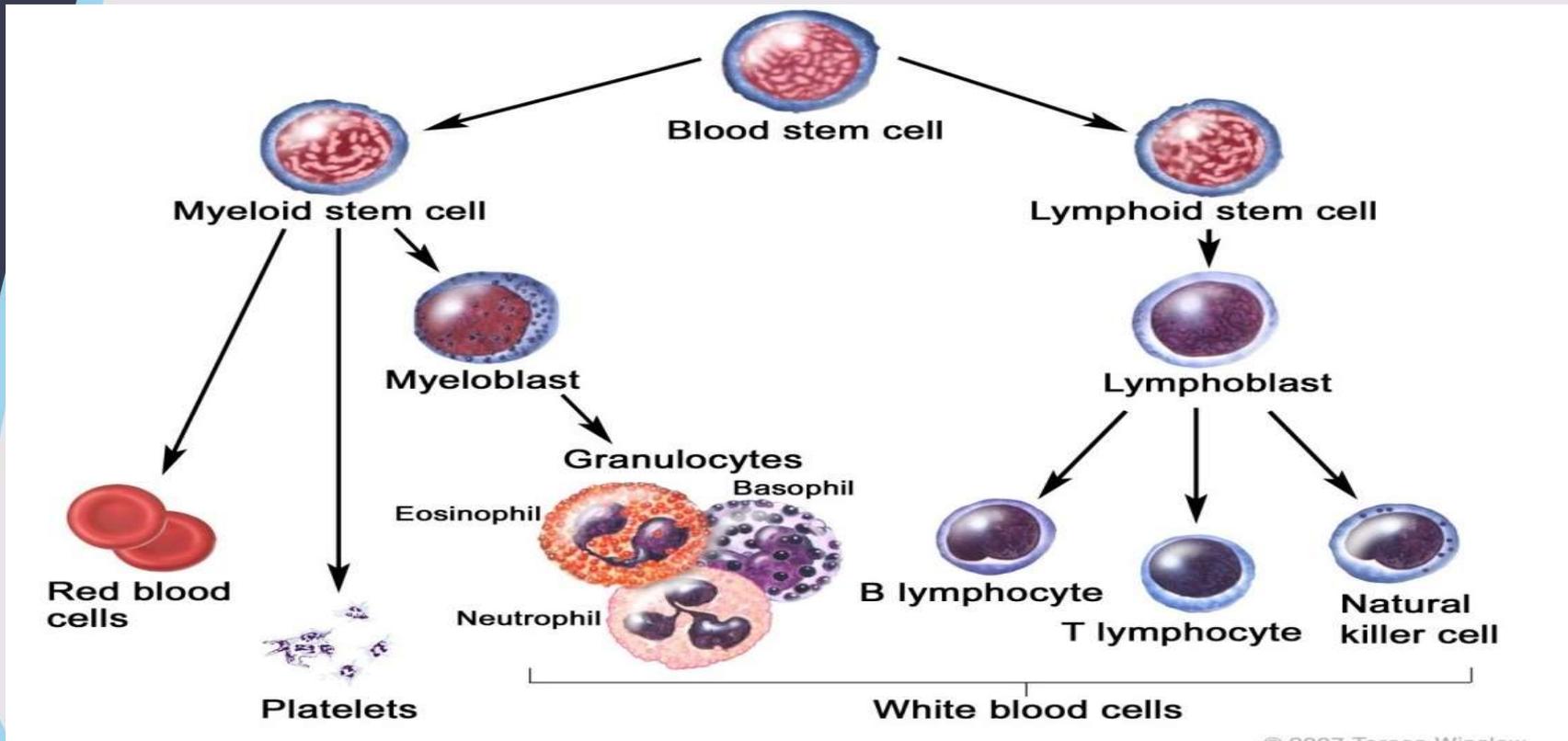


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# DEFINITION

It is the process of **development, differentiation and maturation** of RBCs from primitive stem cells





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## Theories of erythropoiesis

### v Monophyletic theory

Also known as **unitary theory.**

There is a common parent cell of all formed elements of blood.



Alexander A.  
Maximow

### v Polyphyletic theory

Also known as **trialistic theory**

Suggests different group of stem cells gives rise to different blood cells.

L.  
Aschoff





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# Site of Erythropoiesis is

Intravascular erythropoiesis  
 Extravascular erythropoiesis

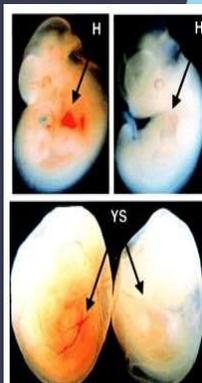
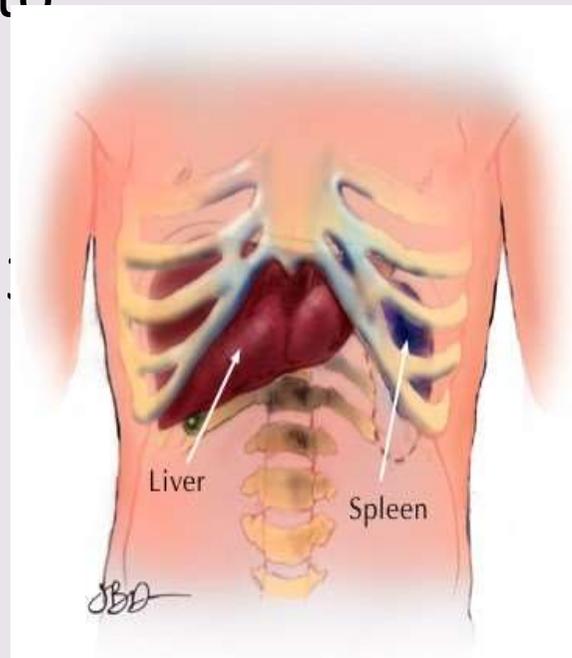
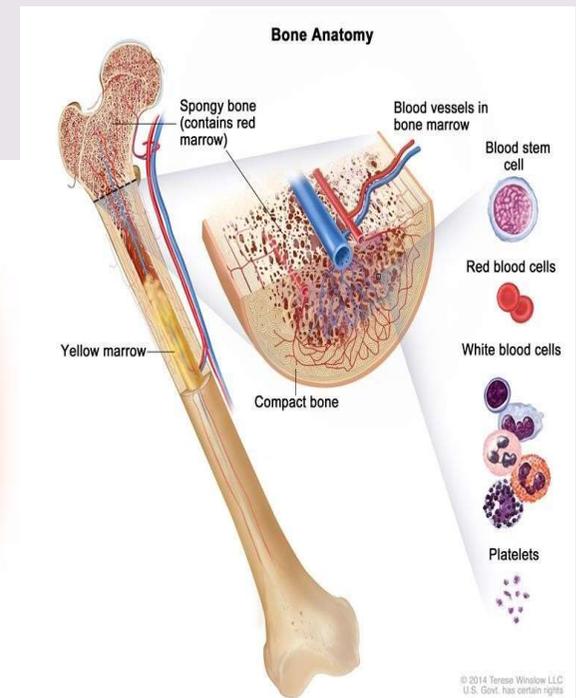
## During intrauterine life

Mesoblastic stage (3<sup>rd</sup> week to 3 months)

Hepatic stage (after 3 months)

Myeloid stage (3<sup>rd</sup> trimester)

## Nucleated RBCs



Yolk sac

Liver & spleen

Bone marrow



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## ✓ In children

- All bones with red bone marrow

Liver & spleen

## ✓ In adults (after 20yrs)

- Ends of long bones like femur, humerus

Skull

Vertbrae

Ribs

Sternum

pelvis

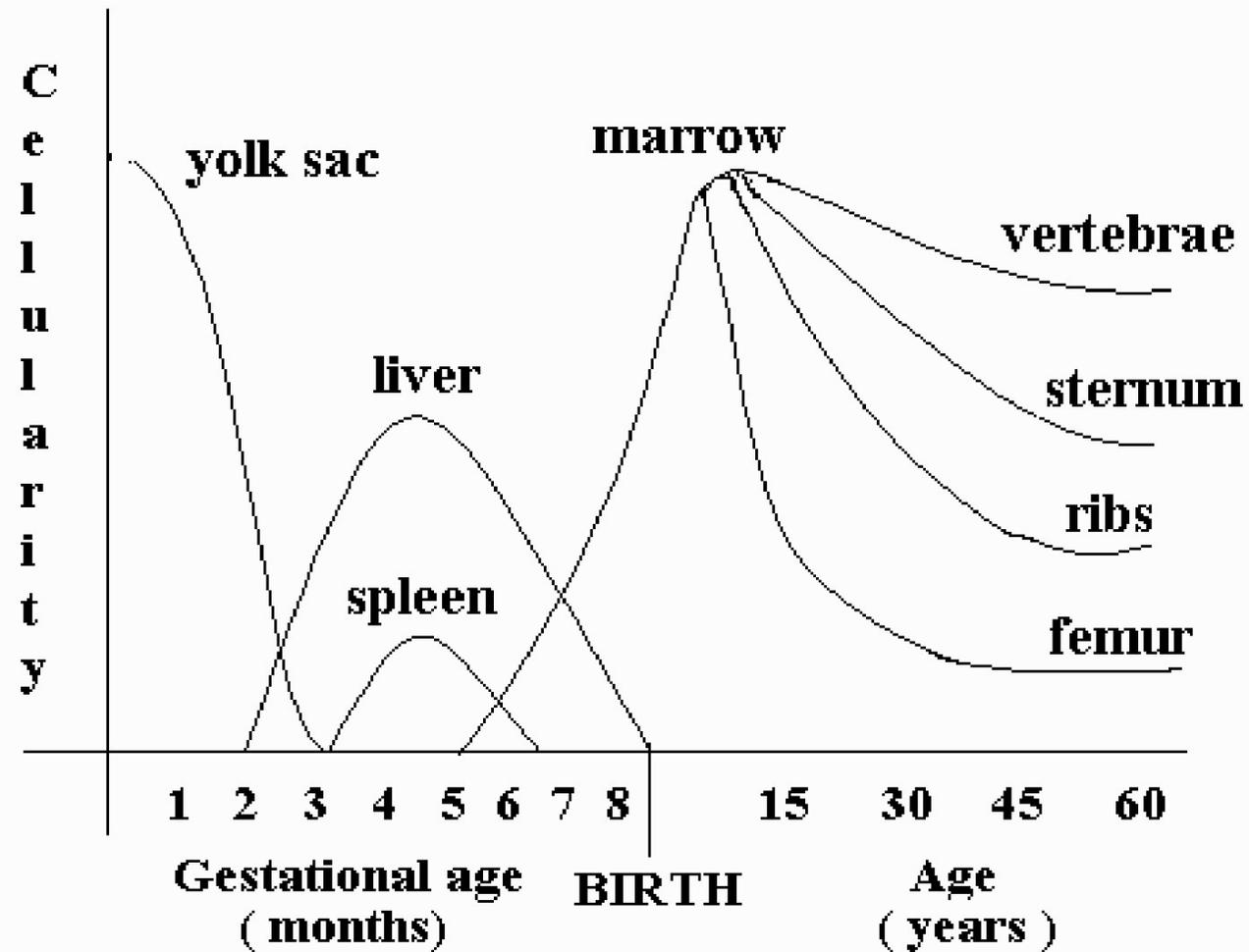




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## SITES OF ERYTHROPOIESIS





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# Pluripotent Hemopoietic stem cell



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# Pluripotent Hemopoietic stem cell

IL-1, IL-6, IL-3 →

← GM-CSF erythro

**BFU-E (Burst Forming Unit Erythrocyte)**

**CFU-E (Colony Forming Unit Erythrocyte)**

← GM-CSF erythro

**PROERYTHROBLAST**

**EARLY NORMOBLAST**

**INTERMEDIATE NORMOBLAST**

**LATE NORMOBLAST**

**RETICULOCYTE**

**ERYTHROCYTE**



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# 1. STEM

## CELLS

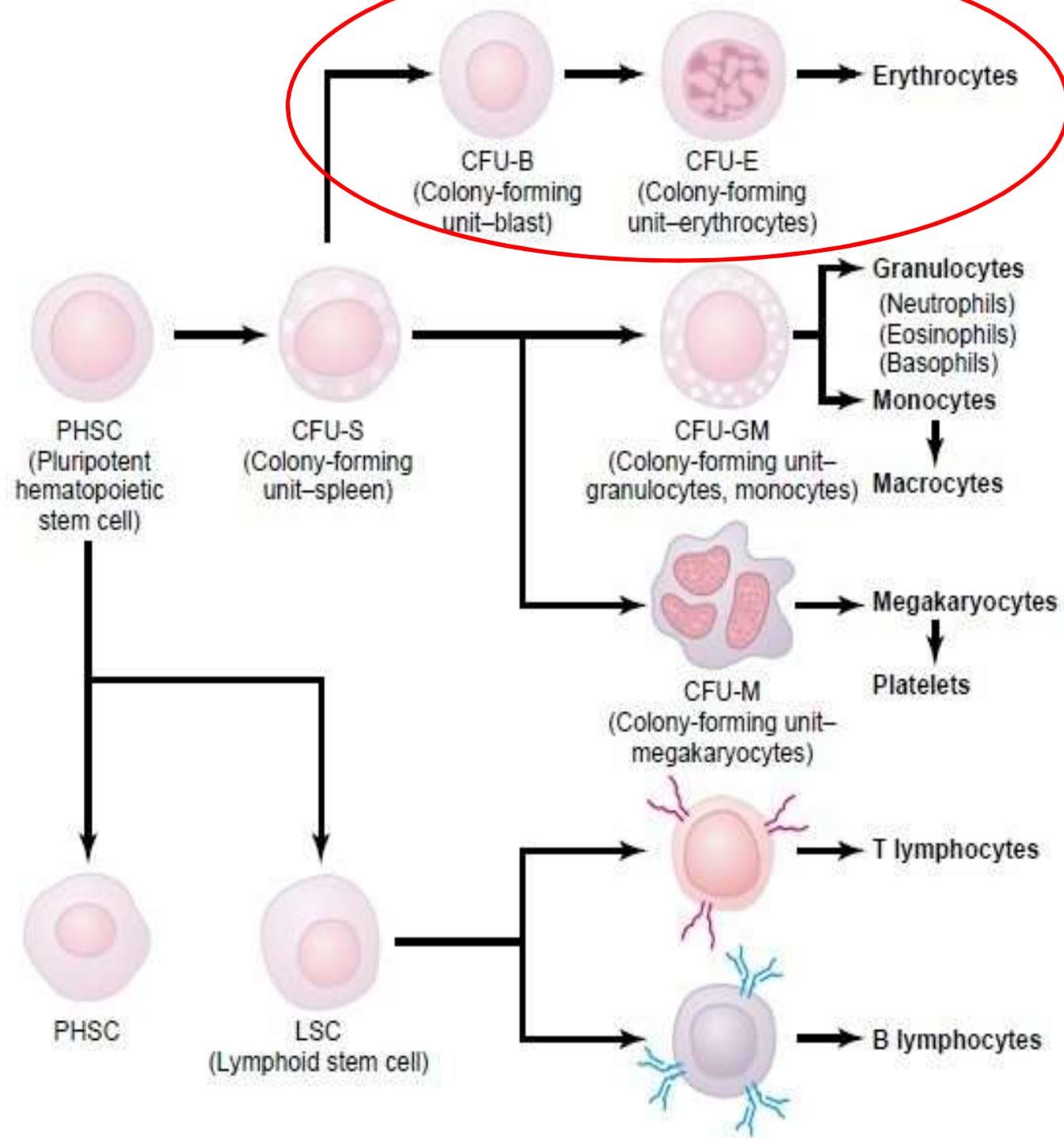
These cells have extensive proliferative capacity and also the:

- ⊖ Ability to give rise to new stem cells (**Self Renewal**)

- ⊖ Ability to differentiate into any blood cells lines

### (**Pluripotency**)

- v Hematopoietic stem cells (HSCs) are bone marrow cells that are capable of producing all types of blood cells. They differentiate into one or another type of committed stem cells (progenitor cells)



**Figure 32-2**

Formation of the multiple different blood cells from the original *pluripotent hematopoietic stem cell* (PHSC) in the bone marrow.



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## 2. Progenitor cells

- v Committed<sup>θ</sup> stem cells lose their capacity for self- renewal.
- v They become irreversibly committed.

## BFU-E & CFU-E

BFU-E Give rise each to thousands of nucleated erythroid precursor cells.

- θ Undergo some changes to become the Colony Forming Units-Erythrocyte (CFU-E)
- θ Regulator: Burst Promoting Activity (BPA)



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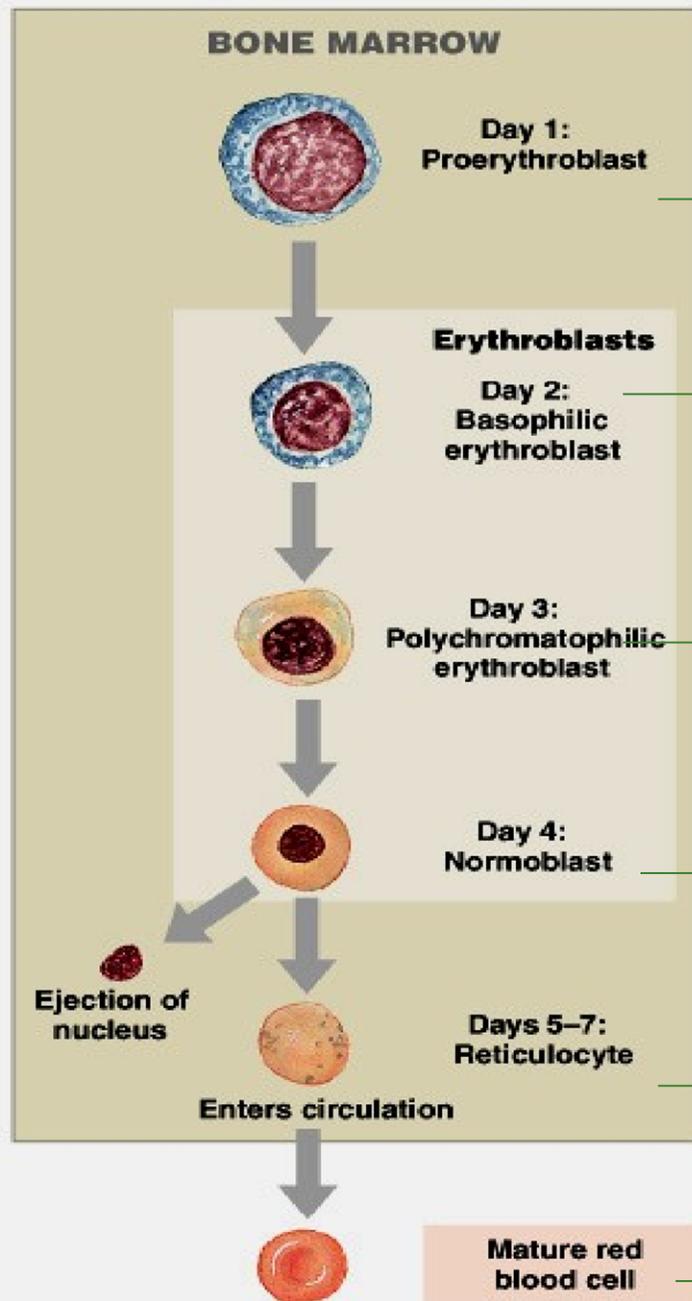
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# Burst forming unit BFU(E)

- v Unipotent progenitor cell
- v Less sensitive to erythropoietin
- v Responds to other stimulus forms

# Colony forming unit CFU (e)

- v Highly sensitive and dependent on erythropoietin
-



## ERYTHROPOIESIS

15-20 $\mu\text{m}$ - basophilic cytoplasm, nucleus with nucleoli.

14-17 $\mu\text{m}$ -mitosis, basophilic cytoplasm, nucleoli disappears.

10-15 $\mu\text{m}$ - 'POLYCHROMASIA' Hb appears, nucleus condenses.

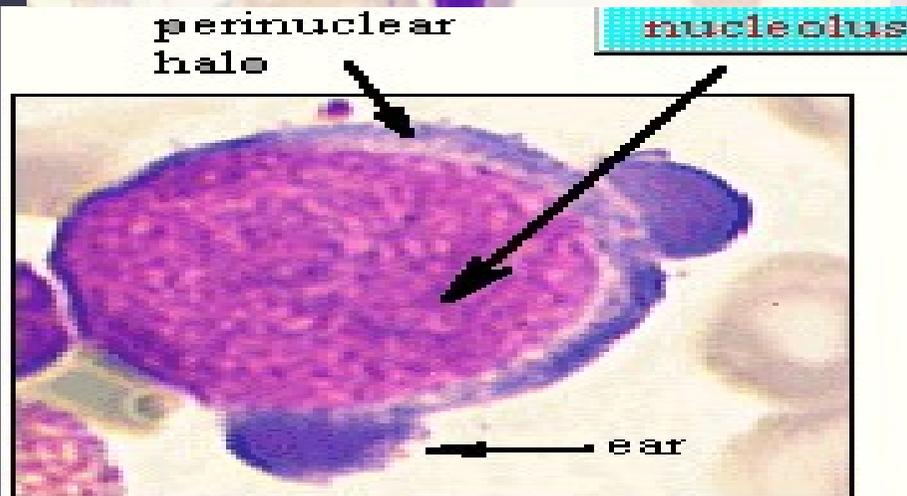
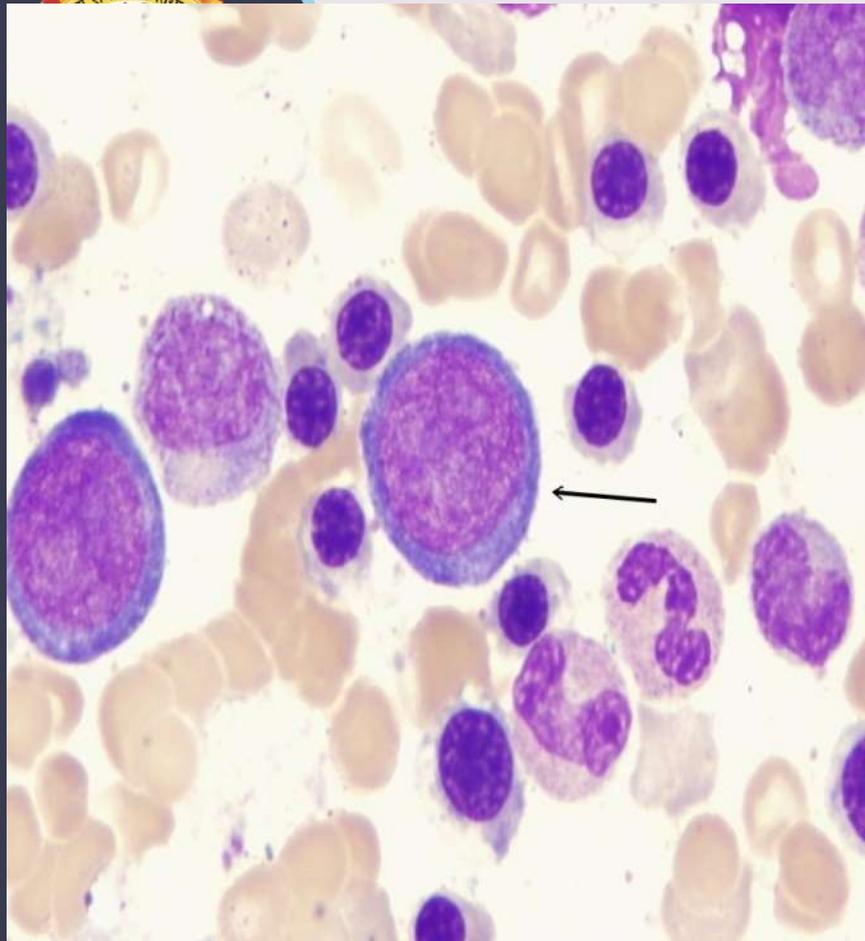
7-10 $\mu\text{m}$ - PYKNOTIC Nucleus. Extrusion, Hb is maximum.

7.3 $\mu\text{m}$ - Reticulum of basophilic material in the cytoplasm.

7.2 $\mu\text{m}$ - Mature red cell with Hb.

### 3. Proerythroblast

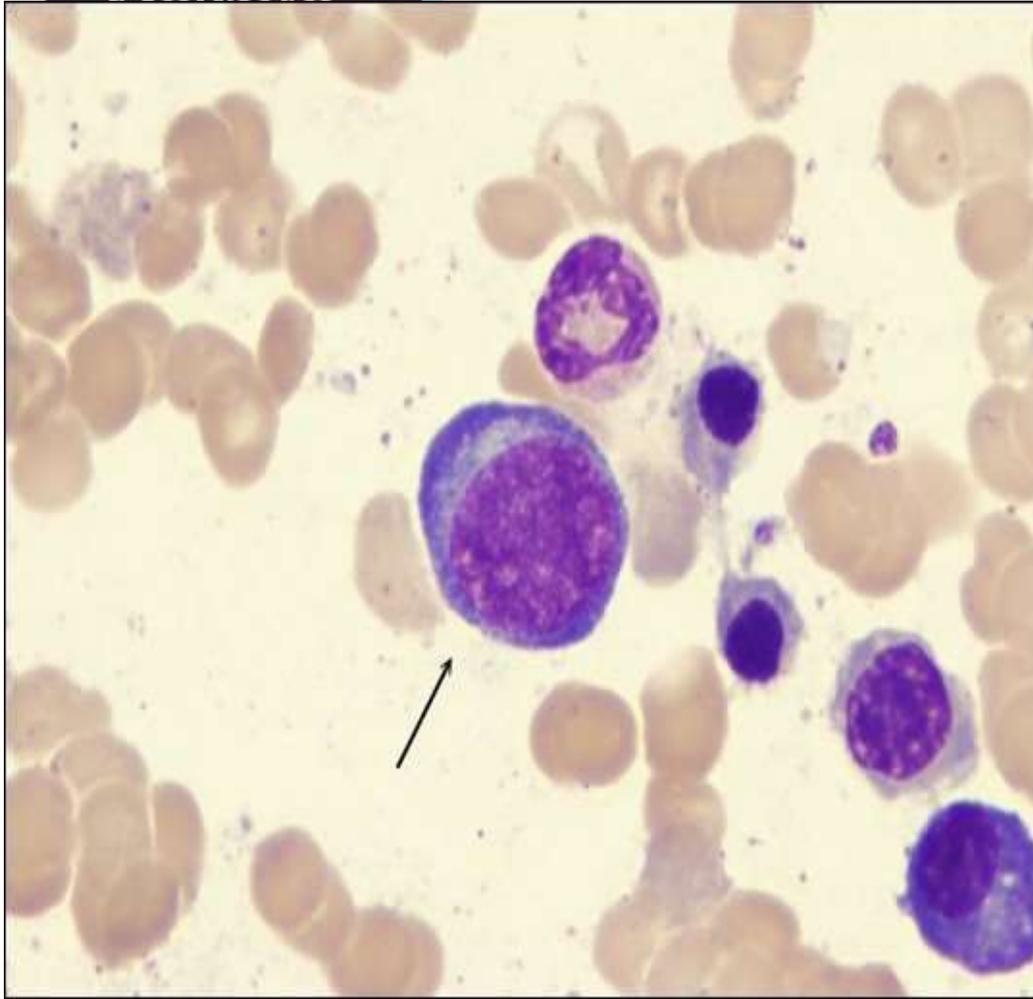
- 15-20 microns
- Nucleus with multiple nucleoli
- Basophilic cytoplasm with perinuclear halo
- No hemoglobin
- Mitosis present





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## 4. Basophilic/ early normoblast



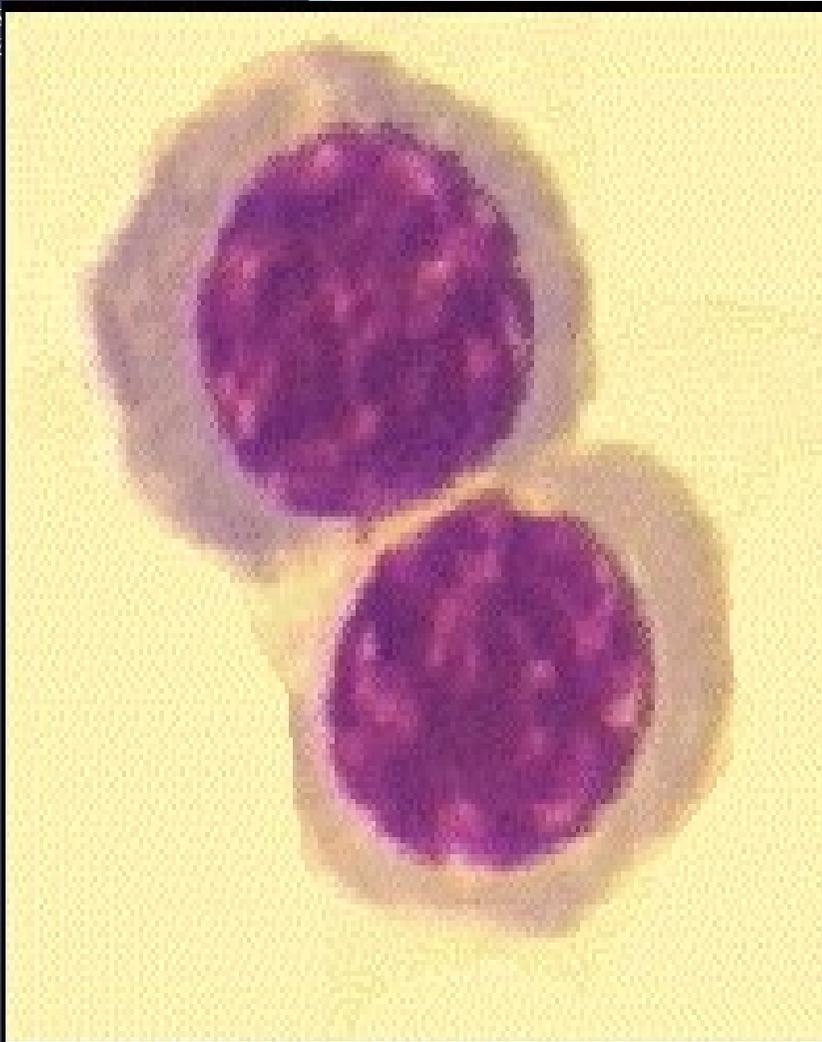
*Bone marrow aspirate smear, Wright-Giemsa stain, 1000x*

- ✓ Slight reduction in size 14-17 $\mu$ m
- ✓ Large nucleus, **nucleoli reduce in number**
- ✓ Basophilic cytoplasm
- ✓ Active mitosis



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## 5. Polychromatophilic/ intermediate normoblast

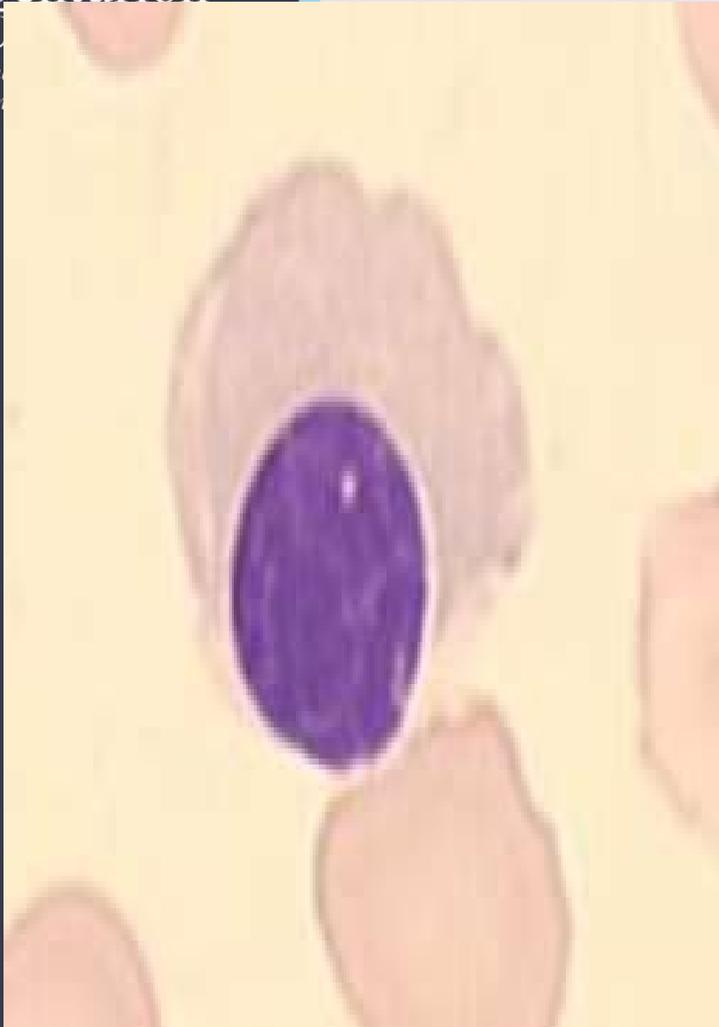


- v 10-15 $\mu$ m size
- v 'POLYCHROMASIA'
- v nucleus condenses  
Chromatin lumps
- v Hb starts appearing
- v Reduced mitoses



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## 6. Orthochromatic normoblast



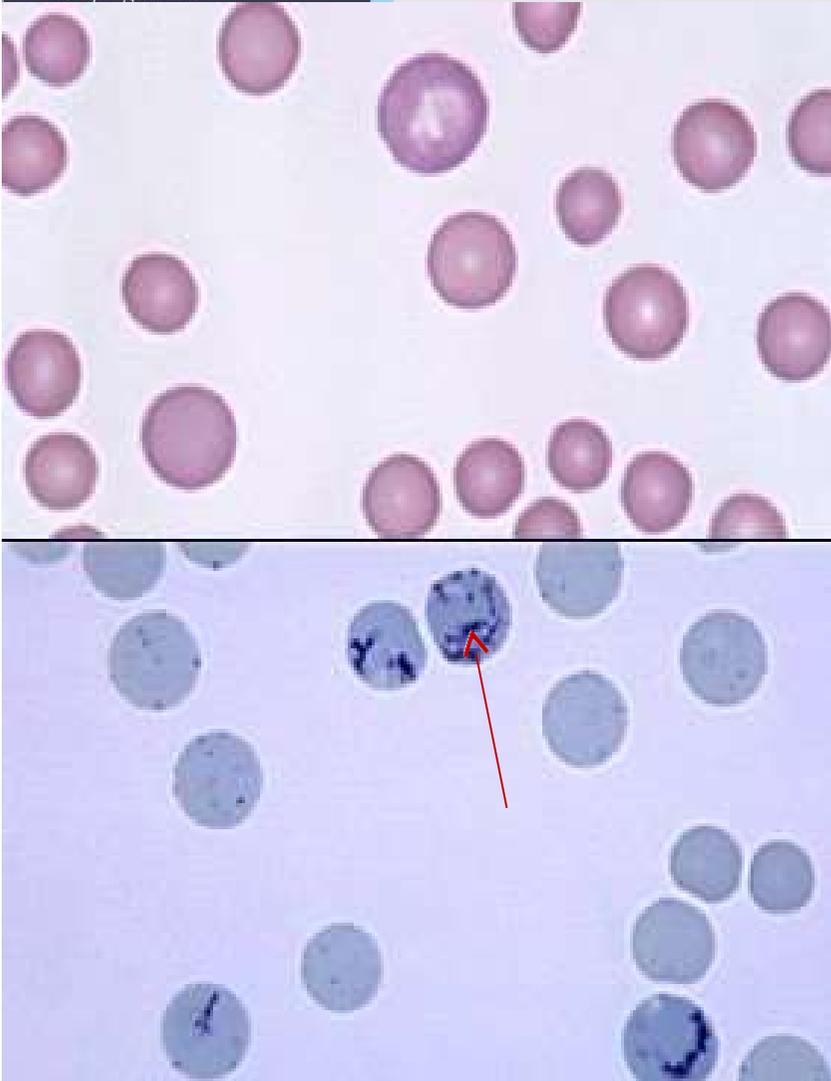
- 7-10 $\mu$ m
- Acidophilic erythroblast which is the last precursor with a nucleus.
- Nucleus is compact & situated near the membrane pyknotic nucleus is extruded
- Cytoplasm is like mature red cell, reflecting a high Hb content.
- Mitosis absent



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# 7. Reticulocyte

- ✓ Reticular nuclear fragments
- ✓ Nucleus extruded
- ✓ Slightly larger than RBCs





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# Reticulocyte



- ✓ Young erythrocytes with granular or reticular filamentous structures.
- ✓ Makes up 0.5-2% of all erythrocytes
- ✓ Vital staining required to make this visible.
- ✓ Reticulocytosis seen following hemolysis or acute blood loss

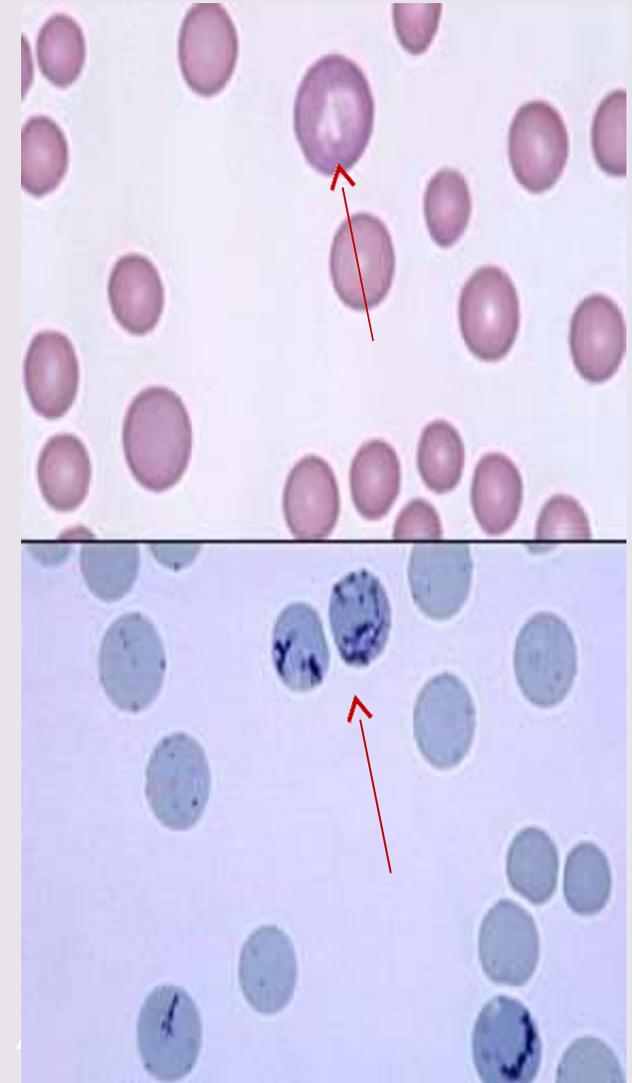


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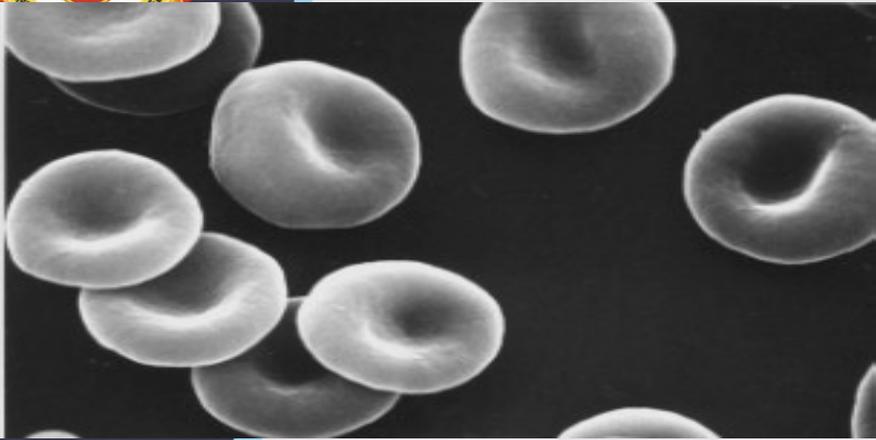
## The Reticulocyte

- θ Has no nucleus
- θ Has no organelles
- θ Is larger than the mature RBC
- θ Is not concave
- θ Has many polyribosomes
- θ In severe anemia, many of these are released into the blood prematurely ◊  
Reticulocyte response.  
Normally 1% of circulating blood are reticulocytes.





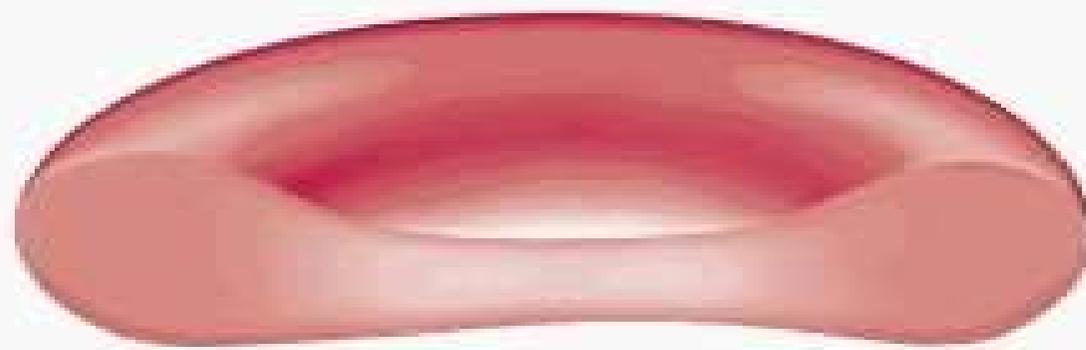
## 8. Mature erythrocyte



- Reddish, circular, biconcave cells
- 7-8  $\mu$
- No visible internal structure
- High Hb content
- Bright at centre due to biconcave shape

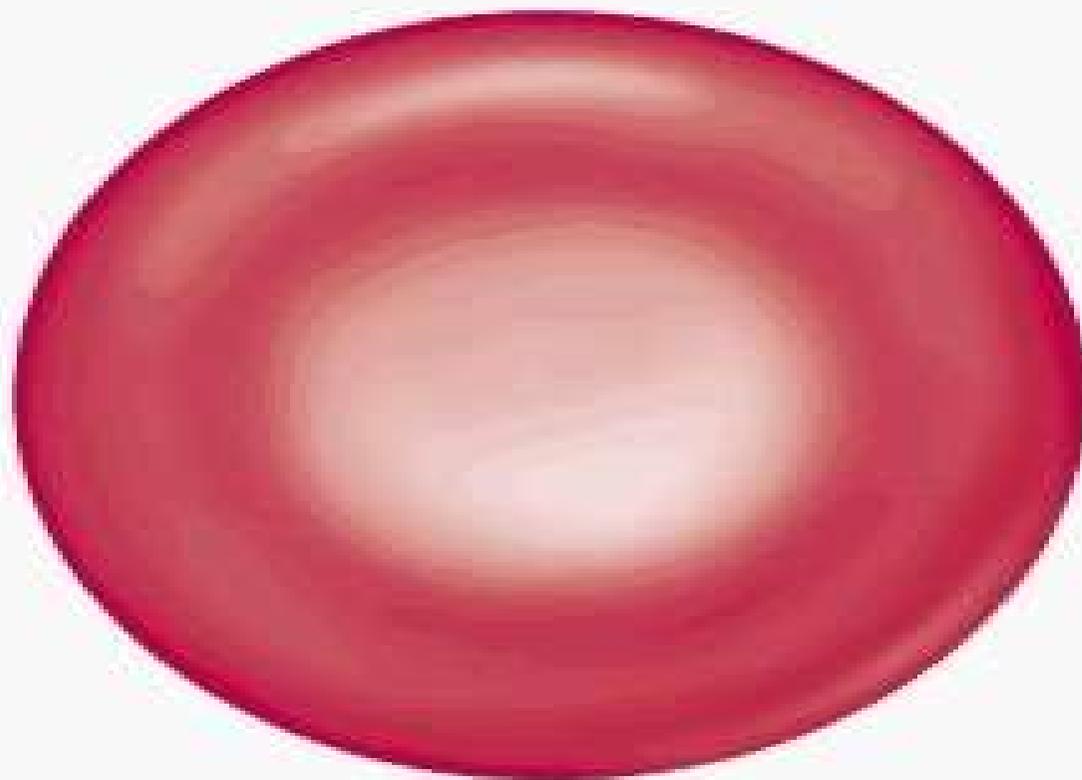


**7.2  $\mu$ m**



Side view

2.0  $\mu\text{m}$



Top view

7.5  $\mu\text{m}$



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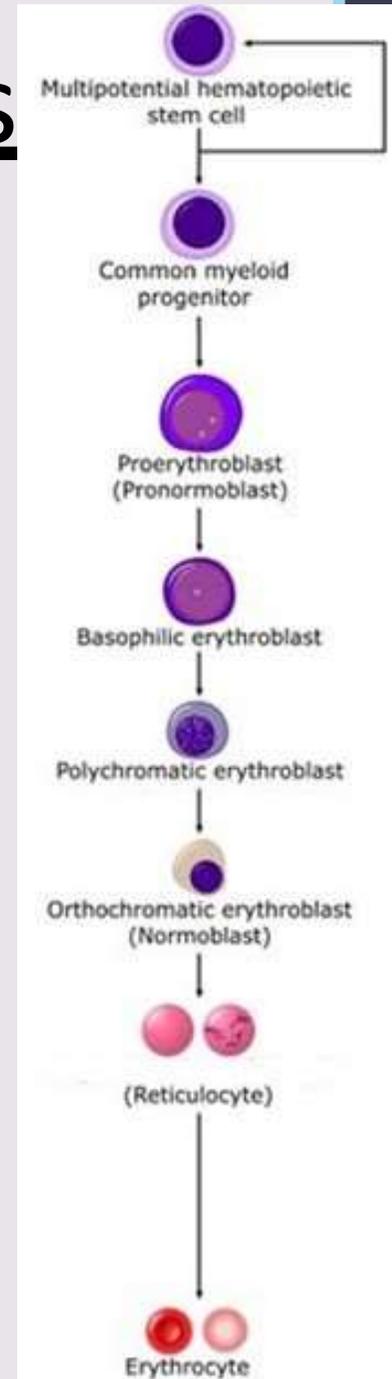
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# Duration of erythropoiesis

HSC to RBC- 21 days

Differentiation phase: from  
pronormoblast to  
reticulocyte phase- 5 days

Maturation phase: from  
reticulocyte to RBC- 2 days





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# Changes during erythropoiesis

- ⊖ Decrease in size
- ⊖ Loss of mitotic activity (later part of intermediate.normo)
- ⊖ Hemoglobinization (intermediate normoblast)
- ⊖ Change of cell shape (from globular to biconcave)
- ⊖ Disappearance of nucleus, mitochondria, RNA, etc
- ⊖ Change of staining (basophilic – eosinophilic)





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# Reticulocyte response

- ∨ Increase in reticulocyte count after treatment of anemia indicates bone marrow activity