RED BLOOD CELLS (RBCs)

- Dr. Urvashi Kapadia

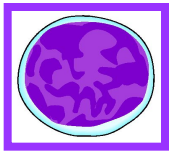
HAEMOPOIESIS

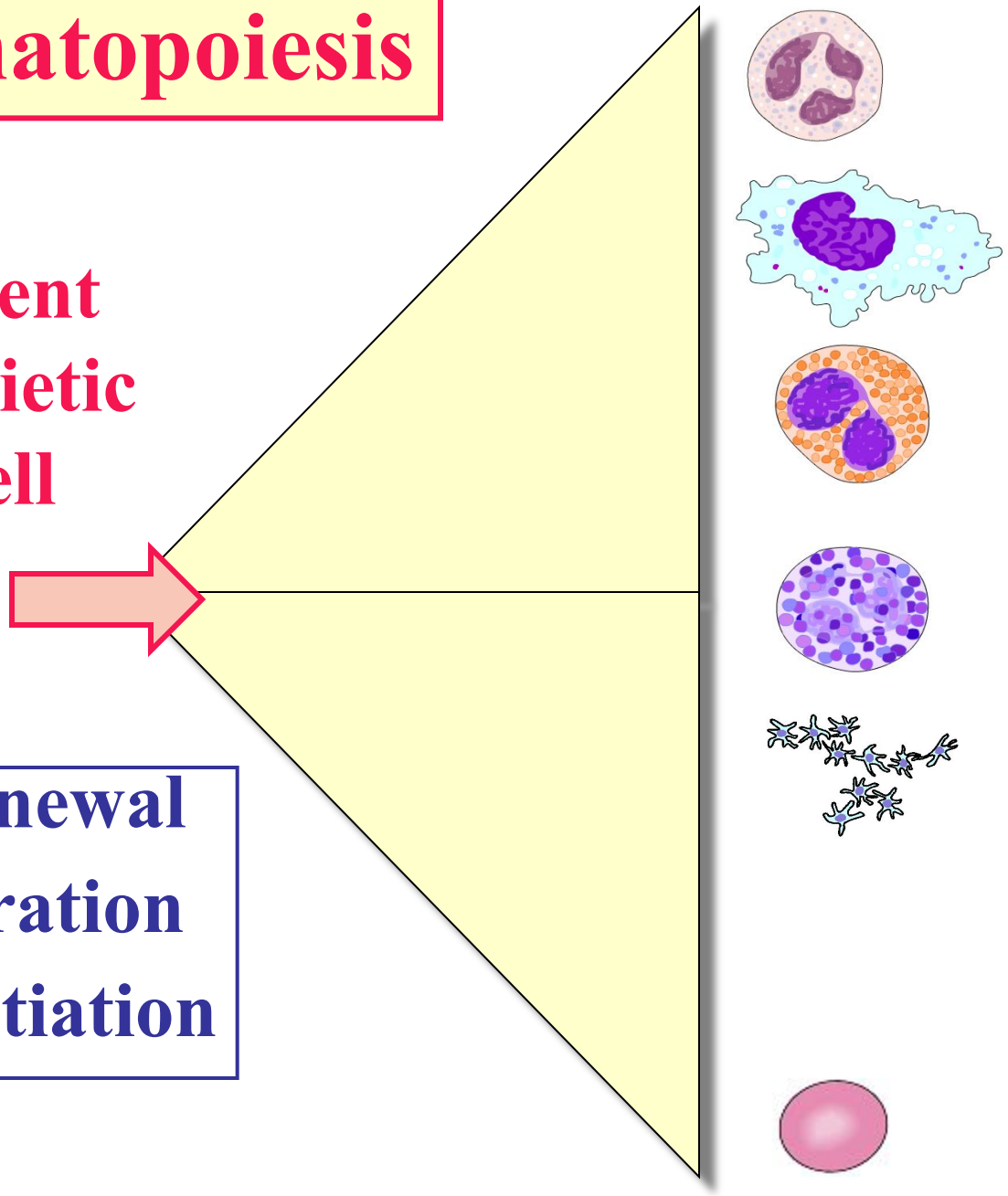
- **Origin, development & maturation of all the blood cells.**

- It includes –
  - Erythropoiesis
  - Leucopoiesis
  - Megacaryocytopoiesis
- Theories of haemopoiesis –
  - monophyletic theory
  - Polyphyletic theory

Hematopoiesis

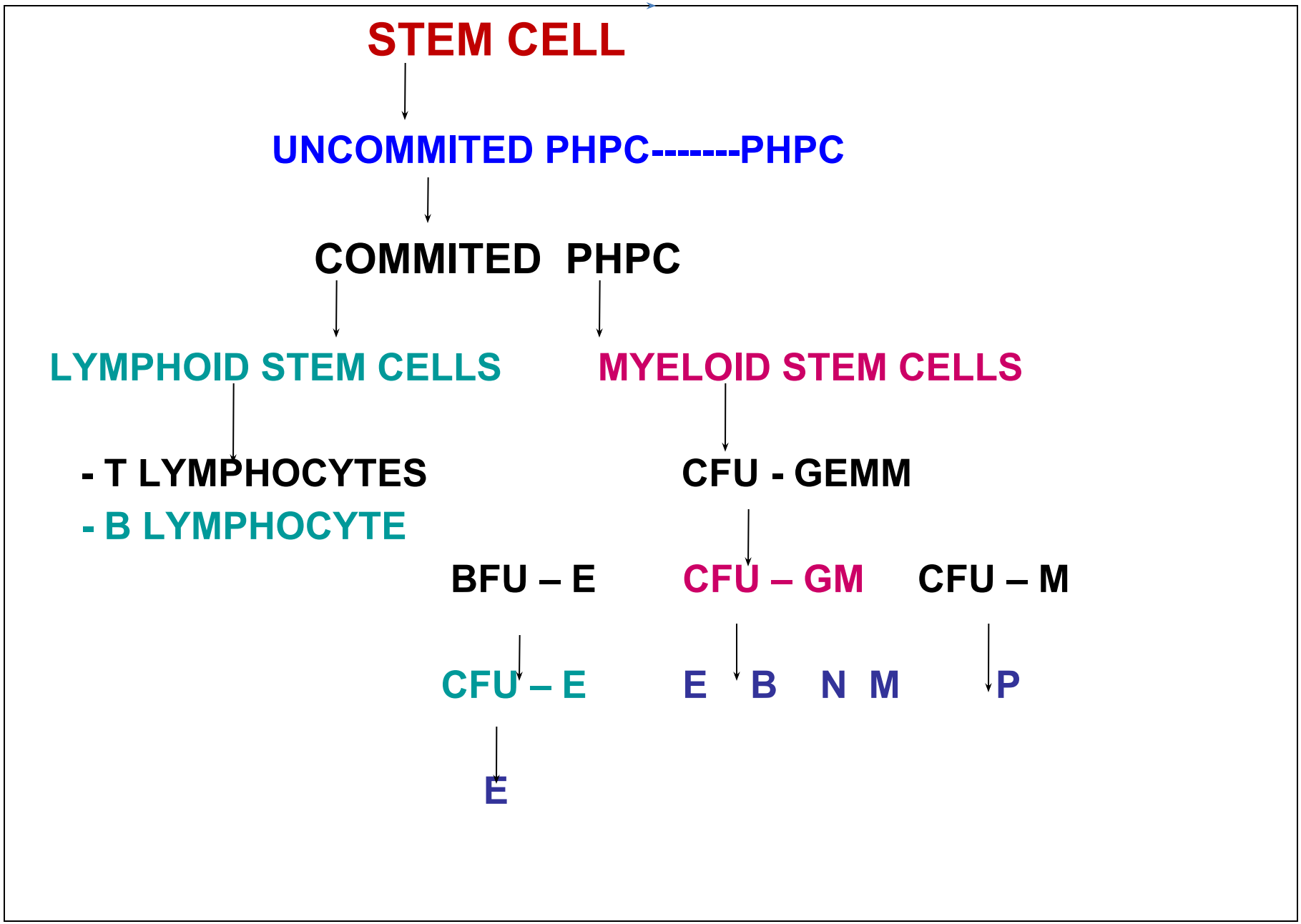
Pluri-Potent Hematopoietic Stem Cell

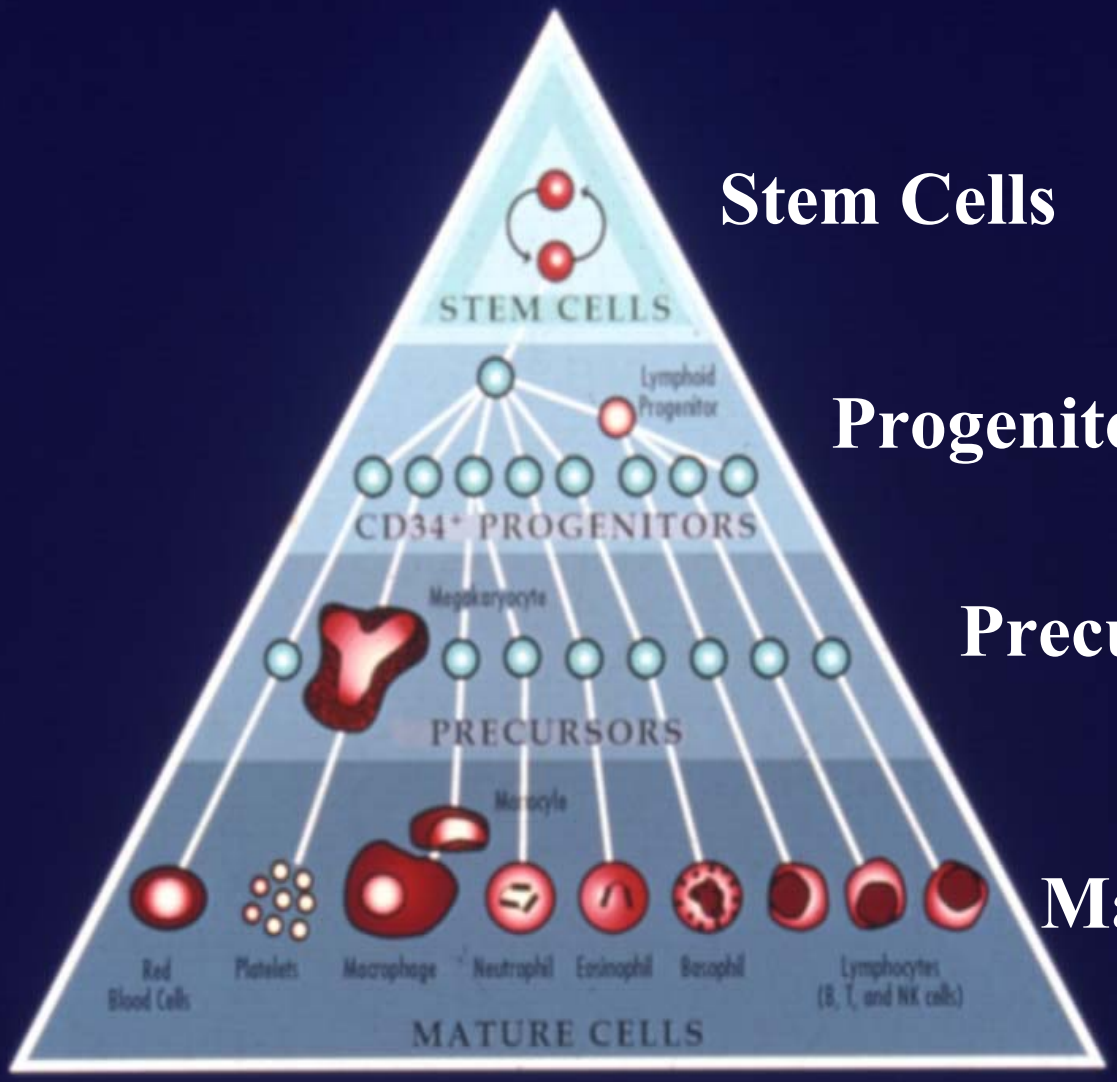
PHSC 



- Self Renewal
- Proliferation
- Differentiation

HAEMOPOIESIS





Stem Cells

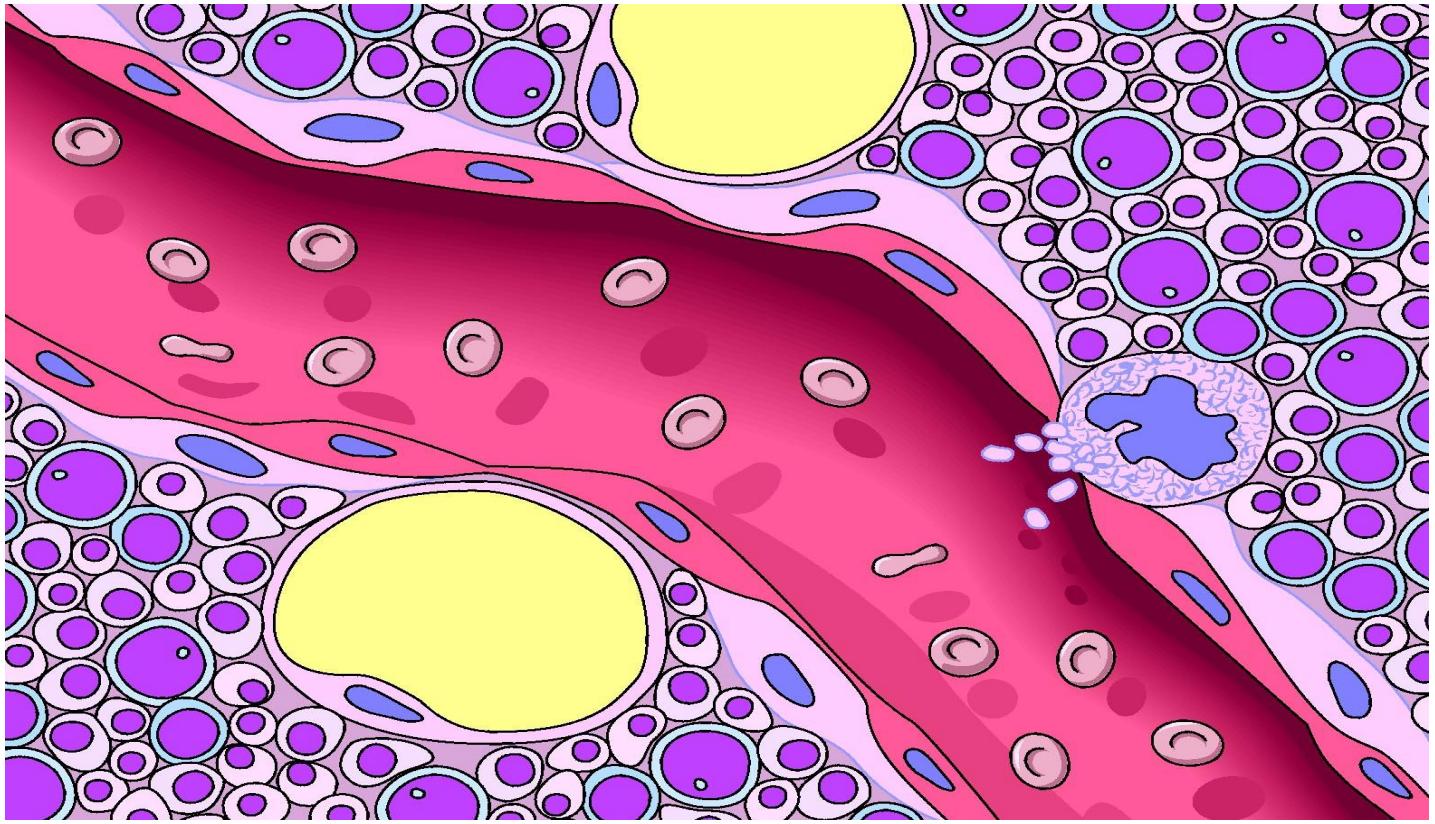
Progenitors

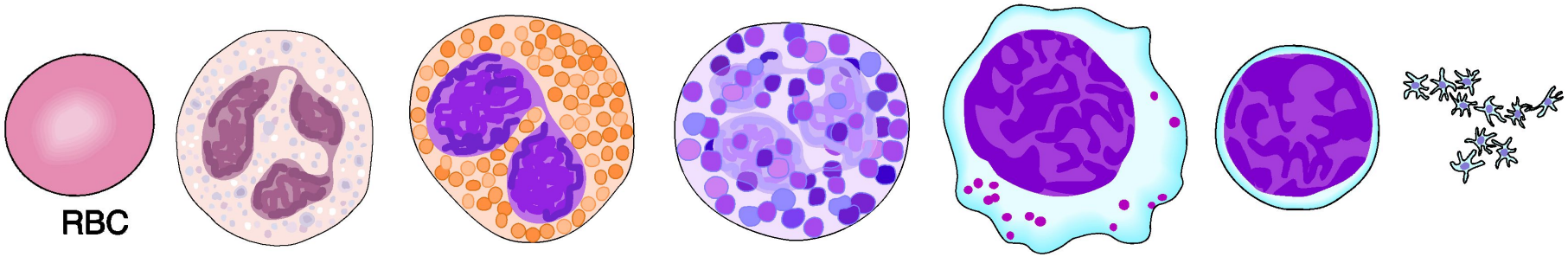
Precursors

Mature Cells

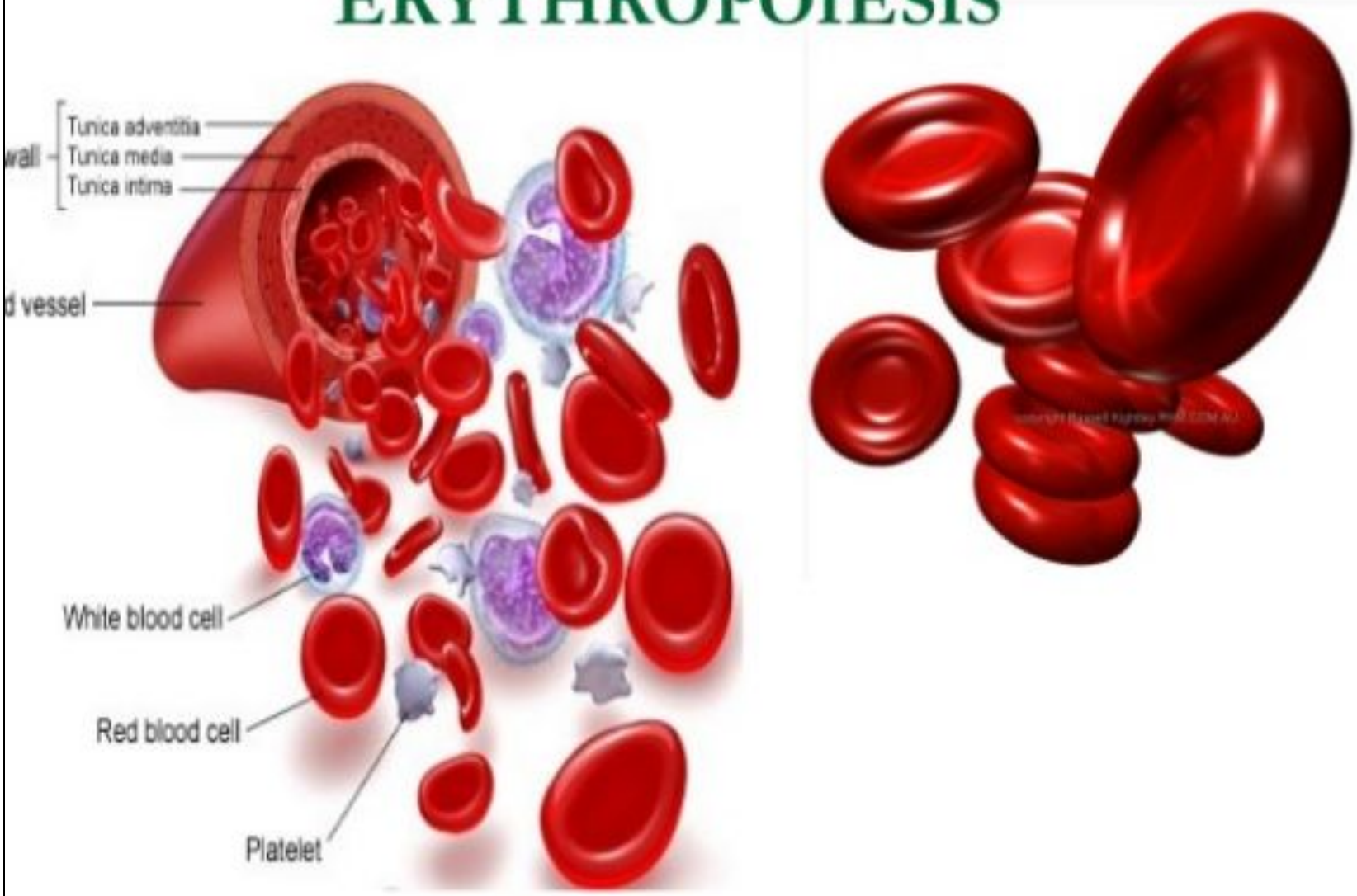
Hematopoiesis

Bone Marrow





ERYTHROPOIESIS



ERYTHROPOIESIS

- **Definition** – Origin, Development & Maturation of RBCs.
- **Sites of Erythropoiesis** –
  - a) During intrauterine life
    - 1) Mesoblastic stage
    - 2) Hepatic stage
    - 3) Myeloid stage
  - b) In children & adults
    - 1) Upto 5 – 6 yrs :- From red bone marrow of all bones
    - 2) From 6 – 20 yrs :-Red BM of long bones & membranous bones
    - 3) After 20 yrs :- Ends of the long bones & All membranous bones

Site of Erythropoiesis

Intravascular erythropoiesis

Extravascular erythropoiesis

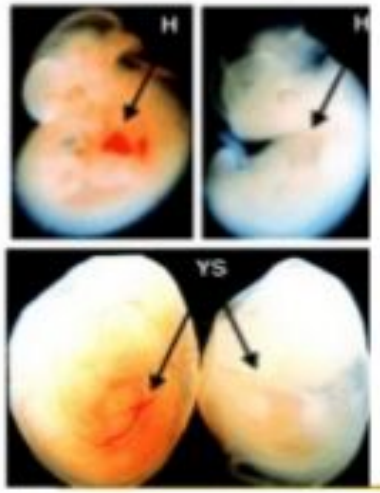
- **During intrauterine life**

  Mesoblastic stage (3rd week to 3 months)

  Hepatic stage (after 3 months)

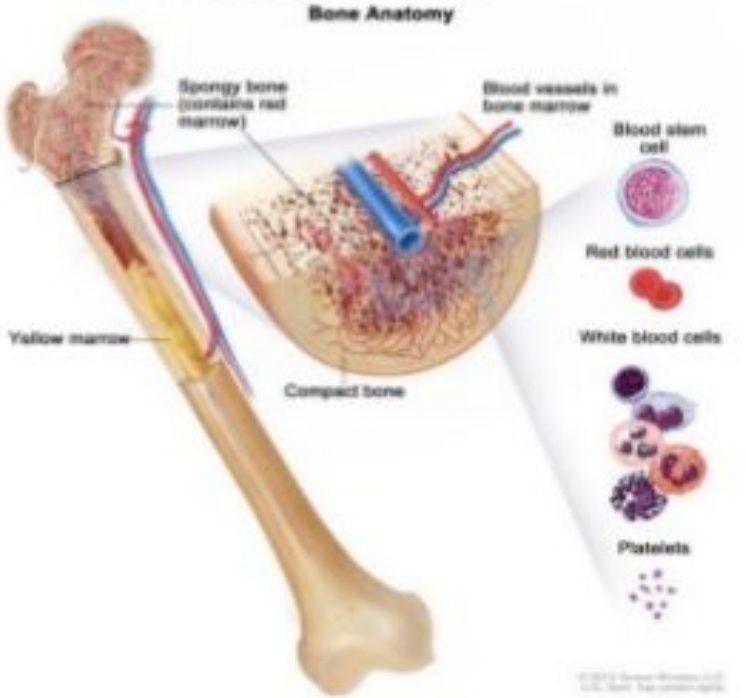
  Myeloid stage (3rd trimester)

Nucleated RBCs

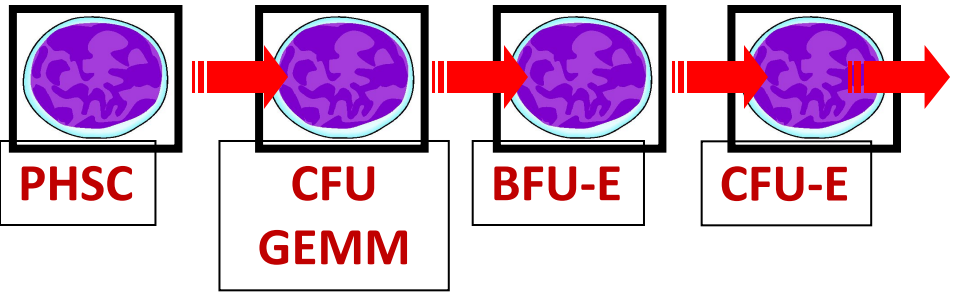


Yolk sac

Liver & spleen



Bone marrow



Erythropoiesis

Pro-Erythroblast

Early (Basophilic) normoblast

Intermediate (Polychromatophilic) normoblast

Late (Orthochromic) normoblast

Reticulocyte

Red Blood Cell

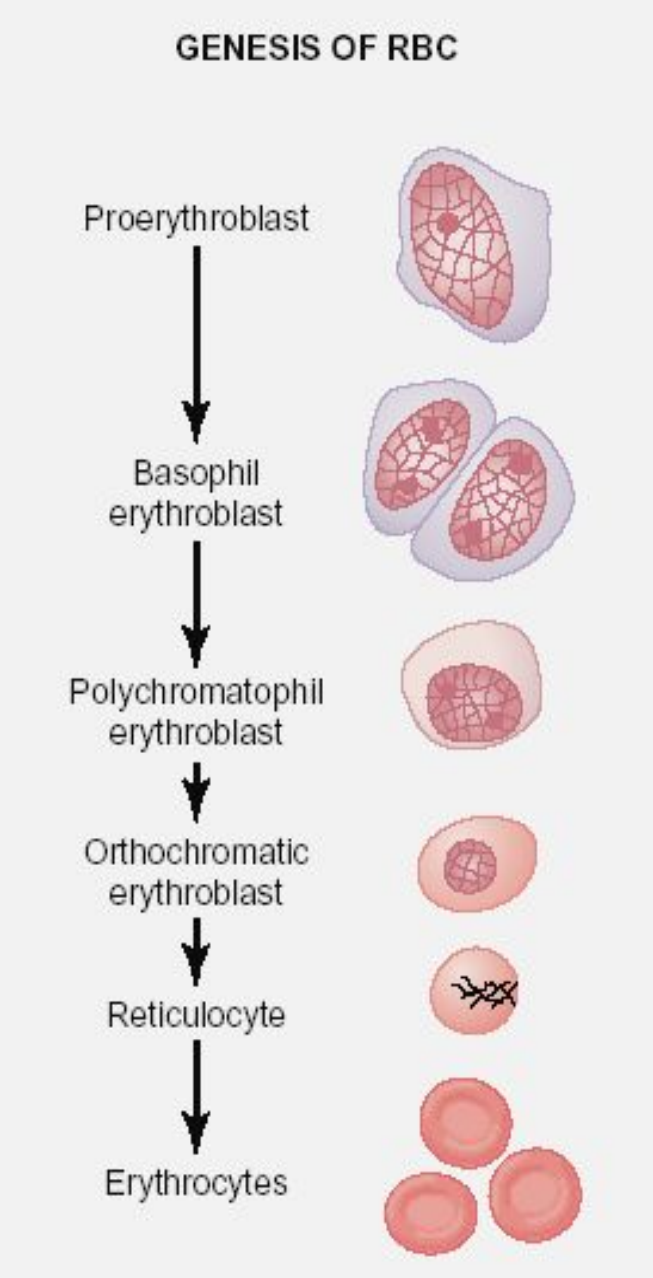
PROERYTHROBLAST First blast cell, first cell of erythrocyte series	Cell size –large,15 -20µm C. plasm- scanty, deeply basophilic. Nucleus- large,3/4 of cell, 2-3 nucleoli, chromatin open. Hb – absent Mitosis – present.
EARLY NORMOBLAST/ Basophilic Erythroblast	Cell size- decreases,14-16 µm C.plasm- increases, basophilic Nucleus- size decreases, no nucleoli, chromatin condenses Hb – absent Mitosis - present

INTERMEDIATE NORMOBLAST/ Polychromatic erythroblast	Cell size - 10-14 µm C.plasm- increases, polychromatic. Nucleus- size decreases, chromatin condenses. Hb- appears Mitosis- present
LATE NORMOBLAST/ Orthochromatic erythroblast	Cell size- 9-10µm C.plasm- increases, more acidic, less basophilic Nucleus- very small (pyknotic), Hb- increases in amount Mitosis – stops here.

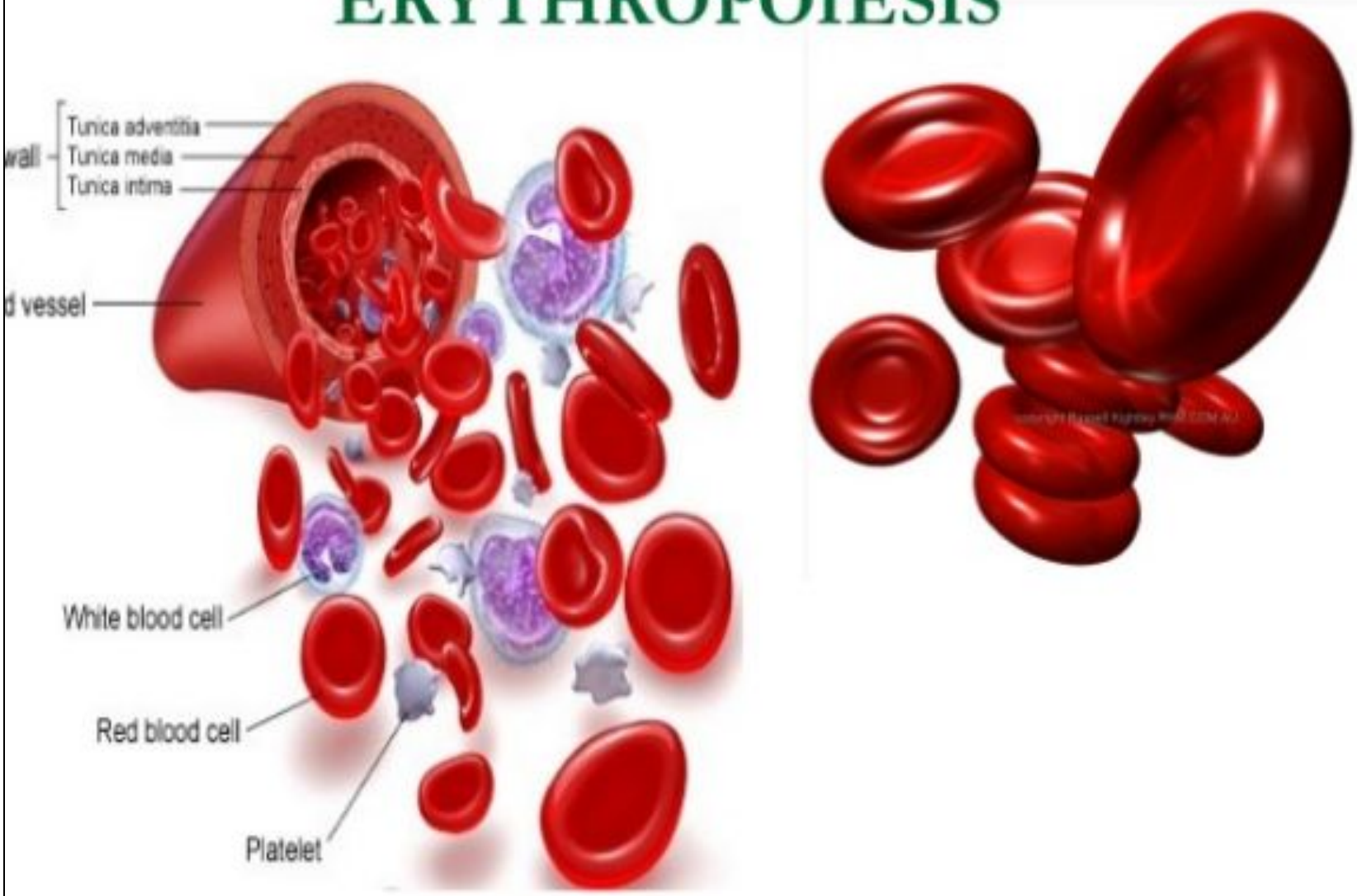
RETICULOCYTES	:Cell size- 8-9µm :C.plasm- increases, RNA present in the form of a reticulum :Nucleus- absent :Hb – increases :Mitosis - absent
ERYTROCYTES	:Cell size- 7.2 to7.4µm :C.plasm- acidophilic :Nucleus- absent :Hb – present :Mitosis - absent

Changes in the cells

- Decrease in cell size
- Size of nucleus – smaller – disappear
- Staining character – basophilic – Polychromatophilic – acidophilic
- Hb appear – intermediate stage – increase in amount till mature RBC
- Mitosis- Upto intermediate normoblast.



ERYTHROPOIESIS



Normal RBC Count

- **Importance:**
- **Must Not fall**
  - To **supply oxygen** from lungs to tissues
- **Must Not rise**
  - **Blood viscosity** may increase
  - May impede blood flow

REGULATION OF ERYTHROPOIESIS

A) General factors

1) Hypoxia - Erythropoietin
2) Thyroxine
3) Growth factors
4) Differentiation factors
5) Vitamins

B) Maturation factors

1) Vitamin B12 (extrinsic factor)
2) Castle's Intrinsic factor(I.F.)
3) Folic acid

C) Factors necessary for Hb formation

General factors

1) **Hypoxia** – Lack of O2 at tissue level

- Hypoxia ----erythropoietin ----RBC production.

- Erythropoietin - Glycoprotein

- Sources : 85% from kidney (from interstitial cells peritubular capillaries)

: 15% from liver , tissue macrophages

- Inactivation : In the liver & kidney

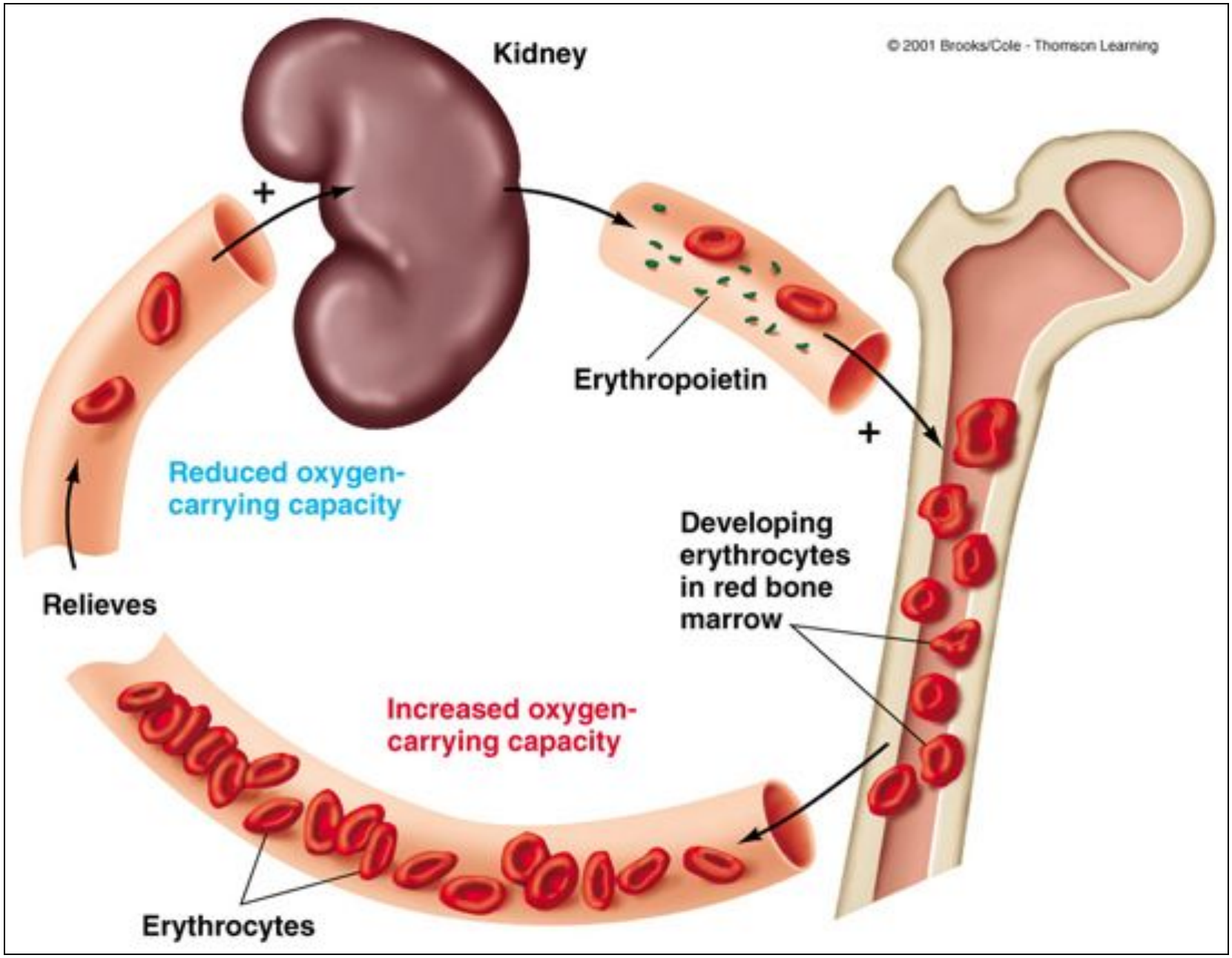
- Excretion : In urine

Mode of secretion

- Hypoxia ----------kidneys

Erythropoietin

RBC production.


Kidney
© 2001 Brooks/Cole - Thomson Learning
+
Erythropoietin
+
Reduced oxygen-carrying capacity
Relieves
Developing erythrocytes in red bone marrow
Increased oxygen-carrying capacity
Erythrocytes

- Actions of Erythropoietin

1) Early differentiatiion of stem cells into proerythroblast -------- mature RBC.

2) Increases release of reticulocytes from the BM.

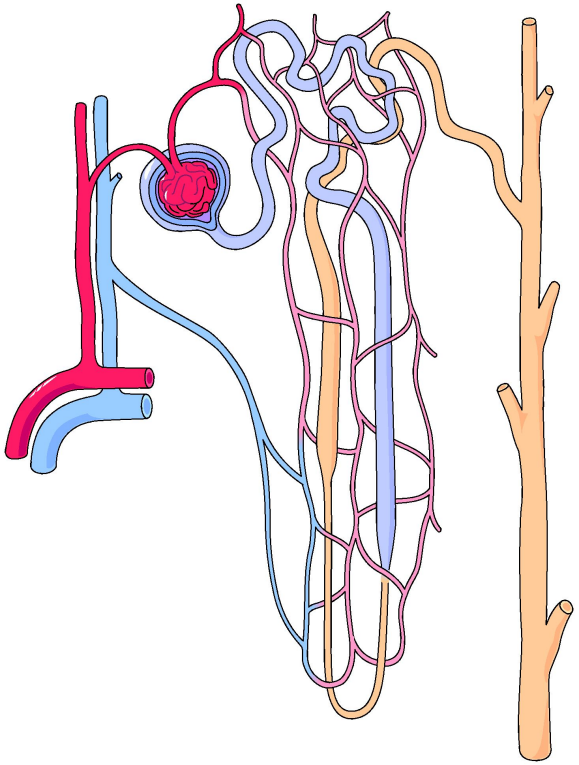
3) Increases synthesis of RNA ,DNA, globin, ferritin. which increases Hb synthesis in normoblasts.

Erythropoietin

Glycoprotein, MW:34,000

Production

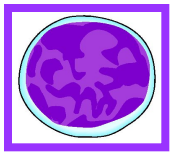
Kidney



Actions

Proerythroblast Formation

Shortens the Maturation Time



Tissue Oxygenation – Most Important Regulator of Erythropoiesis

- **ANY CONDITION** → Decrease Tissue Oxygenation → **Increase Erythropoiesis**
- **Anemia**

  Immediately → **Increase** RBCs production
- **Bone marrow destruction**:

  Hyperplasia of remaining cells

  Increase **production of RBCs** →

- **High altitudes:**
  - Partial pressure of **oxygen in air less**
  - **Decrease** in **oxygen transport** to tissues
  - **Tissue hypoxia**
  - **Result?**
- **Cardiac Failure**
  - **Inefficient pumping by heart**
  - Decreased blood flow to peripheral vessels
  - **Tissue hypoxia**
  - **Result?**

- **Lung diseases:**
  - **Failure of oxygen absorption** in Lungs
  - Blood carries less Oxygen
  - **Tissue hypoxia**
  - **Result?**
- *All conditions have one common problem*

- **HYPOXIA**

Factors affecting Ep production

- Increase :

1) Hypoxia
2) cAMP, NAD, NADP
3) Vasoconstrictors
4) Hemolysates
5) Hormones
   - Thyroxine
   - Ant. Pit. Hormones
   - Androgens

- Decrease

1) Oestrogen
2) Renal diseases
3) Protein deficiency
4) Liver diseases

General factors

2) Thyroxine

3) Growth factors & Differentiation factors

- a) Interleukins – IL – 1, 3 ,6.
- b) GM – CSF : Colony stimulating factor

4) Vitamins – B, C, D, E.

REGULATION OF ERYTHROPOIESIS

A) General factors

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C) Factors necessary for Hb formation

Essential for

Vitamin B12

"AKA"

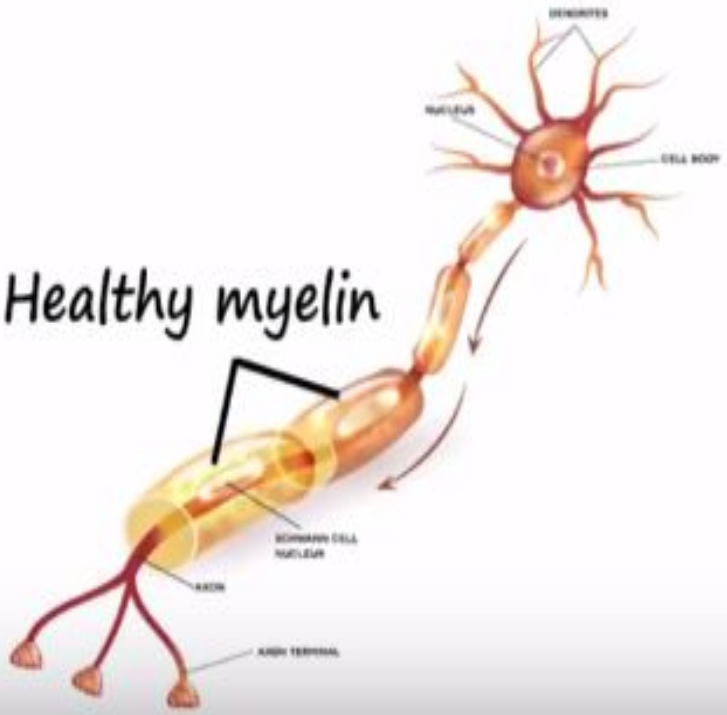
Cobalamin

DNA

Synthesis

Nuclear maturation

Healthy myelin



Maturation factors

1) Vitamin B12 – (Extrinsic factor)

- Functions :

a) Helps in maturation of RBCs.

(conversion of pro erythroblasts-----mature RBC)

b) They are essential for the synthesis of DNA.

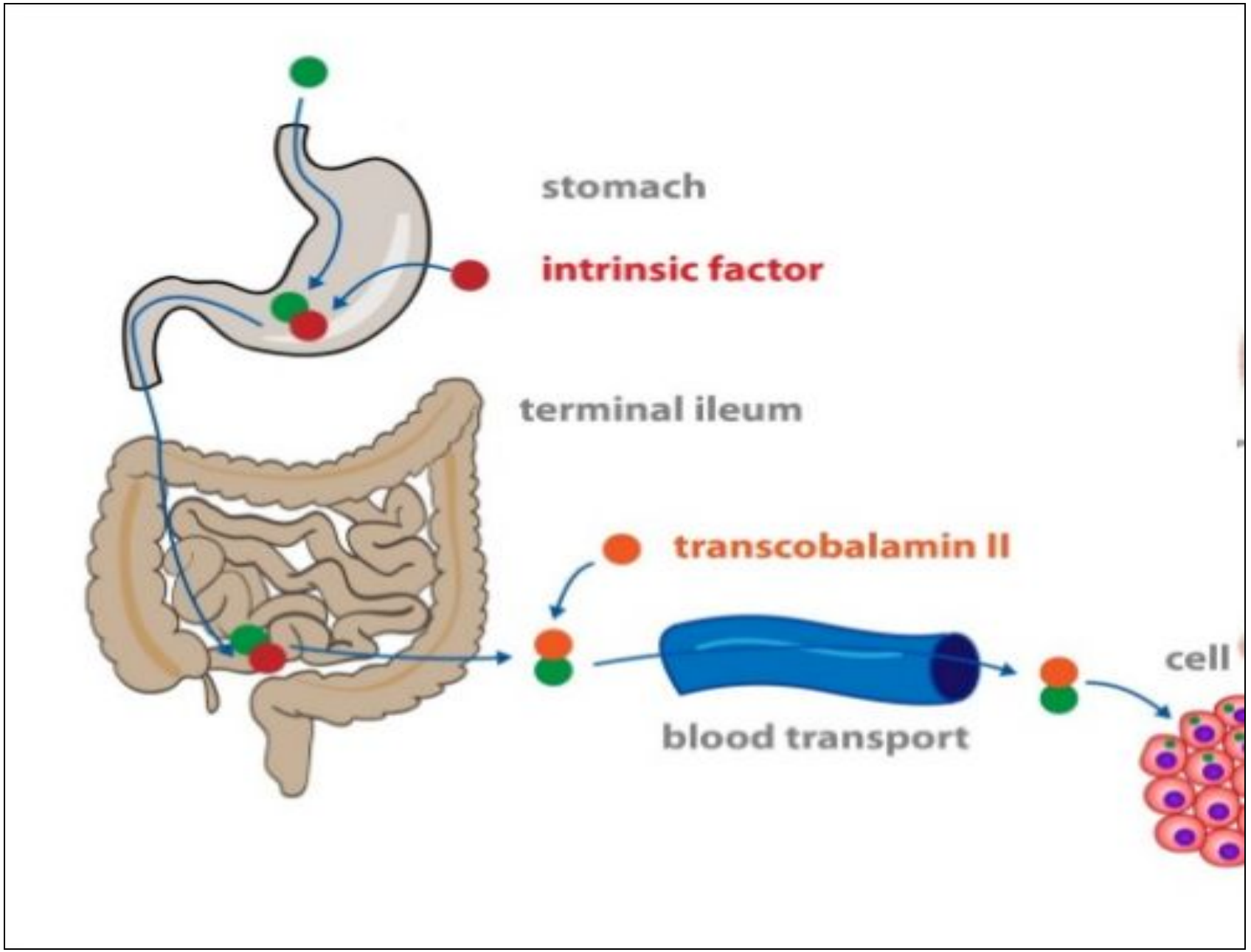
c) Increases WBC & platelet count.

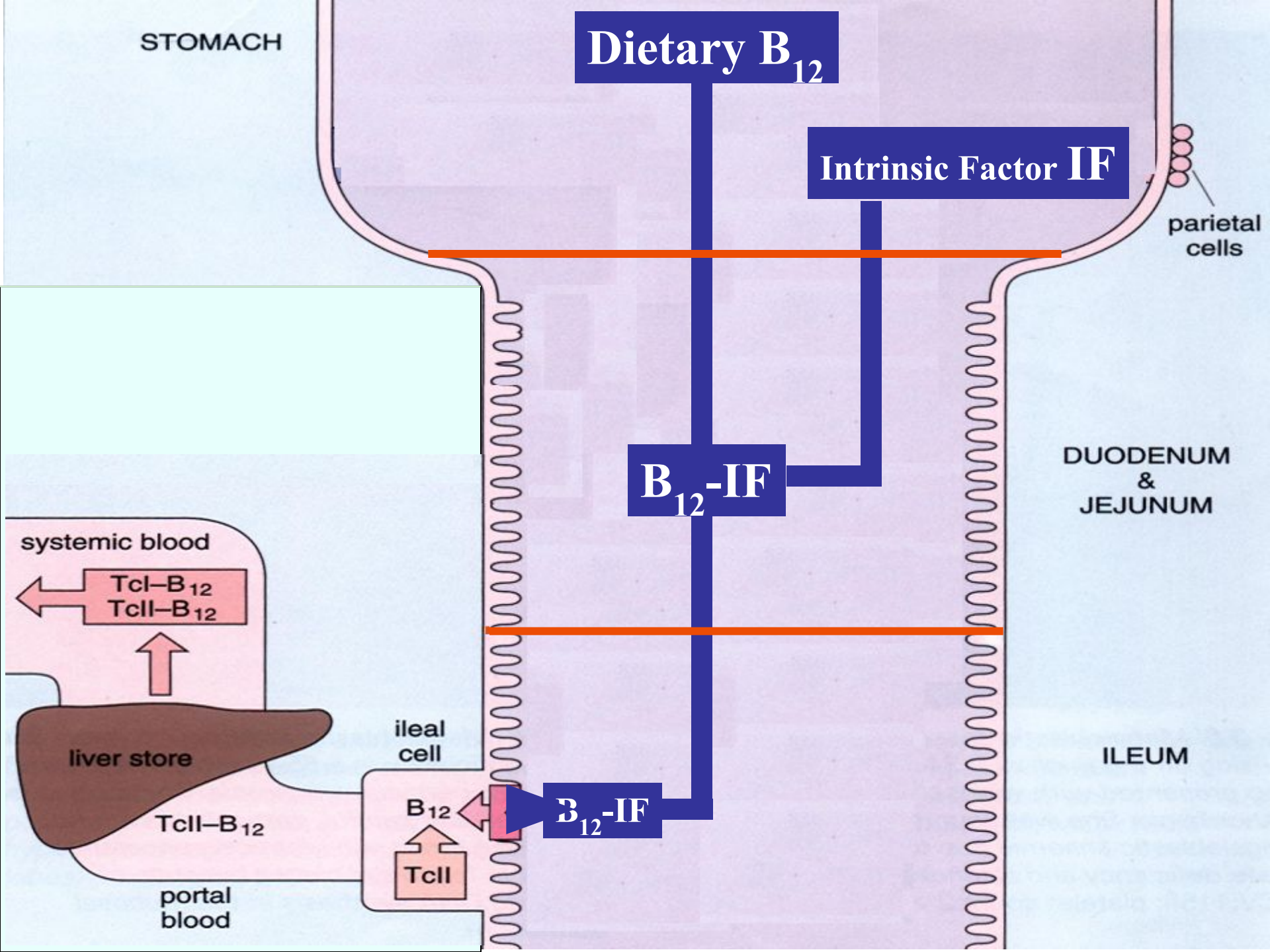
d) Maintains normal activity of CNS.

e) Helps in myelination of nerve fibres.

Vitamin B12 Deficiency

- Vitamin B12 deficiency ------
- Decrease DNA synthesis
- Failure of nuclear maturation & division
- Slow reproduction of cells & abnormality of DNA
- Formation of large cells, cell membrane fragility
- Maturation failure ---- Megaloblastic anemia


stomach
intrinsic factor
terminal ileum
transcobalamin II
cell
blood transport


STOMACH
Dietary B_{12}
Intrinsic Factor IF
parietal cells
B_{12}-IF
DUODENUM & JEJUNUM
systemic blood
TcI–B_{12}
TcII–B_{12}
liver store
TcII–B_{12}
portal blood
ileal cell
B_{12}
TcII
B_{12}-IF
ILEUM

2) Castle's Intrinsic factor (I. F.)

- I.F. with B12 forms haematinic principle which

  helps in maturation of RBC.
- Deficiency of I.F. ----------Loss of vit.B12 due to

  a) Failure of its absorption

  b) Digestive enzyme action

  - Megaloblastic anemia

    or

    Macrocytic anemia

3) Folic acid

- Factors necessary for Hb synthesis

1) **First class proteins & amino acids**
   - For protein part of Hb , globin.

2) **Iron** –For formation of heme part.

3) **Copper** – For absorption of iron from GIT.

4) **Cobalt & nickel** – For utilization of iron.

5) **Vitamins** – Vit. C, riboflavin, nicotinic acid, pyridoxine.

Haemoglobin

- Definition
- Structure
- Synthesis
- Normal values
- Clinically 14.8 gm% Hb is regarded as 100%.
- O2 carrying capacity
  - 1 gm% Hb carries 1.34 ml O2.
  - In males = 21 ml%
  - In females = 18 ml%
- Catabolism of Hb.