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LEARNING OBJECTIVES

- To know the factors required for the RBC synthesis and maturation
- To know about the secretion, functions and regulation of Erythropoietin
- To identify the conditions in which recombinant erythropoietin is used
- To know other factors necessary for the development and maturation of RBC and Haemoglobin

REGULATION OF ERYTHROPOIESIS

- **General factors**
  - Hypoxia → ***Erythropoietin***
  - Growth inducers
  - Vitamins
- **Maturation factors**
  - Vitamin B 12
  - Folic acid
- **Factors necessary for hemoglobin production**
  - Vitamin C →Helps in iron absorption (Fe+++ → Fe++)
  - Proteins → Amino Acids for globin synthesis
  - Iron & copper → Heme synthesis
  - calcium, bile salts, cobalt & nickel.

GENERAL FACTORS.

- Optimum levels of hormone **Erythropoietin** & efficient feedback mechanism controlling erythropoietin.

ERYTHROPOIETIN

A hormone which is needed for Erythrogenesis

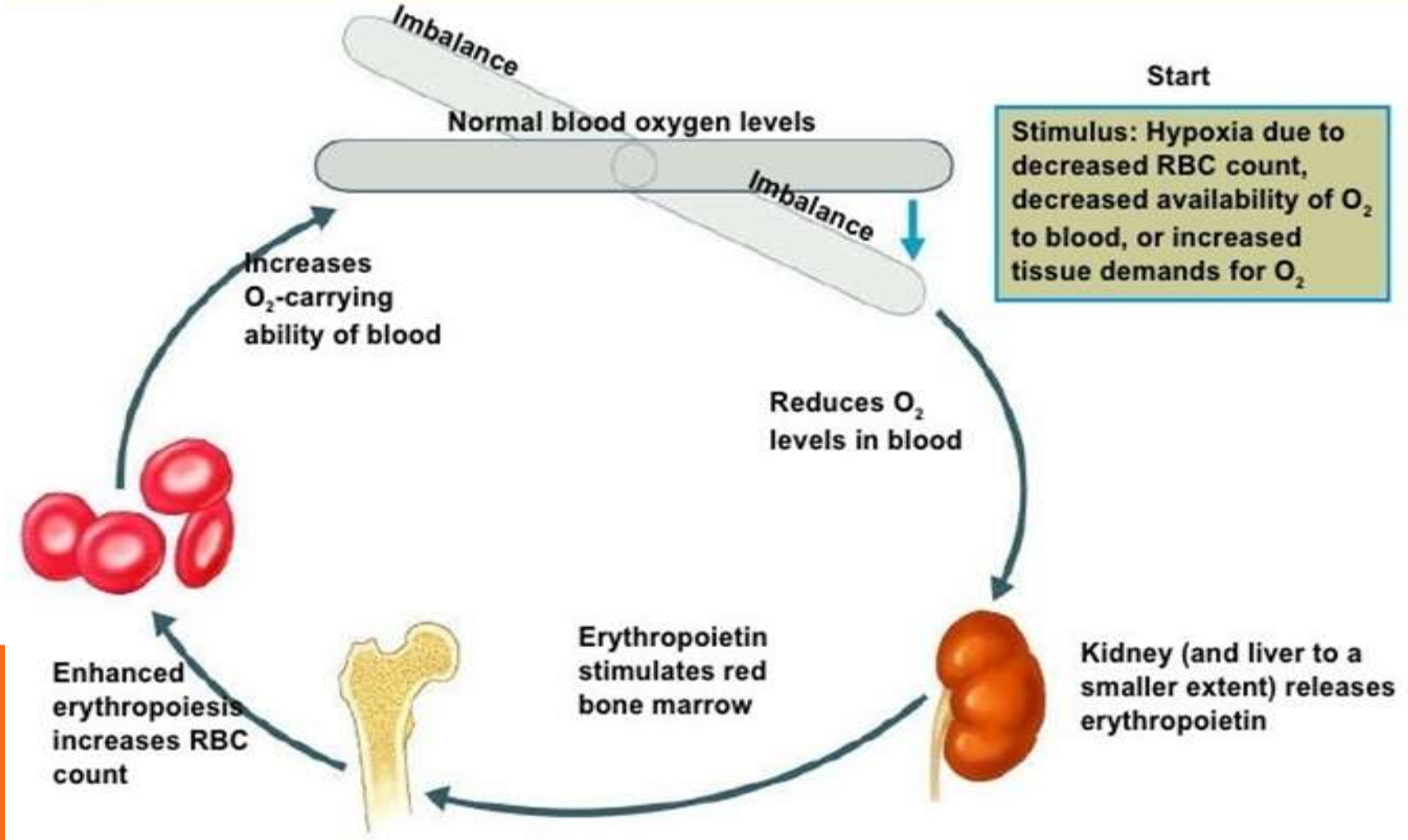
SOURCES OF ERYTHROPOIETIN

- **Erythropoietin** – Glycoprotein with molecular wt 34000.
- **Site of formation-**
  - **90% - epithelial linings and fibroblasts of peritubular capillaries.**
  - **10% - liver & cells of tissue macrophage system. (Kupffer cells) ,**
  - **Fetal liver produce more EPO than kidneys, but in adult kidney production is more**
- **Breakdown**
  - **In liver. Half life is 5 hours**

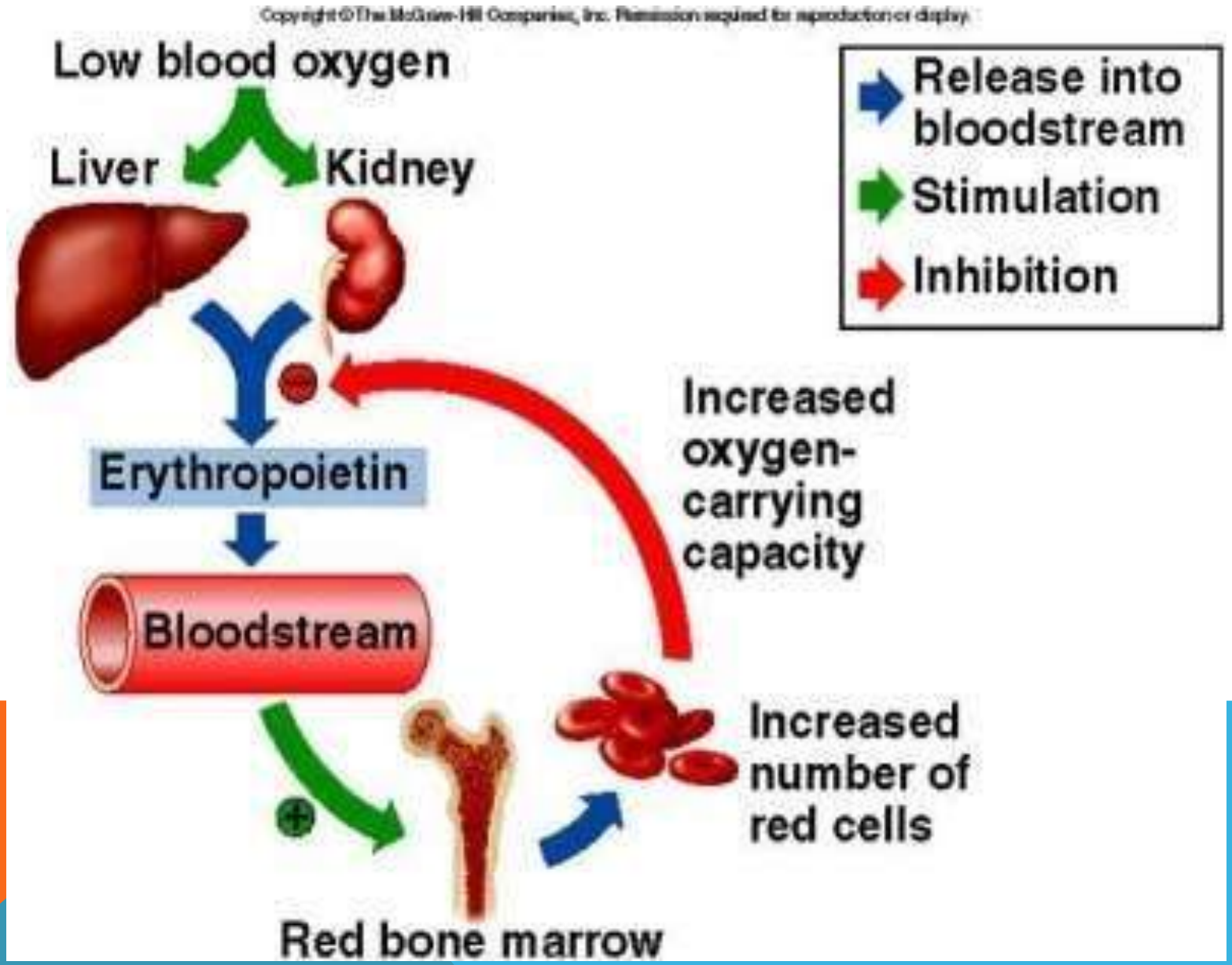
THEORY ERYTHROPOIETIN FORMATION

- **Mainly hypoxia** – is a stimulus for secretion of erythropoietin
- Which causes release of Renal Erythropoietic Factor – *(hypoxic inducible factor-1)*
- Which transcript *hypoxia inducible gene-*
- This binds to hypoxia response element on *erythropoietin gene*
- Inducing transcription of *mRNA*
- form ***Erythropoietin***

Erythropoietin Mechanism



CIRCULATION OF ERYTHROPOIETIN

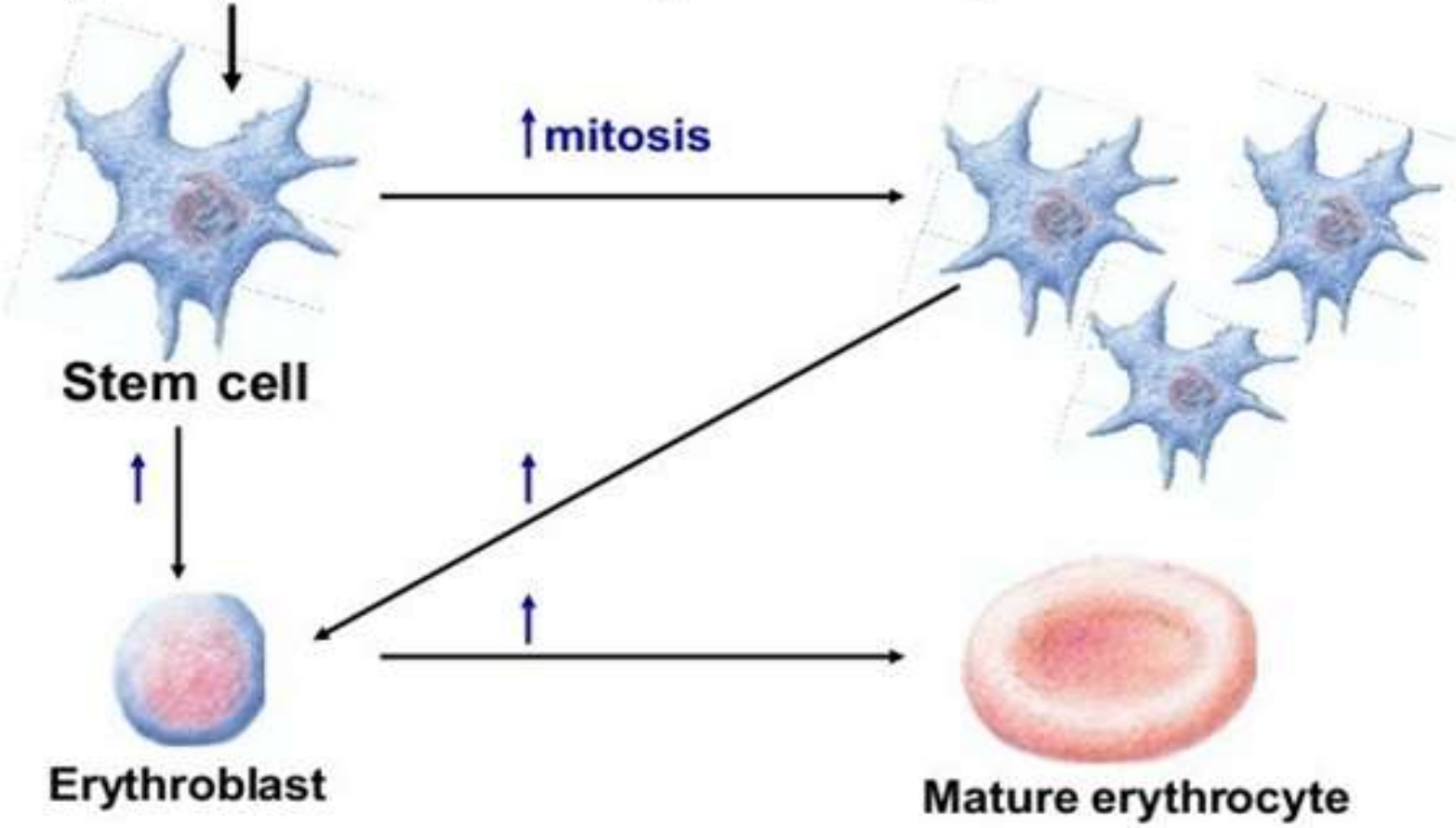


ERYTHROPOIETIN FUNCTIONS

- Main effect on stem cells – in bone marrow is differentiation
- Promotes every stage of RBC synthesis
- Promote Hb synthesis
- Promotes release of RBC from Bone Marrow to Peripheral Circulation.

Mechanism of action:

Erythropoietin acts on specific receptors on stem cells



Erythropoietin causing speeding up of all the stages of development of proerythroblasts into mature erythrocytes

ERYTHROPOIETIN (EPO) FACTS

- Erythropoietin (EPO) is a hormone produced by the kidney in response to Hypoxia (low Oxygen)
- Erythropoietin promotes the formation of red blood cells by the bone marrow.
- The erythropoietin hormone level can be detected and measured in the blood (the EPO test).

  Normal level = 4 to 24 mu/ml

ERYTHROPOIETIN (EPO) FACTS

- Measurement of the blood erythropoietin level can be used to detect ***certain medical conditions.***
- Erythropoietin can be synthesized and used as a treatment of some forms of anemia.
- Erythropoietin has been misused as a performance- enhancing drug by some athletes.

REGULATION OF ERYTHROPOIETIN

Stimuli for production

- **Hypoxia**
- **Products of RBC destruction**
- **High altitude**
- **Anemia**
- **Chronic lung or heart diseases**
- **Catecholamines**
- **Prostaglandins**
- **Androgens**

Inhibition

- Blood transfusion

FACTORS AFFECTING ERYTHROPOIETIN

- **Increase secretion**
  - Hormones – Androgen , Thyroxine, GH, ACTH, Prolactin, Adrenocortical Steroids.
  - Haemolysates – products of RBC destruction.
  - Nucleotides – cAMP, NAD, NADP
  - Vasoconstrictor drugs – that causes renal hypoxia
- **Decrease secretion.**
  - Adenosine antagonists – Theophylline.
  - Oestrogen – decreases synthesis of Globin & depressing erythropoietic response to hypoxia

CLINICAL USES OF ERYTHROPOIETIN

Uses of erythropoietin may include treatment of anemia related to

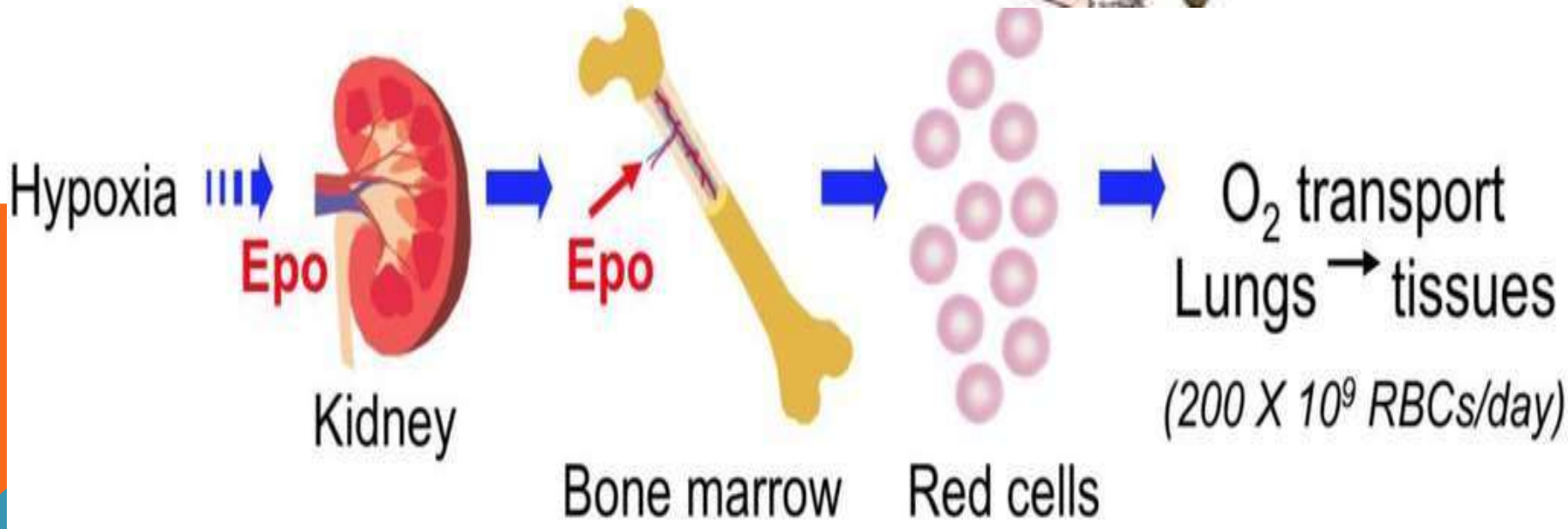
- *Chronic Renal Failure*
- *During medication in AIDS*
- *During chemotherapy, anemia caused by dysfunctional bone marrow (where the blood cells are made), and*
- *Anemia associated with cancer*

CHRONIC RENAL FAILURE (CRF)

- RENAL INSUFFICIENCY -

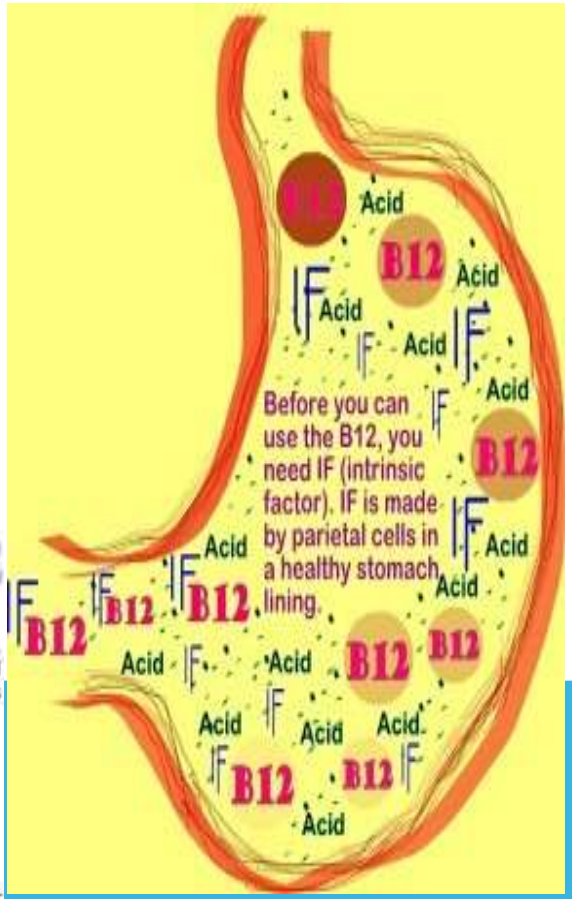
- Headaches
- ↓ Ability to Concentrate Urine
- Polyuria → Oliguria
- ↑ BUN & Serum Creatinine

- Edema
- GFR - progressively decreases from 90 to 30 ml/min
- Mild Anemia
- ↑ BP
- Weakness & Fatigue



SPECIAL MATURATION FACTORS.

- Vit B 12 (extrinsic factor)
- Folic acid
- Intrinsic factor of Castle.



VIT B 12 (EXTRINSIC FACTOR)

- **Vit B12 – Cyanocobalamin or extrinsic factor.**
- **Daily need** – 1-2 µg.
- **Sources** – Milk, Meat, Liver of Animals
  - Also synthesized by bacterial Flora.

VIT B 12 (EXTRINSIC FACTOR)

- **ABSORPTION** – need Intrinsic Factor Of Castle , a glycoprotein secreted by parietal cells of gastric mucosa.
- With it form **Intrinsic Factor- Cyanocobalamin complex**
- Bound to sp receptors in ileum & absorbed by **Endocytosis.**

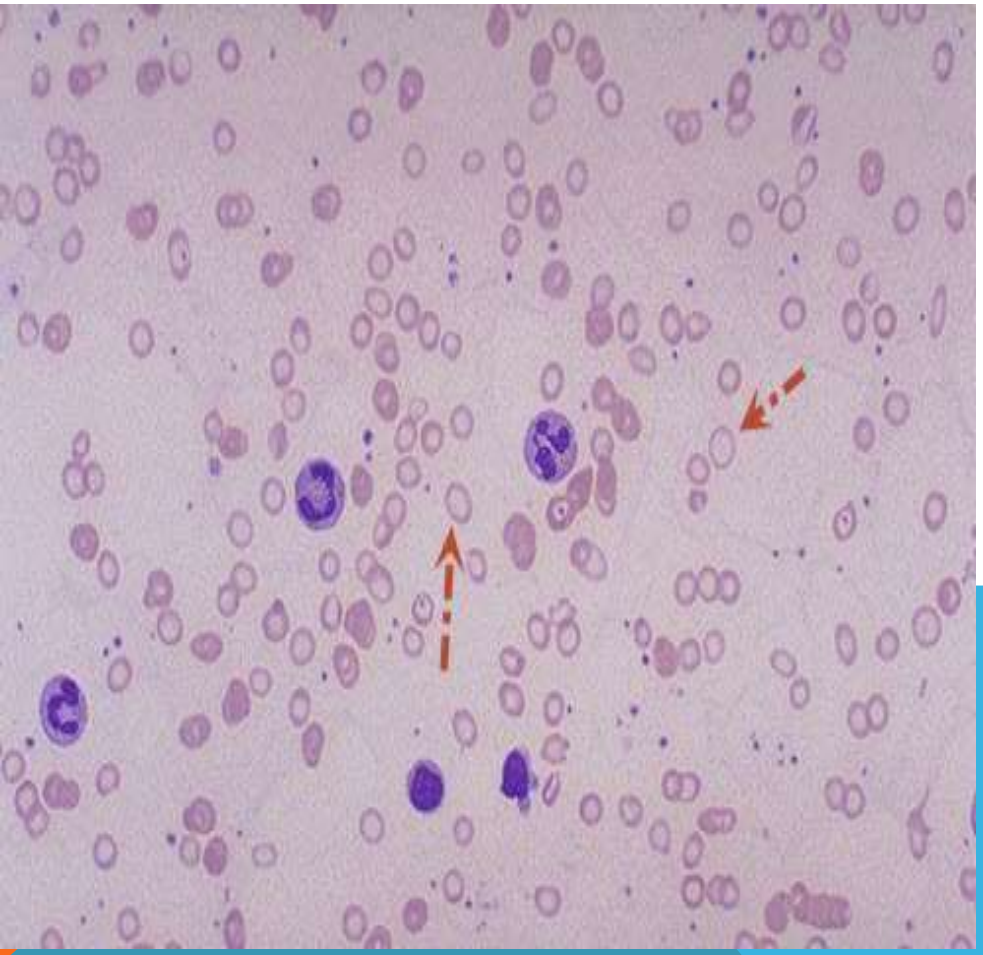
VIT B 12 (EXTRINSIC FACTOR)

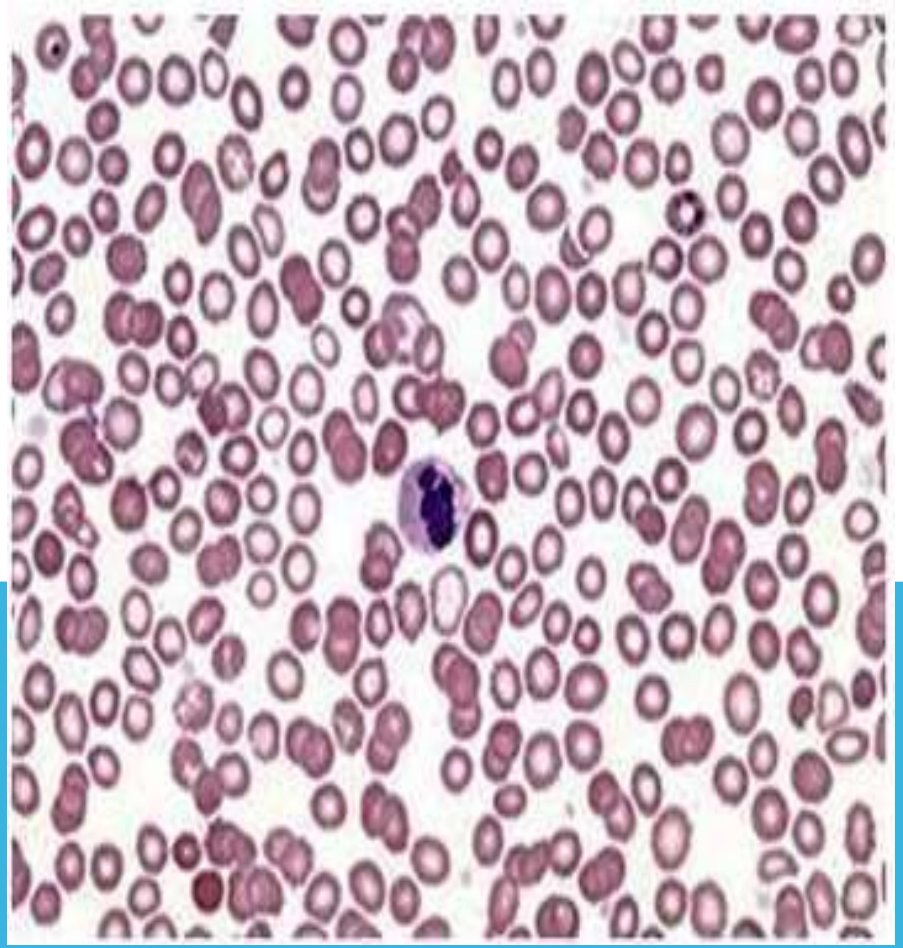
- **TRANSPORT** – in blood transported by combining with Transcobalamin-II
- **STORAGE** – In liver & Muscle
- **ROLE** – required for synthesis of DNA & maturation of cell.

FOLIC ACID

- **Folic acid** – Pteroylglutamic acid.
- **Daily requirement** – 100 µg.
- **Sources** – leafy veg, pulses, yeasts, liver.
- From breakdown of Polyglutamate to Monoglutamates.

IRON DEFICENCY ANEMIA





THANK YOU