Regulation Of Erythropoiesis

By:
Dr Asma Jabeen
**General Factors:**
- Hypoxia- Erythropoietin
- Growth inducers
- Vitamins

**Maturation factors**
- Vitamin B12
- Folic acid

**Factors necessary for hemoglobin production:**
- Vitamin C
- Proteins
- Iron & copper
- Calcium, bile salts, cobalt, nickel

**State of bone marrow & liver**
Erythropoietin

A glycoprotein hormone (MW 34000)

Source:

- 90% from the kidney (fibroblast like cells from renal interstitium + tubular epithelial cells and 10% from the liver (mainly from the liver in fetal life).

Function:

- Stimulates the production of proerythroblasts from stem cells
- Speeds up all stages of development of erythroblasts into mature RBCs
Regulation (control of secretion):

1. Hypoxia the main stimulus- Increased levels of hypoxia inducible factor-1 (HIF) bind to hypoxia response element on erythropoietin gene. Cause increased erythropoietin synthesis

2. Adrenaline, noradrenaline and some Prostaglandins
3. Adenosine (adenosine antagonist decrease EPO secretion)
4. Cobalt salts

Clinical uses:

1. Chronic renal failure
2. Aplastic anemia
3. Anemia with chronic diseases
Tissue Oxygenation

Decreases

Factors that decrease oxygenation
1. Low blood volume
2. Anemia
3. Low hemoglobin
4. Poor blood flow
5. Pulmonary disease
Release of Erythropoietin due to hypoxia

Physiological:
- High altitude

Pathological:
- Cardiac failure
- Lung diseases
- Anemia
- Low blood volume
Erythropoietin Mechanism

Stimulus: Hypoxia due to decreased RBC count, decreased availability of O₂ to blood, or increased tissue demands for O₂

Normal blood oxygen levels

Imbalance

Enhanced erythropoiesis increases RBC count

Kidney (and liver to a smaller extent) releases erythropoietin

Erythropoietin stimulates red bone marrow

Increases O₂-carrying ability of blood

Reduces O₂ levels in blood
Minerals

1. **Iron (Fe)** is essential for formation of heme part of Hb.
2. **Copper (Cu)**
   - Cu essential for erythropoiesis, transported in the plasma by ceruloplasmin (which catalyze the oxidation of ferrous iron to ferric)
   - Co-factors in Hb synthesis

3. **Cobalt (Co)**
   - Stimulate erythropoiesis though stimulation of erythropoietin secretion from the kidney
   - synthesis of Vit. B12
Role of vitamins

Vitamin $B_{12}$ (cyanocobalamin) & Folic acid

- Rapidly growing and reproducing erythropoietic cells depend on nutritional status of individual

- Both are required for synthesis of DNA (each is required for Thymidine triphosphate synthesis, an essential building block of DNA)

- Deficiency cause failure of nuclear maturation and cell division due to diminished, abnormal DNA
Vitamin B12 deficiency
pernicious anemia

Folic acid deficiency
malabsorption, sprue

Erythroblasts failing to proliferate
Rapidly, produce macrocytes → large
Irregular, oval, fragile cells
Vitamin B$_{12}$

- For absorption, **intrinsic factor** is required
- Absorbed in terminal ileum
- After absorption, stored in the liver
- Released slowly as needed by bone marrow
- The minimum requirement for normal red cell maturation is 1 to 3$\mu$g
- Deficiency symptoms occur after 3 or 4 years

Lack of intrinsic factor, decreases availability of vitamin B12 because of faulty absorption
Folic acid (Pterylglutamic acid)

- Normal constituent of green vegetables, some fruits and meats (liver)
- Destroyed by excessive cooking
- Defective absorption in sprue usually of both Vitamin B12 & folic acid leads to maturation failure of red blood cells
Thyroxine:

- Thyroxine accelerates the process of erythropoiesis at many levels.
- Polycythemia is common in hyperthyroidism
State of bone marrow & Liver

Healthy bone marrow is essential for normal erythropoiesis
Destruction by irradiation, drugs or toxins leads to aplastic anaemia

Healthy Liver is essential for normal erythropoiesis as it the site for:

1. Storage of Vit. B12 & iron
2. synthesis of 10% of EPO

Chronic liver disease leads to anaemia
Factors necessary for hemoglobin formation in RBC:

- **Proteins** of high biologic value
- **Iron** for heme synthesis
- **Copper** for iron absorption from GIT
- **Cobalt and Nickel** for utilization of iron during hemoglobin formation
- **Vitamin C**, riboflavin, nicotinic acid and pyridoxine
THANK YOU