Anti-Anemic Drugs

Pharmacology Team

المذكرة عبارة عن سلايدات الدكتورة بالاضافة الى نوتات التيم

Ps: the notes are in orange color or gray squares

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Antianaemics:

1- Iron.

2- Vitamin B12

3-Folic Acid.

4- Erythropoietin

Team Note:

Anemia :

Inabilty of blood to carry oxygen (tissue hypoxia)

-Low RBc -

- Low HB -

types :

1- iron difcncy Anemia (small RBC)

Hypochromic or microcytic anemia

No suffcent iron which is rqured for good content of HB

2- Megalopalstic Anemia (large RBCs with no function)

Folic acid anemia -

vit B 12 anemia -

3- hemolytic anemia

4- aplastic anemia

Iron:

Forms of iron

Total body iron = 4 gm distributed as

1. Hemoglobin = 2/3 amount.

2. Stored forms

- Available Forms Ferritin & haemosiderin in intestinal mucosal cells and in macrophages in liver, spleen & bone.

- Non available Forms: myoglobin, cytochromes, various enzymes

Team Note:
Iron in ..

Reduced form → Ferrous

Oxidized form → Ferric

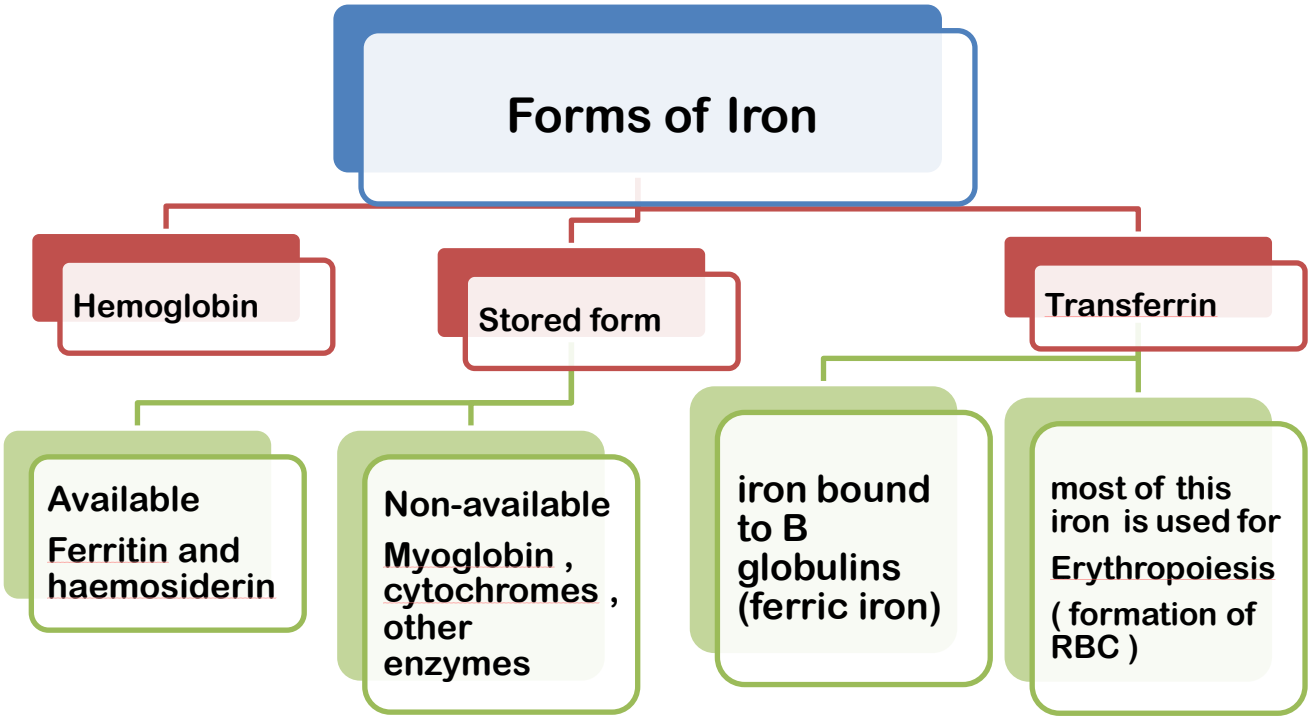
3. Transferrin: (circulating iron)

  - iron bound to B globulins (ferric iron)
  - most of this iron is used for erythropoiesis.

Daily requirement

- 5 mg for male.
- 15 mg for female & children.
- available in meat, grain and vegetables

Team Note:



Iron absorption

Iron is absorbed from upper part of small intestine in ferrous form (active transport).

2. Vitamin C, acidic medium, amino acids & fructose ↑ absorption.

3. Antacids & tetracyclines ↓ absorption.

4. Converted to ferric in the mucosal cells

Excretion no efficient way for excretion

minimal lost in saliva, sweat, or by exfoliation (peeling off) of intestinal mucosal cells containing ferritin into stool.

USES OF IRON THERAPY

1. Microcytic or hypochromic anemia.
2. Usually given orally

Oral iron preparations

widely used in iron deficiency anemia

Ferrous sulphate Ferrous gluconate.

Ferrous succinate Ferrous fumarate.

Side Effects of oral iron therapy

1. GIT disturbances: Nausea, abdominal cramps and diarrhea or constipation.
2. Black stool.
3. Teeth staining.

Parenteral Iron therapy

Rare use

Iron dextran

Iron sucrose

Iron sodium gluconate.

Uses

1. Non compliance of oral iron therapy.
2. Severe malabsorption syndrome.

3. Marked blood loss.

Adverse Effects

1. Local pain & tissue staining (I.M.).

2. Hypersensitivity reactions. (Urticaria up to anaphylactic reactions I.M. , I.V).

3. Headache, fever.

Acute iron toxicity

Causes: accidental ingestion of iron tablets by children.

Symptoms:

1. Severe gastritis, vomiting, bloody diarrhea, abdominal pain.
2. Circulatory collapse (shock).
3. Metabolic acidosis, coma, death.

Treatment

Gastric lavage: 1% Na HCO_3 $\rightarrow$ insoluble iron salts.

Antidotes

Deferoxamine intramuscularly or intravenous infusion $\rightarrow$ complex with ferric iron $\rightarrow$ excreted in urine.

Chronic Iron Toxicity

Causes.

1. Congenital (hemochromatosis).

Genetic abnormality of iron absorption

2. Repeated blood transfusion.

3. Chronic hemolytic anemia (Thalassaemia).

Treatment

1. Deferoxamine

2. Intermittent phlebotomy.

Iron

drugs	mechanism	use	Adverse effect
-Oral iron preparations widely used in iron deficiency anemia Ferrous sulphate Ferrous gluconate. Ferrous succinate Ferrous fumarate. - Parenteral Iron therapy Rare use Iron dextran Iron sucrose Iron sodium gluconate.	Iron absorption Iron is absorbed from upper part of small intestine in ferrous form (active transport). 2. Vitamin C, acidic medium, amino acids & fructose ↑ absorption. 3. Antacids & tetracyclines ↓ absorption. 4. Converted to ferric in the mucosal cells Excretion no efficient way for excretion minimal lost in saliva, sweat, or by exfoliation (peeling off) of intestinal mucosal cells containing ferritin into stool.	Microcytic or hypochromic anemia. Parenteral Iron therapy Uses 1. Non compliance of oral iron therapy. 2. Severe malabsorption syndrome. 3. Marked blood loss.	Side Effects of oral iron therapy 1. GIT disturbances: Nausea, abdominal cramps and diarrhea or constipation. 2. Black stool. 3. Teeth staining. Parenteral Iron therapy Adverse Effects 1. Local pain & tissue staining (I.M.). 2. Hypersensitivity reactions. (Urticaria up to anaphylactic reactions I.M. , I.V). 3. Headache, fever

iron toxicity

Kind of toxicity	cause	Symptoms:	treatment
Acute iron toxicity	Causes: Accidental ingestion of iron tablets by children.	Symptoms: -Severe gastritis, vomiting, bloody diarrhea, abdominal pain. -Circulatory collapse (shock). -Metabolic acidosis, coma, death.	Gastric lavage: 1% Na HCO3→ insoluble iron salts. Antidotes Deferoxamine intramuscularly or intravenous infusion → complex with ferric iron → excreted in urine
Chronic Iron Toxicity	Congenital (hemochromatosis). *Genetic abnormality of iron absorption* 2. Repeated blood transfusion. 3. Chronic hemolytic anemia (Thalassaemia).		1. Deferoxamine 2. Intermittent phlebotomy.

Vitamin B12 (cobalamin)

- Vitamin B12 is not synthesized in human
- Should be supplied by dietary sources as eggs, dairy products & liver.
- Daily requirement 2 µg - 3 µg.
- It is absorbed from GIT in presence of intrinsic factor.
- Intrinsic factor is a protein secreted by parietal cells of the stomach.
- It may be absent in patients having pernicious anemia.
- Full absorption of vitamin B12 requires intrinsic factor (gastric mucosa)+ receptors mediated transport system in ileum. It is stored mainly in the liver (3- 5 mg).

Preparations available

1. Cyanocobalamin. ← Given I.M

2. Hydroxocobalamin (preferable). ← It's a life time treatmen

Hydroxocobalmin is more bound to plasma protein ⟶ ↑ t ½ longer half life .

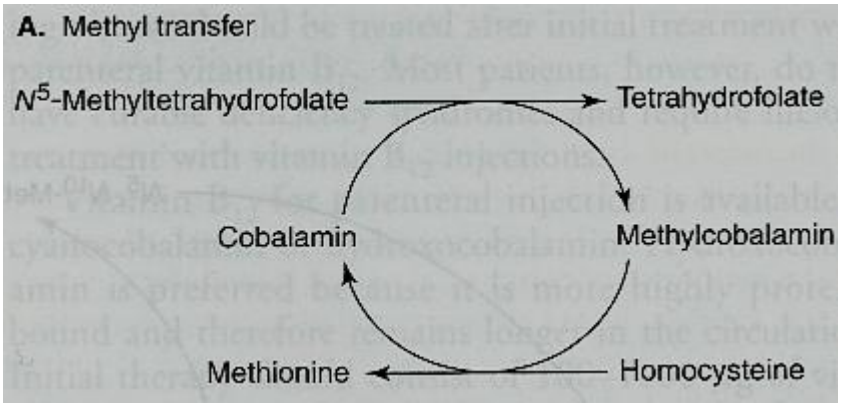
Team Note:

Who can't syntheize the intrnsic factor → pericious anemia

- **gnetically →** congenital
- **abnormalty of absorption ..** Rs of Vit B12 are defcted on the intestine
- **operation →** gasrtoctomy

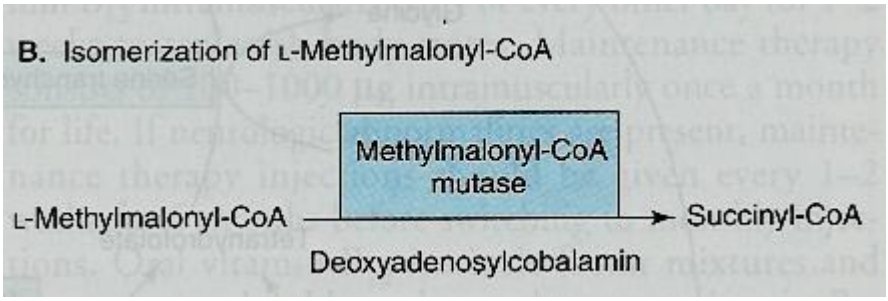
Function of vitamin B12

1. Conversion of homocysteine into methionine this is required in folic acid metabolism and DNA synthesis (necessary for red blood cells production).



Function of vitamin B12

2.Conversion of methylmalonyl CoA to succinyl-CoA essential for lipid metabolism & normal neuronal function of the brain.



USES of VITAMIN B12

1. Naturally occurring pernicious anemia (life long therapy, I.M.)

2. Neurological abnormalities.

3. Gastrectomy.

4. Cyanide poisoning (hydroxocobalamin).

naturally occurring pernicious anemia occurs due to vitamin b 12 deficiency

1. Lack of intrinsic factor.
2. Diseases that interfere its absorption in the ileum as.

e.g. inflammatory bowel disease

characterized by :

1. Megaloblastic anaemia.

2. Neuropathy.

Team Note:

Megaloblastic anaemia. → Means doesn't has DNA synthesis

Neuropathy → When having vit B 12 deficiency

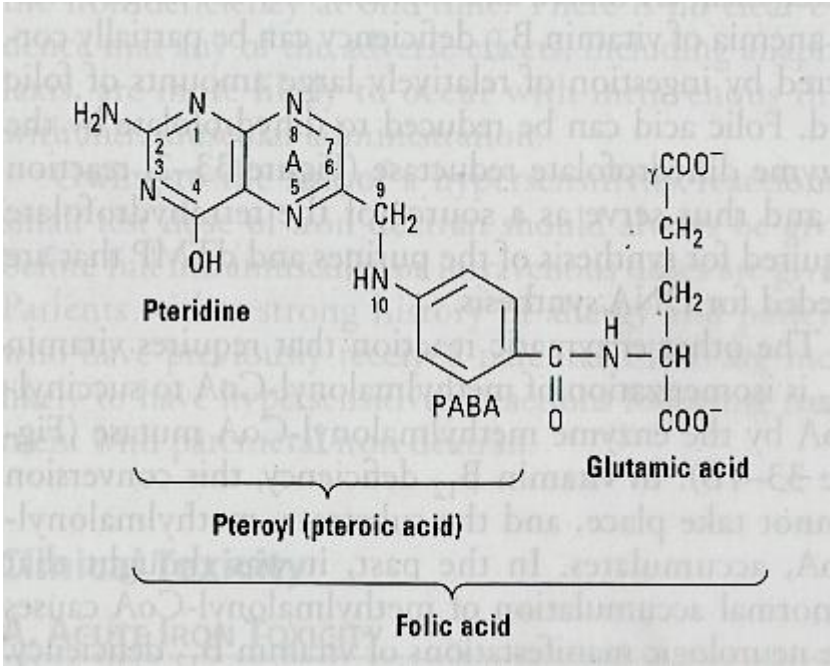
But when having the both problems he will has pernicous anemia

Vitamin B12 (cobalamin)

Preparations available	mechanism	Function	USE
1. Cyanocobalamin. 2. Hydroxocobalamin (preferable). Hydroxocobalmin is more bound to plasma protein ⟶ ↑ t ½ longer half life .	Vitamin B12 is not synthesized in human ▪ Should be supplied by dietary sources as eggs, dairy products & liver. ▪ Daily requirement 2 µg - 3 µg. ▪ It is absorbed from GIT in presence of intrinsic factor. is a protein secreted by parietal cells of the stomach. ▪ It may be absent in patients having pernicious anemia. ▪ Full absorption of vitamin B12 requires intrinsic factor (gastric mucosa)+ receptors mediated transport system in ileum. It is stored mainly in the liver (3- 5 mg).	1. Conversion of homocysteine into methionine this is required in folic acid metabolism and DNA synthesis (necessary for red blood cells production). 2. Conversion of methylmalonyl CoA to succinyl-CoA essential for lipid metabolism & normal neuronal function of the brain.	Naturally occurring pernicious anemia occurs due to vitamin B 12 deficiency -Lack of intrinsic factor. -Diseases that interfere its absorption in the ileum as. e.g. inflammatory bowel disease characterized by : 1. Megaloblastic anaemia. 2. Neuropathy.

Folic acid

Chemistry



Folic acid

Sources

- **Present as in green vegetables, liver, kidney & yeasts (methyl tetrahydrofolates).**
- **Folic acid**
- **Daily requirement 100 µg.**

Kinetics → Means how is it absorped

In intestine:

- **Folic acid or dietary folates are absorbed completely by active transport system.**

Team Note:

Folate→ as in food

Folic acid → as a drug

In cells:

Means removal

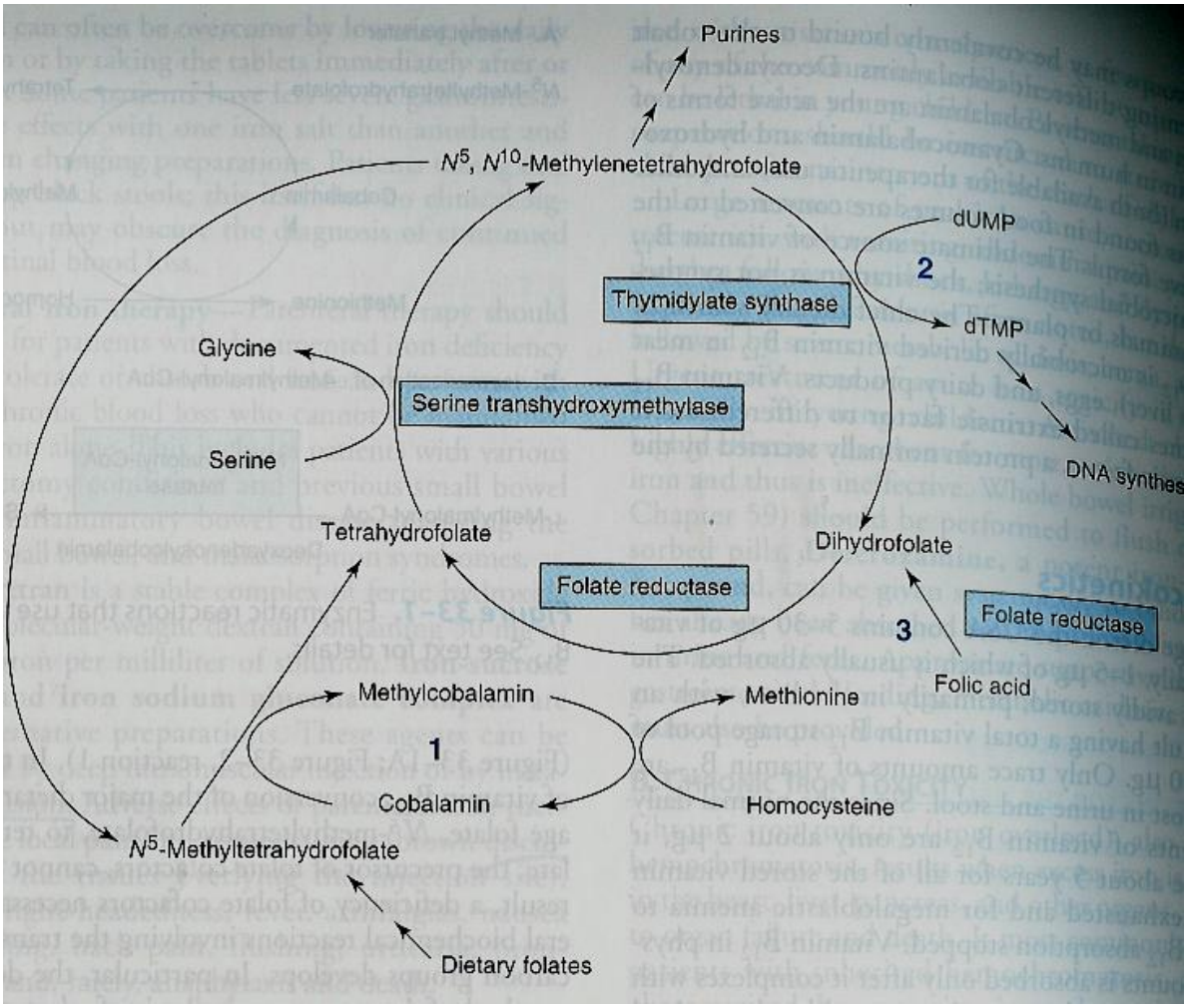
- **Folic acid is reduced to dihydrofolate then tetrahydrofolate *by dihydrofolate reductase enzyme*.**

Folic acid (drug)→ dihydrofolate → tetrahydrofolate

Actevated when combined with ***polyglutamate***

- **Folates is demethylated to tetrahydrofolate.**

- **Active form is *tetrahydrofolate polyglutamate***
- **Vitamin B12 is required for activation of folic acid**



Functions

Folic acid is necessary for

1. Synthesis of purines & pyrimidines.

2. Amino acid metabolism

Deficiency

Causes

1. Poor diet (alcoholics is common).

2. Pregnancy (increases the risk of neural tube defect in the fetus).

3. Drugs (phenytoin, phenobarbitone).

4. Premature Infants.

Enzyme inducer

5. Hemolytic Anaemia.

6. Folate antagonists

- **Sulphonamides, methotrexate**

USES

1. Megaloblastic anaemia (folic acid deficiency).

2. Pregnancy *to avoid risk of neural tube defect in newborns*

3. During cytotoxic therapy (Methotrexate).

Preparations

Synthetic folic acid (tablets & parenteral).

Contraindications ← Can't take it instead of vit B12

Pernicious Anaemia (Vitamin B12 deficiency)

Folic acid can aggravates the neurological symptoms although blood picture may improve.

Erythropoietin (Epotein)

Team Note:
If the patient has renal failure & anemia we give him ERYTHROPIETIN

- **A hematopoeitic growth factor**
- **stimulate the proliferation and differentiation of erythrocyte precursors in the bone marrow.**
- **glycoprotein hormone released mainly from the kidney (90%; the remainder in the liver and other tissues) in response to hypoxia.**

Team Note:
It's a hormone so we can't give it orally because it will be destructed by the acid in GIT

- ❑ **Synthesized by (recombinant DNA technology).**
- ❑ **Subcutaneously (SC) or intravenously (i.v.).**
- ❑ **Plasma half life is 4 h.**
- ❑ **Given 3 times weekly**

USES

anaemia due to renal failure.

1. **anaemia in HIV-infected patients.**
2. **anaemia in cancer patients.**
3. **Bone marrow depression**

Team Note:
In cancer or HIV the concentration of erythropoietin will decrease ,, so we give it to the patient as a medication

Adverse Effects

1. **hypertension.**
2. **Influenza-like syndrome.**
3. **Increased incidence of thrombosis.**
4. **Convulsions.**
5. **Allergic reactions.**

Summary

1. **Microcytic hypochromic anemia**

   Iron orally

1. **Megaloblastic anemia Folic acid orally**
2. **Pernicious anemia Vitamin B12 i.m.**
3. **Anemia due to renal failure or bone marrow failure erythropoietin s.c. or i.v.**