THERAPEUTICS OF HAEMATINICS

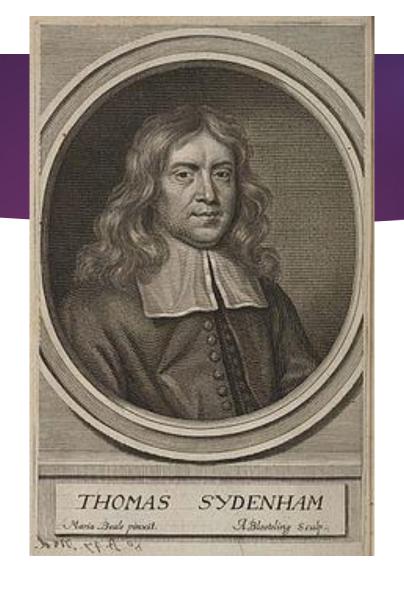
Haematinics are agents that required for formation of blood and used in the treatment of anaemia.





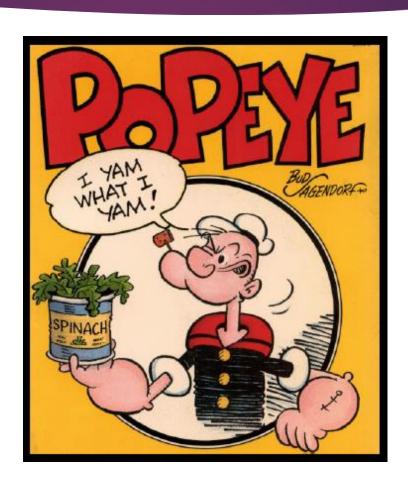


- time of Hippocrates.
- The earlier applications of iron were more often symbolic, with the idea that iron was indicative of strength and was imbued with some peculiar force by Mars, the god of war.
- The Greek physicians employed iron for the cure of weakness, with a view to impart to the patient the strength of iron.



▶ Sydenham (1624-1689) belongs the credit of introducing iron into clinical medicine for the treatment of anemia.

IRON



Iron distribution in normal adults.1

	Iron Content (mg)	
	Men	Women
Hemoglobin	3050	1700
Myoglobin	430	300
Enzymes	10	8
Transport (transferrin)	8	6
Storage (ferritin and other forms)	750	300
Total	4248	2314

- ▶ Daily diet: 10–15 mg; absorbption 5–10%
- ► Location: duodenum and proximal jejunum
- Heme iron directly absorbed
- Nonheme iron reduced to ferrous (Fe 2+) absorbed
- Iron is transported in the plasma bound to transferrin

- No mechanism for excretion
- Small amounts are lost in the feces by exfoliation of intestinal mucosal cells, trace amounts are excreted in bile, urine, and sweat
- Regulation of iron balance: absorption Vs storage

INDICATIONS

- Iron deficieny
 - ▶ Iron deficiency due to dietary lack or to chronic blood loss.
- Pregnancy
- Malabsorption syndromes
- Premature neonates
- Early treatment of pernicious anemia

Oral preparations

- ferrous sulfate
- ferrous gluconate
- ferrous fumarate
- ferrous succinate

- Iron salts provide different amounts of elemental iron.
- ▶ In an iron-deficient individual, about 50–100 mg of iron can be incorporated into hemoglobin daily, and about 25% of oral iron given as ferrous salt can be absorbed.
- ► Therefore, 200–400 mg of elemental iron should be given daily to correct iron deficiency most rapidly.
- Treatment with oral iron should be continued for 3–6 months after correction of the cause of the iron loss to replenishes iron stores.

Some commonly used oral iron preparations.

Preparation	Tablet Size	Elemental Iron per Tablet	Usual Adult Dosage for Treatment of Iron Deficiency (Tablets per Day)
Ferrous sulfate, hydrated	325 mg	65 mg	2-4
Ferrous sulfate, desiccated	200 mg	65 mg	2-4
Ferrous gluconate	325 mg	36 mg	3-4
Ferrous fumarate	325 mg	106 mg	2-3

Adverse effects

- Constipation
- Epigastric pain, Heartburn, bloating, Nausea & Vomiting
- Teeth staining
- Blackened stool
- Metallic taste (Start with low dose then increase the dose higher)

Prevention GI disturbances: ?? Takes immediately after or with meals

Reduction of iron content in each dose

Parenteral iron therapy

- Iron dextran, sodium ferric gluconate complex and iron sucrose.
- Parenteral therapy should be reserved for
 - patients with documented iron deficiency who are unable to tolerate or absorb oral iron
 - patients with extensive chronic anemia who cannot be maintained with oral iron alone. Eg CKD

Oral Vs Parenteral

- Intravenous administration eliminates the local pain and tissue staining that often occur with the intramuscular route.
- Adverse effects of intravenous iron dextrain therapy include headache, light-headedness, fever, arthralgias, nausea and vomiting, back pain, flushing, urticaria, bronchospasm, and, rarely, anaphylaxis.
- Owing to the risk of a hypersensitivity reaction, a small test dose of iron dextran should always be given before full doses are given.

▶ Oral iron should not be given 24 h before start i.m. and for 5 days after the last i.v. injection.

- ► For patients treated chronically with parenteral iron, it is important to monitor iron storage levels to avoid the serious toxicity associated with iron overload.
- ▶ Parenteral administration—which bypasses this regulatory system at absorption—can deliver more iron than can be safely stored.

READ..!!

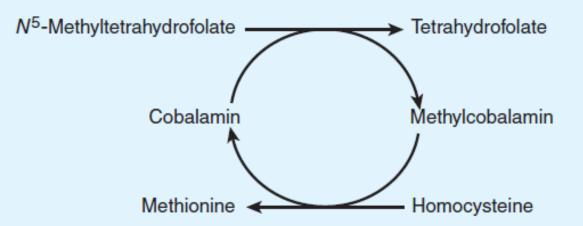
- Interactions
- ▶ Acute iron overdose
- ▶ Chronic iron overload
- ► Iron-Chelating agents

- Complex cobalt containing compounds
- Cyanocobalamin and hydroxocobalamin

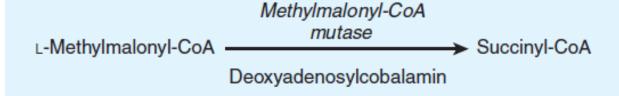
- synthesized only by microorganisms
 - ▶ Sources: Liver, Kidney, sea fish, egg yolk

Daily Requirement: 1 – 3 mcg (Pregnancy and Lactation3 – 5 mcg)





B. Isomerization of L-Methylmalonyl-CoA



- Read...!!
 - Methylfolate trap
 - ▶ Why ?? Neurological manifestations of Vit B12 deficiency

- Absorption: Present in food as protein conjugates attaches to specific receptor in mucosa – absorbed by active transport
- Transport: In combination with transcobalamin II (TCII)
- Storage: In liver 4/5th of Body`s Vit.B12
- Degradation: Not degraded in body excreted mainly in Bile enterohepatic circulation
- Parenteral -IM and SC administration excreted via urine

Normal B-12 absorption:

- Dietary B-12 binds to R factor in saliva and gastric juices.
- In duodenum, pancreatic enzymes promote dissociation from R factor and binding to Intrinsic Factor (IF)
- F-B12 complex taken up by ileal receptors.
- Released into plasma bound to transcobalamines TC I, II, or III.

Indications

- Pernicious anaemia :deficiency of IF
- Dietary deficiency: vegetarian
- Malabsorption syndromes :
 - ▶ Blind loop syndrome ,Crohn's disease, ileal resection
- Gastrectomy
- †requirements:
 - pregnancy, hemolytic anemia, hepatic disease
- ► Neurologic syndromes of Vit B12 deficiency

Preparations

- Hydroxocobalamin is preferred to cyanocobalamin
 - highly protein-bound and therefore remains longer in the circulation

- ▶ **Initial therapy** should consist of 100–1000 mcg of vitamin B 12 intramuscularly daily or every other day for 1–2 weeks to replenish body stores.
- ► Maintenance therapy consists of 100–1000 mcg intramuscularly once a month.

Response

- ► Feel better: 2 days
- Reticulocyte peak: 5-7 days
- ▶ Hb, RBC, Ht ↑: first week □ normalize: 2 months
- ▶ Watch: hypokalemia!!

- ▶ If injections are refused/ bleeding disorder
 - Alternative: snuff , aerosol , oral
- Large daily oral doses (1000 micrograms)

Depleted stores must be replaced by parenteral cobalamin before switching to the oral preparation.

Interactions

- Reduction of absorption of B 12 from GI tract
 - Excessive consumption of ethanol
 - Prolonged use of cholestyramine, colchicine
 - ► Large doses of ascorbic acid may destroy B12

FOLIC ACID

Daily requirement: 0.2 mg per day (0.8 mg in pregnancy and lactation)

Kinetics:

- Absorption: As polyglutamates in food glutamates split off and absorbed in upper intestine Reduction to DHFA and methylation also occurs at same site
- ► Transport: as methyl-THFA partly bound to plasma protein
- Store: tissues extract FA rapidly and store as polyglutamates in cells.
- Metabolism in the liver, Excretion in Urine

Deficiency

- Inadequate dietary intake
- Malabsorption (upper GIT coeliac disease, tropical sprue etc.)
- Chronic alcoholism
- Increased demand (pregnancy)
- drug induced (phenytoin, phenobarbitone, MTX etc.)

Indications

- Megaloblastic anaemia: due to nutritional deficiency,
- Pernicious anaemia (adjuvant role with Vit. B12)
- Malabsorption syndromes
- Antiepileptic therapy
- Pregnancy Prophylaxis: 1 mg per day routinly in pregnancy
- Methotrexate toxicity: Folinic acid

- Parenteral administration of folic acid is rarely necessary, since oral folic acid is well absorbed even in patients with malabsorption syndromes.
- Folate deficiency is treated with oral folic acid (1 to 5 mg/day orally) for four months, or until complete hematologic recovery occurs.
- A dose of 1 mg folic acid orally daily is sufficient to reverse megaloblastic anemia, restore normal serum folate levels, and replenish body stores of folates in almost all patients.

- Therapy should be continued until the underlying cause of the deficiency is removed or corrected
- ► Folic acid supplementation to prevent folic acid deficiency should be considered in high-risk patients, including pregnant women, patients with alcohol dependence, hemolytic anemia, liver disease, or certain skin diseases, and patients on renal dialysis.

▶ ADRs: Non toxic orally, sensitivity by injections rarely

ERYTHROPOIETIN

- ► A hormone produced by peritubular cells of Kidney
- Recombinant human erythropoietin (Epoetin a, β)
- Administerd IV or SC
- ► Half life: 6 10 Hours
- Required for erythropoiesis: anaemia and hypoxia sensed by kidney cells – EPO secretes and acts on marrow:
 - Stimulates proliferation of colony forming cells of erythroid series
 - Induces Hb formation and erythroblast maturation
 - Release of reticulocytes

ERYTHROPOIETIN...

Indications

- Anaemia of chronic renal failure 25 100 U/kg SC or IV
- Anaemia with AIDS patients treated with zidovudine
- Cancer chemotherapy induced anaemia
- Preoperative increased blood production

ERYTHROPOIETIN...

ADRs

- Nonimmunogenic ADRs occur due to increase in haematocrit,
 viscosity and peripheral resistance
- Increased clot formation in AV- shunts
- Hypertensive episodes
- Seizure
- Flu like symptoms

