# treatment of iron deficiency anemia

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# Red blood corpuscles (RBC) laboratory data

- Haemoglobin (Hb) concentration: (13-18gm/dl)
- RBCs count: (4,5-5,5 millions/cm)

**Absolute values of RBC**

- Packed cell volume (PVC): (40-50%)
- Mean corpuscular volume (MCV): (85-95 fl)
- Mean corpuscular haemoglobin concentration (MCHC): (30-35%)

**Reticulocyte count:** (0,2-2,0% of RBC count)

# RBC absolute values in various types of anaemia

- Hypochromic RBC: MCH <28pg
- Normochromic: MCH 28-32pg
- Microcytic RBCs: MCV <85fl
- Macrocytic RBCs: MCV >95fl
- Normocytic RBCs: MCV 85-95fl
- Reticulocytosis: Reticulocytes >2%

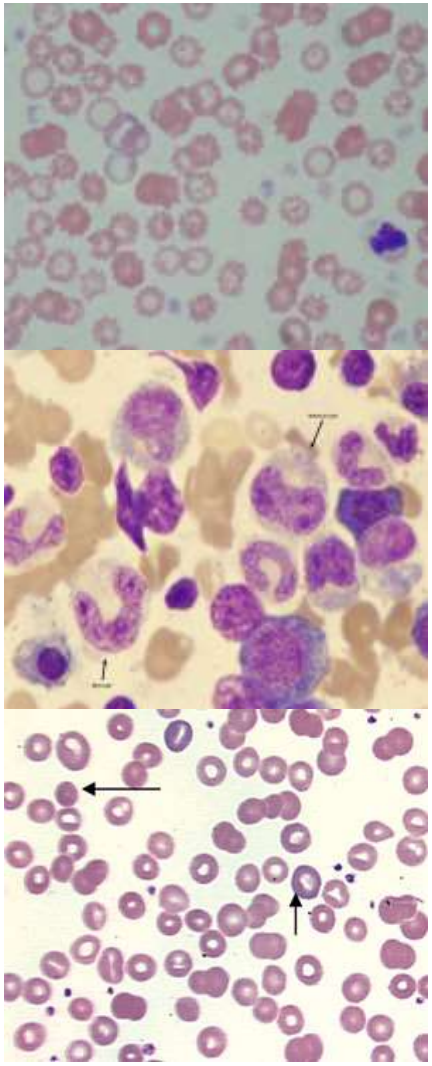
# Types of anaemias

- **Deficiency anaemias**: (Fe, vit B12, folic acid)
  - **Iron deficiency anaemia**
  - **Megaloblastic (pernicious) anaemia (B12 Deficiency)**
  - **Megaloblastic anaemia of folate deficiency**
- **Aplastic anaemia**: (depression of bone marrow)
- **Haemolytic anaemia**: (++ destruction of RBCs)
- Anaemias due to **haematological diseases**

# Microscopic diagnosis of deficiency anaemias

- **Iron deficiency anemia:**
  - Is diagnosed by presence of : microcytic hypochromic RBC

- **Pernicious (megaloblastic anemia):**
  - Is diagnosed by presence of : macrocytic megaloblastic RBC



# Iron (Fe)


- Total male body (70kg) content: **4 gm**
- Body **distribution** of Fe:
  - **Circulating blood haemoglobin** (within red cells): 70%
  - **Tissues stores for Hb synthesis** (liver, spleen, bone marrow): 20% (ferritin and haemosiderin)
  - **Tissues stores not for Hb synthesis** (myoglobin, cytochromes): 10%
- **Daily requirements** for adult men= **1.0-1.5 mg/day**
  - * Increased daily doses is required for:
    - Pregnant and menstruating women (1,0-3,0 mg/day)
    - During rapid growth periods

# Iron (Fe)

- Average **healthy diet** contains (**10-20 mg Fe/day**)
- **Normal** adults **absorb 5-10%** of the dietary Fe, while in **pregnancy** or Fe deficiency absorption **rises up to 30%**

# Iron (Fe)

Food iron is found in 2 forms:

- Haem Fe
- Non-haem Fe

- **Haem Fe**:
  - Is derived from the **Hb & myoglobin** found in **meat** and accounts for 10-25% of ingested Fe in well economic communities (up to 20% is absorbed)
  - Prior to absorption the **Haem Fe is cleaved from the globin**.
  - Absorption is influenced by **body Fe stores**.
    - The more deficiency, the greater the absorption
  - Iron is relatively **well absorbed**

- **Non-haem Fe:**
  - Is supplied by **plant and dairy products**.
  - It is **not well absorbed**.
  - Non-haem Fe consists mainly of **Fe salts** which are **bound to foods** and therefore must be hydrolyzed or solubilised prior to absorption.
  - **Consumption** of non-haem Fe **with haem Fe increases** non-haem Fe **absorption**

# Fe absorption

- Fe is present in 2 states: **ferric ($Fe^{3+}$) and ferrous ($Fe^{2+}$).**

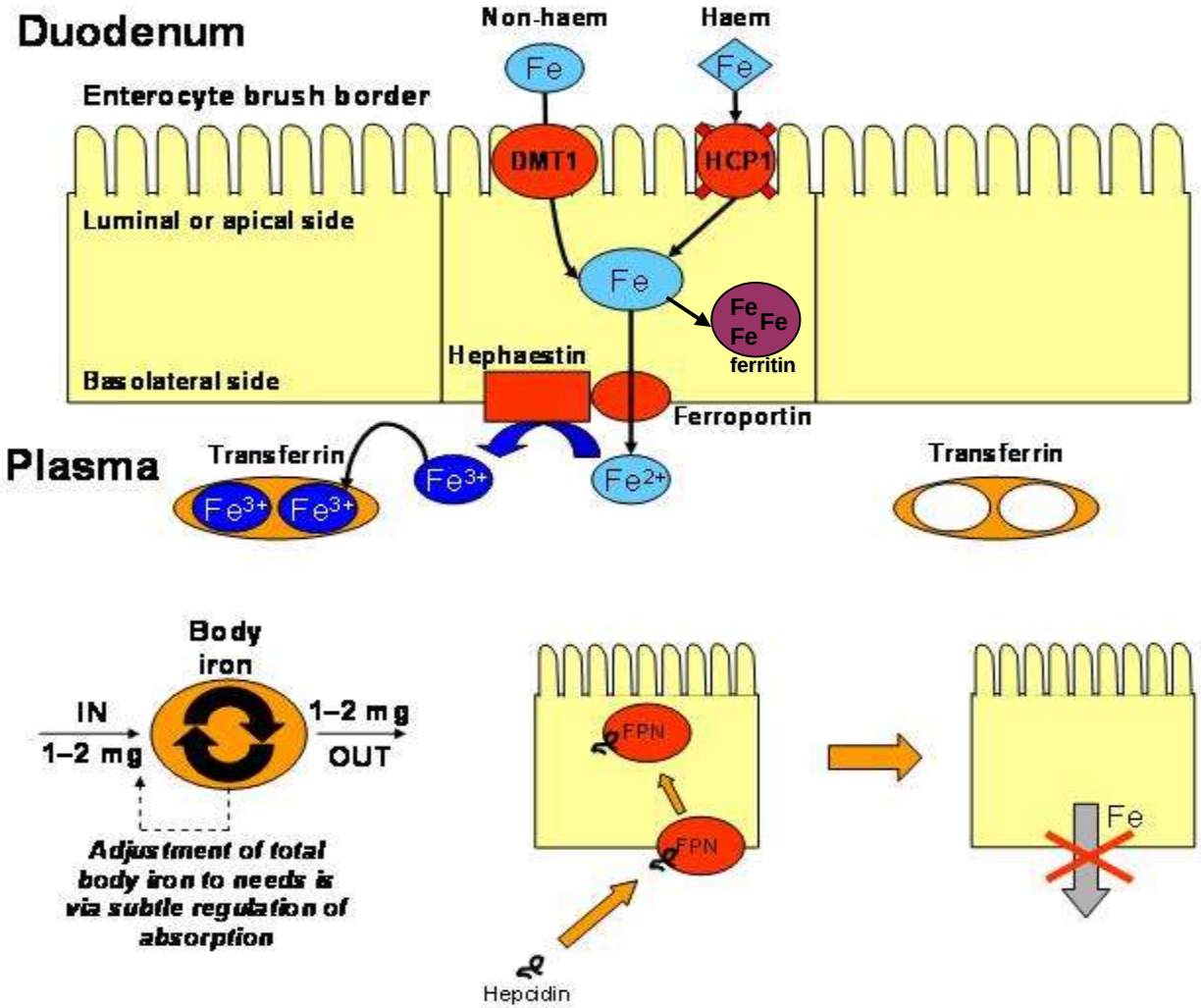
- At **neutral pH** most iron is in the **$Fe^{3+}$ state**, which is **insoluble & not absorbed**

- **Gastric acidity** is essential for **converting $Fe^{3+}$ to $Fe^{2+}$.**

- **$Fe^{2+}$** form is **best absorbed** compared with $Fe^{3+}$ form
- **Ascorbic acid** (vit. C) **promotes** conversion of **Fe to $Fe^{2+}$** form

- **Absorption** is **primarily** influenced by the **amount** of **Fe stores**.

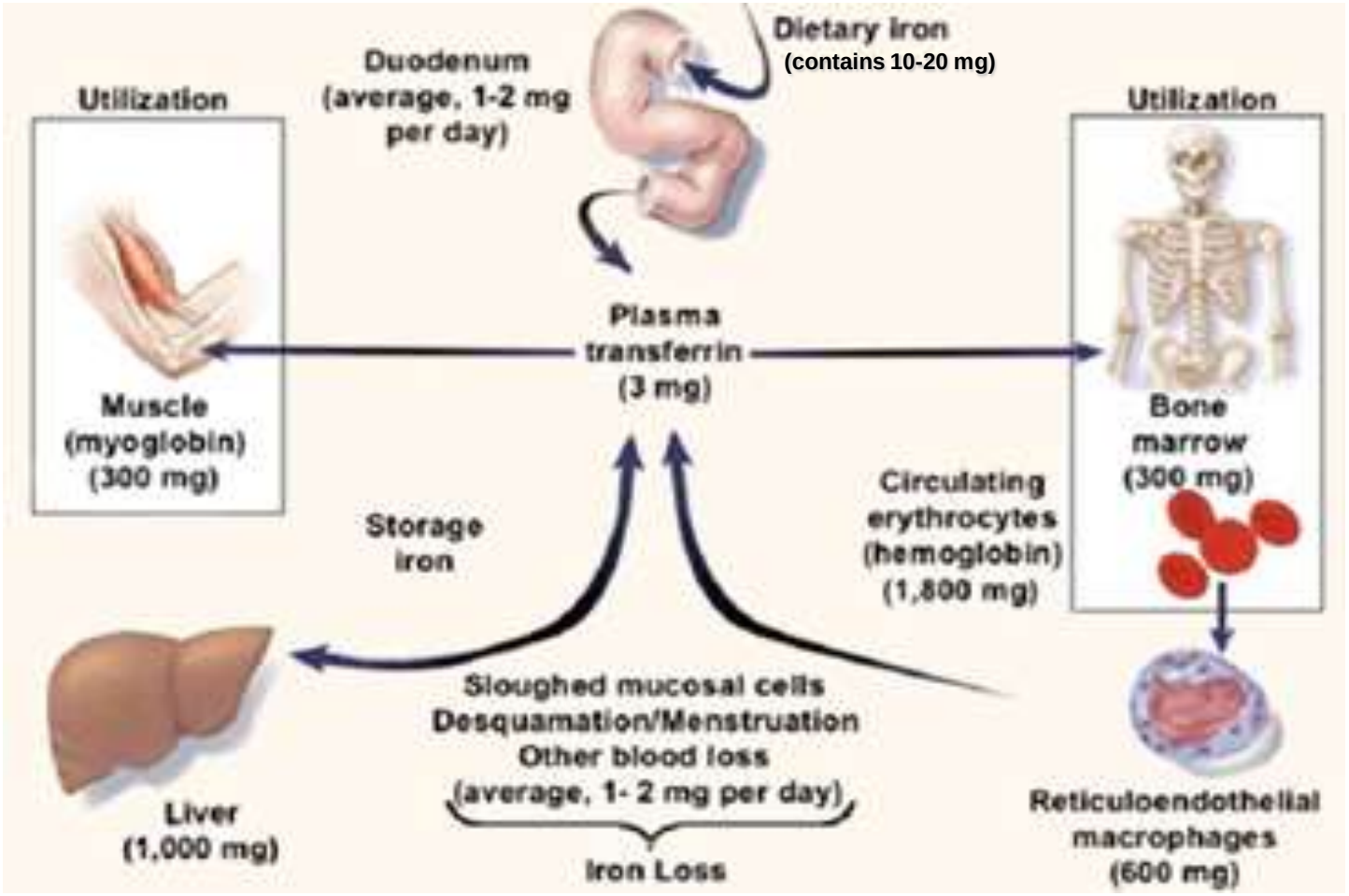
# Intestinal Fe absorption




(*hormone) is produced by hepatocytes when iron stores are full. Inflammation can also stimulate hepcidin production*

***DMT1*** *(divalent metal transporter-1),* ***HCP1*** *(haem carrier protein-1),* ***FPN*** *(ferroprotein) basolateral transporter*

# Normal iron store and distribution




Iron is bound and transported in the body via transferrin and stored in ferritin molecules. Once iron is absorbed, there is no physiologic mechanism for excretion of excess iron from the body other than blood loss i.e., pregnancy, menstruation or other bleeding.

# Factors affecting Fe absorption

- **Increased absorption:**
  - Increased demands
  - Reducing agents that increase ferrous forms e.g. HCl, Vit.C, SH groups of amino acids
- **Decreased absorption:**
  - Gastric resection
  - Mal-absorption syndrome (small intestine abnormalities; e.g. autoimmune diseases, tumors)
  - Others

# Indications of Fe therapy

- **Fe deficiency anaemia**:
  - Chronic blood loss (excessive menstruation, haemorrhoids)
  - Occult GIT bleeding (with peptic ulcer or NSAID)
  - Treatment of the cause is mandatory
- **Prophylaxis in pregnancy** (start from 4$^{th}$ month)
- **Mal-absorption syndrome (Parenteral Fe indicated)**
- **Premature babies** (human and cow milk are deficient in Fe)
- **During treatment of pernicious anemia with vit. B12 or folic acid** (due to depletion of Fe stores by rapid RBC formation)

# Treatment of Iron deficien Anaemia

- Find cause & treat if possible
- Diet with increased iron content e.g. red meat
- Iron supplements:
  - These include:
    - **Oral iron**
    - **Parenteral iron**

# Iron therapy: Oral Fe preparations


- Ferrous sulphate
  - Is most commonly used and is cheap
  - **In iron 200 mg tab, it** contains about 65 mg of elementary Fe
  - **Given with or after meal**, to reduce GIT disturbances
  - Treatment should be **given until Hb becomes normal**, then a **lower dose** of Fe is **continued for 2 month** to replenish Fe stores

# Iron therapy: Oral Fe preparations

- Side effects of oral Fe therapy include:
  - GIT disturbances:
    - heart burn, diarrhoea or sometimes constipation, nausea
  - Allergic reactions
  - Black stool (Fe doesn't interfere with test for occult blood)

- **Organic ferrous salts :**
  - These cause **less gastric irritation & produce better compliance**
  - Ferrous gluconate
  - Ferrous fumarate
  - Others : For children or elderly, **solution or syrup preparations** are available such as Ferrous glycine sulphate, Iron edetate

# Iron therapy:
# Oral Fe preparations

- **Slow release preparations** (e.g. spansules) would slowly release iron in intestine for absorption
- This causes **less gastro-intestinal side effects** and **improves** patient **compliance** esp. in elderly

**! Note : Oral iron corrects the anemia as quick as parenteral iron !**

# Iron therapy: Parenteral Fe preparations


- **Indications** of parenteral therapy:
  - If oral therapy causes or aggravates GIT disturbances
  - In mal-absorption syndrome (where Fe is not absorbed)
  - Non-compliance to oral therapy

# Iron therapy: Parenteral Fe preparations

- **Iron sorbitol citric acid complex:**
  - Given by deep **IM injection daily** or on **alternate days** 100 mg/d .
  - Rapidly absorbed into blood, bound to transferrin, and is stored in liver and bone marrow.
  - Excess unbound iron (about 30%) is **excreted in urine** which may thus becomes dark transiently.
  - It can **irritate kidney**

- **Iron dextran (ferric hydroxide with dextran ):**
  - Given by **IM, slow IV infusion**
  - In blood, it is not bound to transferrin
  - Most adult patients with anemia need about 1 - 2 g (or 20 – 40 ml) of parenteral iron
  - A small test dose (0.25 - 0.5 ml) is used first to exclude any allergy
  - **Total dose infusion (TDI):**
    - The calculated total dose of Fe required to be administered parenterally to correct anaemia and replenish Fe stores:

**mg of Fe= Hb deficit (in gm %) X body weight (Kg) X 3**

**Note: Oral Fe must be stopped 24 h before parenteral iron, and not resumed for at least 5 days after last injection**

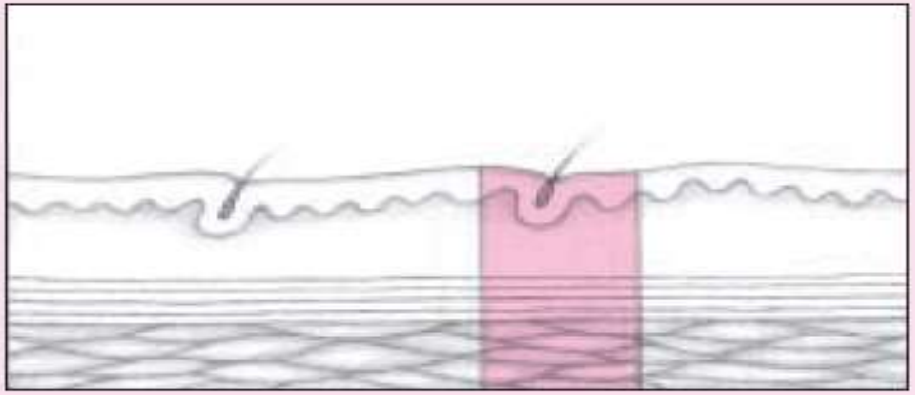
- **Side effects of parenteral iron :**
  - Local side effects
    - Parenteral iron include pain and black-brown staining at site of injection; IM iron, this can be decreased by the Z-technique of injection
  - Systemic side effects :
    - Dizziness, disorientation, arthralgia, and metallic taste
    - Allergy : esp. occur with IV iron in TDI; they include urticaria , hypotension, **anaphylactic shock.**

Adrenaline, cortisol, H1-anti-histamines, and facilities for CPR (cardiopulmonary resuscitation) must be available so that they can be used quickly in anaphylaxis

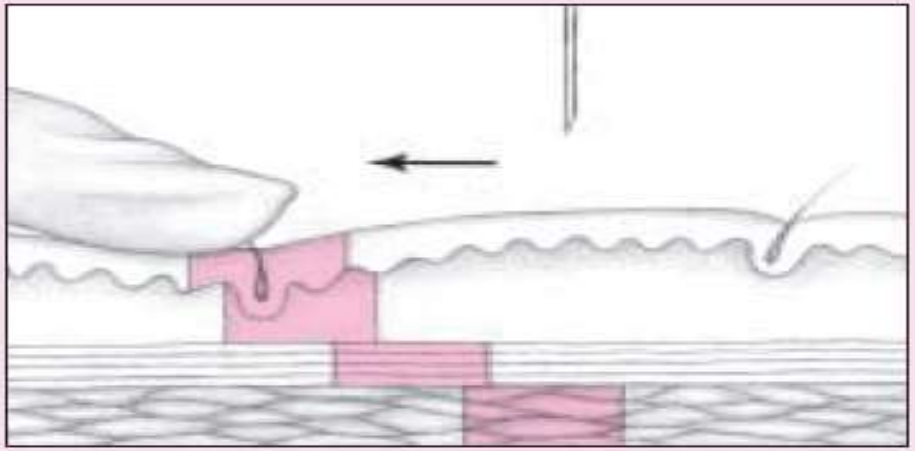
# Displacing the skin for Z-track injection

By blocking the needle pathway after an injection, the Z-track technique allows I.M. injection while minimizing the risk of subcutaneous irritation and staining from such drugs as iron dextran. The illustrations below show how to perform a Z-track injection.

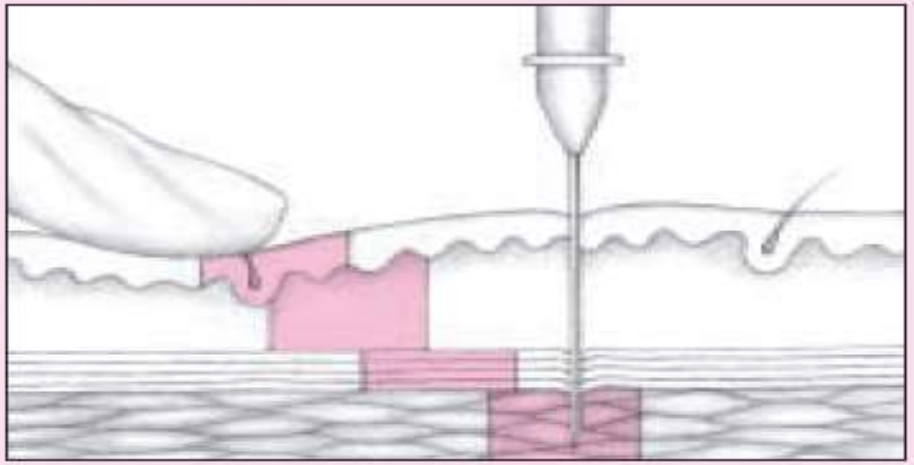
Before the procedure begins, the skin, subcutaneous fat, and muscle lie in their normal positions.



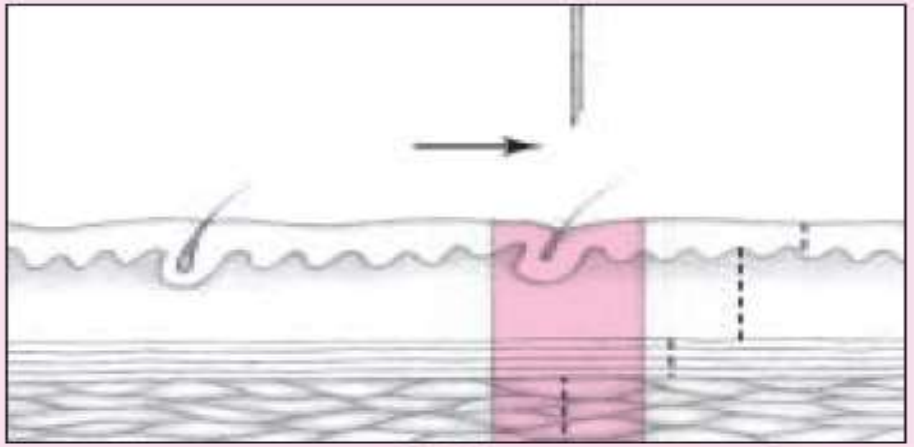
To begin, place your finger on the skin surface, and pull the skin and subcutaneous layers out of alignment with the underlying muscle. You should move the skin about ½" (1 cm).



Insert the needle at a 90-degree angle at the site where you initially placed your finger. Inject the drug and withdraw the needle.



Finally, remove your finger from the skin surface, allowing the layers to return to their normal positions. The needle track (shown by the dotted line) is now broken at the junction of each tissue layer, trapping the drug in the muscle.



# Iron toxicity:
# Acute Iron toxicity

- May occur in children (accidental ingestion)
- Iron is a corrosive metal; as little as 10 tablets can cause serious toxicity or death in children
- Its incidence has decreased by use of child-proof drug containers.
- **Clinical manifestations** include:
  - Acutely, toxic amounts of iron impairs oxidative phosphorylation and mitochondrial function leading to cell death.
  - GIT manifestations (necrotizing gastro-enteritis with abdominal pain, vomiting , bloody diarrhea, hepatic injury)
  - CNS and metabolic manifestations (Metabolic acidosis, hypoglycaemia, encephalopathy, convulsions, coma and death)

- **Treatment of acute Fe toxicity:**
  - **Gastric lavage**: Sodium **bicarbonate** (which by making pH alkaline would decrease iron absorption) or with **Desferrioxamine** (that binds iron and prevent its absorption in intestine; desferrioxamine itself is not absorbed by intestine)
  - **Raw egg or milk** to bind and precipitate Fe
  - **Haemofilteration** or exchange transfusion in serious anuric cases
  - Supportive treatment for shock, metabolic acidosis, liver damage, and encephalopathy

# Iron toxicity: Chronic iron toxicity or haemochromatosis

- It s a genetic disorder where individuals adsorb more Fe than normal
- The increased Fe in the body is deposited in the major organs (liver, heart, pancreas)
- Treatment:
  - **Phlebotomy** (blood withdrawal): a single venesection of 500ml of blood remove ~200-250mg of Fe. It can repeated weekly
  - **Desferrioxamine** by intermittent IM injection