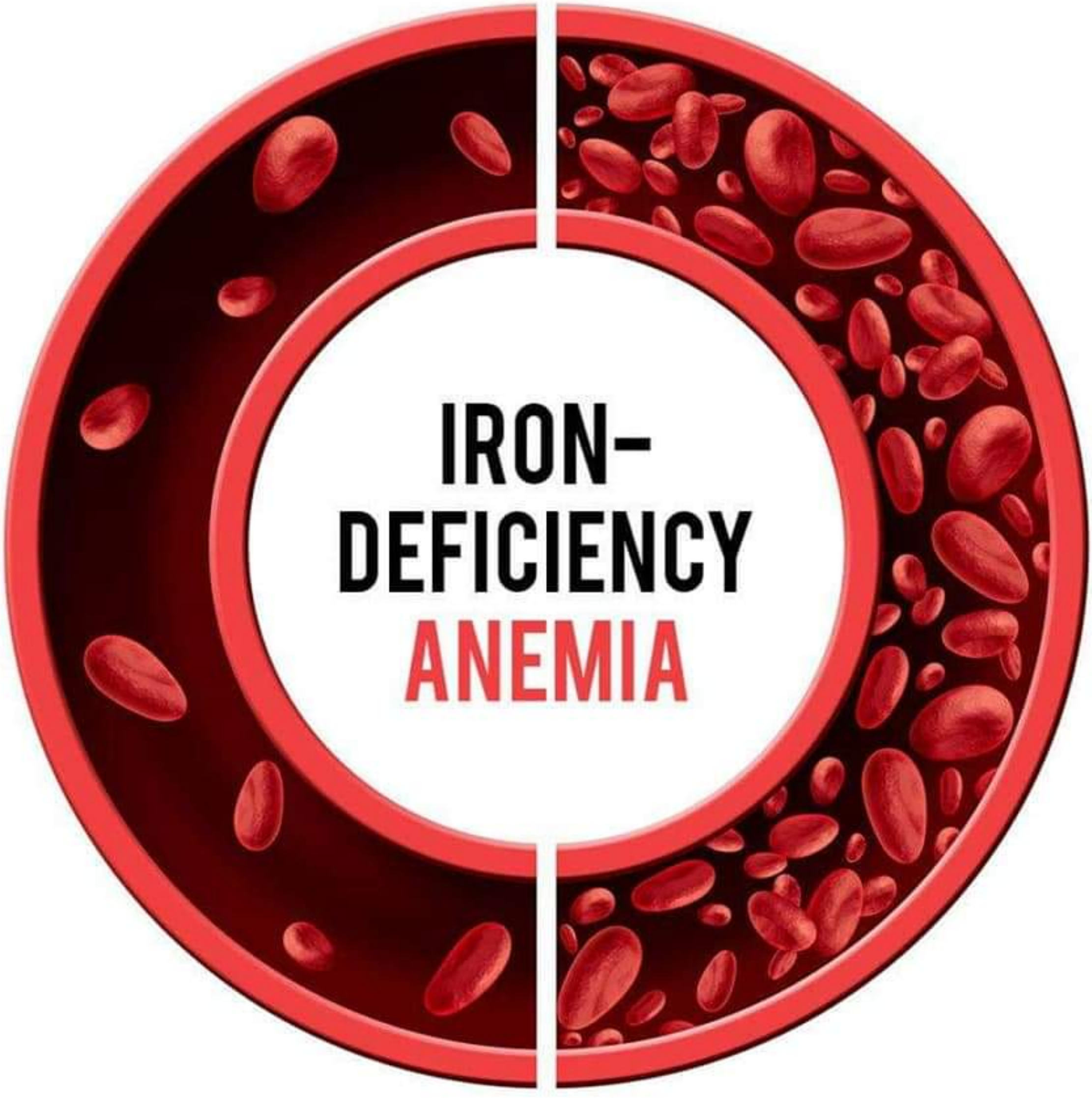

IRON-
DEFICIENCY
ANEMIA

# Clinical Presentation

- Patients may present with :

a) No signs or symptoms coming to medical attention only because of abnormalities noted on laboratory tests

b) Features of the underlying disorder responsible for the development of iron deficiency

c) Manifestations common to all anemias

d) One or more of the few signs and symptoms considered highly for iron deficiency

# Symptoms due to anemia

- Easy fatigability


- Palpitation

- Tinnitus

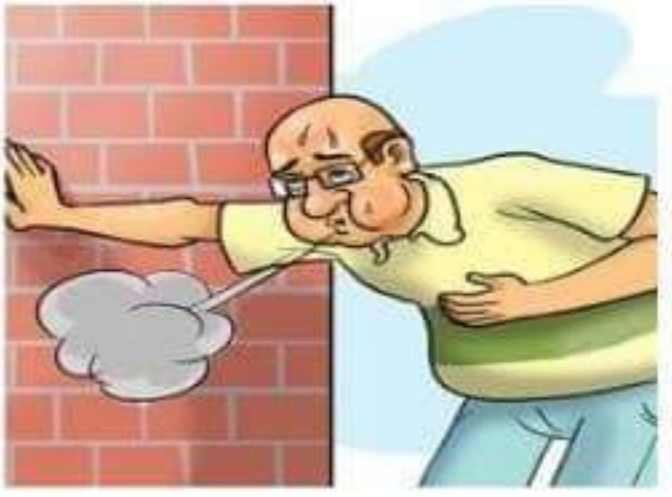
- Headache

- Irritability

- Lightheadedness

- Angina

- Breathlessness



# Symptoms independent of anemia

- Pagophagia ( highly specific symptom of iron deficiency)

- Restless legs

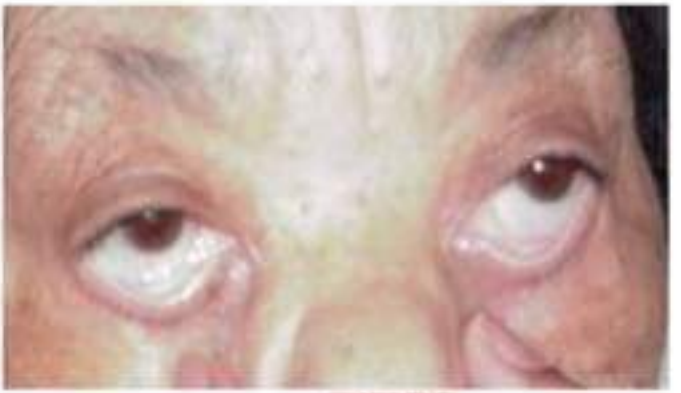
- Dysphagia

- Hair loss

- Parasthesias

# Signs of iron deficiency anemia

- Pallor



- Glossitis

- Angular stomatitis

- Koilonychia

- Tachycardia

-increased heart rate and cardiac output

- Plummer –Vinson syndrome:

-microcytic hypochromic anemia

-atrophic glossitis

-esophageal webs in middle aged women

These mucosal abnormalities are premalignant and occasionally carcinoma develops at the site.

# Laboratory Findings

## Serum iron profile

| | Normal range |
|---|---|
| Serum ferritin | 15-300µg/L |
| Serum iron | 50-150µg/dL |
| Serum transferrin saturation | 30-40% |
| Total iron binding capacity (TIBC) | 310-340µg/dL |
| Serum transferrin receptor (TFR) | 0.57-2.8µg/L |
| Red cell protoporphyrin | 30-50µg/dL |

## Peripheral blood

RBC count

Hemoglobin concentration

Red cell indices:

-MCV

-MCH

-MCHC

-RDW

Reticulocyte count : normal or decreased

# Peripheral smear

## Erythrocytes

-Microcytic hypochromic

-Anisocytosis (earliest recognizable morphologic change of erythrocytes)

-Pencil cells (elongated hypochromic elliptocytes)

-Target cells (sometimes)

Leukocytes

Normal

Platelet

Thrombocytosis :

- due to chronic blood loss
- in actively bleeding patients

Thrombocytopenia :

- associated with more severe anemia
- occurs almost as frequently as thrombocytosis in infants and children
- in adults either as the presenting hematologic problem or early during response to iron therapy for anemia

# Bone Marrow

Cellularity: variable

M : E ratio : variable

Erythropoiesis:

-erythroblasts smaller than normal

-narrow ragged rims of cytoplasm containing little hemoglobin

Myelopoiesis : normal

Megakaryopoiesis : normal

**Gold standard for diagnosis of iron deficiency**

-Assessment of iron stores by evaluating the amount of iron in marrow macrophages.

-Decreased or absence of hemosiderin evaluated after staining by the simple Prussian blue method.

Technical barriers

1.Marrow aspiration (invasive method)

2.Differentiation of iron from within macrophages from artifacts is not easy

3.Patients transfused with or treated with parenteral iron

4.Seen also in chronic myelogenous leukemia and myelofibrosis

# Differential Diagnosis

| Tests | Iron deficiency | Anemia of chronic disease | Thalassemia | Sideroblastic anemia |
|---|---|---|---|---|
| Smear | Microcytic hypochromic | Normocytic normochromic | Microcytic hypochromic with target cells | Variable |
| Serum iron | < 30 | <50 | Normal to high | Normal to high |
| TIBC | <360 | <300 | Normal | Normal |
| Percent saturation | <10 | 10-20 | 30-80 | 30-80 |
| Ferritin ( µg/L) | <15 | 30-200 | 50-300 | 50-300 |
| Hemoglobin pattern on electrophoresis | Normal | Normal | Abnormal with β thalassemia; can be normal with α thalassemia | Normal |

## Other differential diagnosis of microcytic hypochromic anemia

Normal or increased body iron stores:

- Iron-refractory iron-deficiency anemia
- Atransferrinemia
- Aceruloplasminemia
- Divalent metal transporter 1 (DMT1 or SLC11A2) deficiency
- Heme oxygenase 1 deficiency

# Management of iron deficiency

Goal :

-To repair anemia

-To provide stores of at least 0.5-1 g of iron

(sustained treatment for 6-12 months after correction of anemia needed to allow for repletion of iron stores)

Recognition and treatment of the underlying cause should be done.

# Oral Iron therapy

-For adults, up to 300 mg of elemental iron/day, as 3-4 iron tablets ( each containing 50-65mg elemental iron)

-Taken on an empty stomach(gastrointestinal irritation is common)

-Absorption is enhanced by orange juice, meat,poultry,fish.

-Absorption inhibited by cereals,tea,milk.

-A dose of 200-300mg of elemental iron per day should result in the absorption of iron up to 50mg/d.

-In children, optimal dosage is 1.5-2.0mg elemental iron per kg body weight given orally three times a day. (palatable elixirs and syrups preferred)

# Oral Iron Preparations

| Generic name | Tablet (iron content), mg | Elixir (iron content), mg in 5ml |
|---|---|---|
| Ferrous sulphate | 325 ( 65)<br>195 (39) | 300 (60)<br>90 (18) |
| Extended release | 525 (105) | |
| Ferrous fumarate | 325 (107)<br>195 (64) | 100 (33) |
| Ferrous gluconate | 325 ( 39) | 300 (35) |
| Polysaccharide iron | 150 (150)<br>50 (50) | 100(100) |

## Side effects of oral iron therapy

i)heartburn

ii)nausea

iii)vomiting

iv) abdominal cramps

v)diarrhoea or constipation

vi)staining of teeth

vii)metallic taste

❖ Response to treatment :

-Depends on the erythropoietin stimulus and rate of absorption

-Reticulocyte count should begin to increase within 4-7 days after initiation of therapy and peak at 1-

1 ½ weeks

-Hemoglobin concentration :

After 4-5 weeks : halfway back to normal

After 2 months or sooner : normal level

❖ Failure of oral iron therapy may be due to:

a) Incorrect diagnosis

b) Failure of patient to take the prescribed medication

c) Inadequate prescription

d) Continuing of iron loss in excess of intake

e) Malabsorption of iron

# Iron Tolerance Test

- To determine the patient's ability to absorb iron
- Two iron tablets given to the patient on empty stomach.
- Serum iron measured serially over the subsequent 2 hours.
- Normal absorption results in an increase in the serum iron of at least 100µg/dL.
- If iron deficiency persists, may be necessary to switch to parenteral iron therapy.

# Parenteral iron therapy

Indications:

- Severe iron deficiency anemia
- Unable to tolerate oral iron
- Non compliance
- Loses iron (blood) at a rate too rapid for the oral intake to compensate for the loss (e.g., hereditary hemorrhagic telangiectasia)
- Has a disorder of the gastrointestinal tract, like ulcerative colitis, in which symptoms may be aggravated by iron therapy
- Unable to absorb iron from the gastrointestinal tract

## Types of parenteral iron preparation

-Iron dextran

-Iron sucrose (Venofer)

-Sodium ferric gluconate (Ferrlecit)

-Ferric carboxymaltose

Formula for calculation of amount of iron needed by a patient:

**Body weight (kg) x 2.3 x (15- patient's hemoglobin, g/dL) + 500 or 1000 mg (for stores)**

Parenteral iron is given in 2 ways :

-Administer total dose of iron required to correct the hemoglobin deficit and provide the patient with at least 500mg of iron stores

-Give repeated small doses of parenteral iron over a protracted period.

Common in dialysis center.

## Iron dextran

-Contains 50mg of iron per millimeter of solution

-Can be given IM or IV

-Complication : anaphylactic reaction

(Having epinephrine, oxygen and facilities for resuscitation available)

-Test dose (25mg) is given initially to test for hypersensitivity. If this is well tolerated, the full dose may be given.

-Smaller doses can be given (each dose consisting of only 2ml or less)

-Total dose infusion can be given.

-If larger doses is to be given (>100mg), the iron preparation should be diluted in 5% dextrose in water or 0.9% NaCl solution. The iron solution can then be infused over a 60-90 minute period or at a rate convenient for the attending nurse.

Iron sucrose

- 20mg of iron per milliliter
- Recommended administration : 5ml (100mg of elemental iron) administered no more frequently than three times a week.
- Can be administered to patients manifesting sensitivity reactions to iron dextran or sodium ferric gluconate.

Sodium ferric gluconate

- 12.5 mg of elemental iron per milliliter
- Recommended administration : 125mg of elemental iron with the preparation eluted in 100ml of 0.9% NaCl and given intravenously over a period of one hour.
- Side effects almost similar to iron dextran, but less severe.

## Ferric carboxymaltose (Injectafer)

-First third generation intravenous iron.

-50 mg of elemental iron per milliliter

-For patients weighing 50kg or more : Give Injectafer in two doses separated by at least 7 days. Give each dose as 750mg for a total cumulative dose of 1500mg of iron per course.

-For patients weighing less than 50kg : Give Injectafer in two doses separated by at least 7 days. Give each dose as 15mg/kg body weight.

- After intravenous administration, it is found in the reticuloendothelial system ; liver, spleen and bone marrow. The iron slowly dissociates from the complex is used for hemoglobin synthesis.

- Advantages of ferric carboxymaltose:

1. Doesn't contain dextran or modified dextrans and doesn't react with dextran antibodies therefore the risk of anaphylactic reactions is very low.
2. Unlike iron sucrose, it has a nearly pH (5.0 to 7.0) and physiological osmolarity.
3. More stable than sodium ferric gluconate and iron sucrose, producing a slow delivery of of iron to the binding site and has an acute toxicity in animals 1/5 that of iron sucrose.
4. Much higher doses over a short period of time can be administered:
   - fewer administrations needed
   - increase patient's comfort
5. Better suited for outpatient use.
   -lesser number of infusions required
   -test dose not required
   -higher dose can be administered

Side effect of parenteral iron therapy

-pain, abscess at the site of injection

-staining of skin ( Z track method to reduce staining)

-arthralgia

-skin rash

-low grade fever

-hypotension

-myalgia

-headache

-abdominal pain

-nausea

-vomiting

-dizziness