# Lecture_5

# Sideroblastic anemia

# &

# Anemia in CKD

**Fifth year students**

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# Sideroblastic anemia

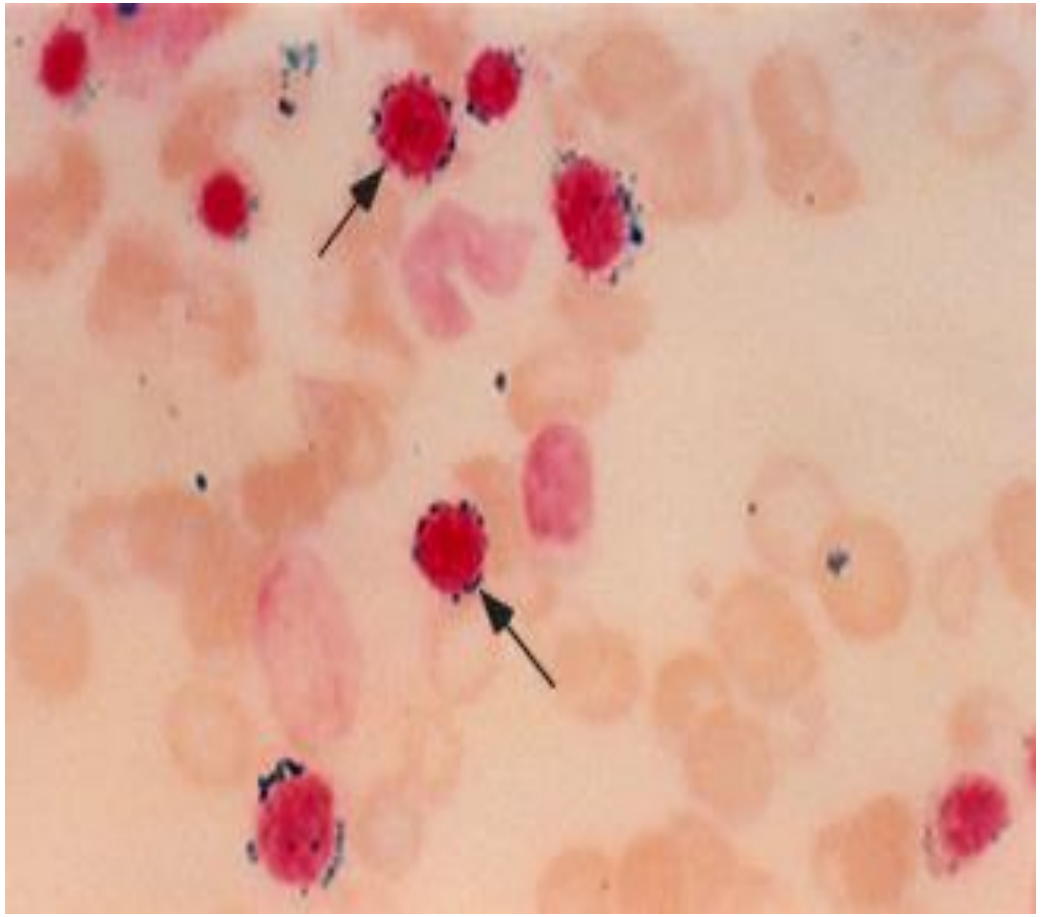
- is a form of anaemia resulted from failure of incorporation of iron into the heme molecule despite the availability of adequate iron store

- This is a refractory anaemia with hypochromic cells in the peripheral blood and increased marrow iron

- Sideroblastic anemia  is defined by the presence of many pathological ring sideroblasts in the bone marrow
- Sideroblastic anemia is primarily a laboratory diagnosis, made on the basis of bone-marrow examination with Prussian blue stain

- A sideroblast is an erythroblast (normoblast) that has stainable iron deposits in mitochondria surrounding nucleus

- Ringed sideroblasts are hallmark



## Etiology of Sideroblastic anemias

A. Hereditary

1) X-linked are further divided into
   - pyridoxine-responsive (>50%) due to δ-amino levulinic acid synthase (ALAS-2) deficiency
   - pyridoxine-resistant due to ABC7 gene mutation presented with andemia and CNS abnormality
2) Autosomal recessive sideroblastic anemia has been described in Jews of Persian descent
3) DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy, and deafness) syndrome is associated with sideroblastic anemia that is responsive to vitamin B-1 (thiamine).

## B. Acquired causes :

1) clonal (myelodysplastic syndrome)
2) nonclonal (metabolic) types
   - Nutritional deficiencies (copper, vitamin B-6)
   - Lead poisoning (disputed by some authorities as a cause)
   - Zinc overdose
   - Alcohol
   - Drugs (anti-TB, chloramphenicol, progesterone, phenacetin, busulfan)
   - Hypothermia
   - Idiopathic

➢Vitamin B-6 (pyridoxine) acts as a coenzyme in the first, rate-limiting step in heme formation catalyzed by δ-ALAS

# Clinical features

- Mostly nonspecific clinical effects, which may exist for several years before being identified:
  - Pallor
  - anorexia
  - Fatigue & weakness
  - dizziness
  - enlarged lymph nodes

- Heart and liver failure may develop from excessive iron deposition in these organs, causing dyspnoea, exertional angina, slight jaundice, and hepatosplenomegaly

- Hereditary sideroblastic anaemia is associated with increased GI absorption of iron, causing signs of hemosiderosis

- Additional symptoms in secondary sideroblastic anemia depend on the underlying cause

## Diagnosis

1. **CBC:**

- hypochromic or normochromic, and slightly macrocytic erythrocytes
- Unlike iron deficiency anemia, sideroblastic anemia lowers Hb and raises serum iron and transferrin levels
- In turn, faulty Hb production raises urobilinogen and bilirubin levels
- Platelet and WBC levels remain normal, but thrombocytopenia or leukopenia occasionally occurs

2. **Bone Marrow:** Ringed sideroblasts on bone marrow aspirate, stained with Prussian blue confirm the diagnosis, RBC precursors may be megaloblastic, with anisocytosis (abnormal variation in RBC size) and poikilocytosis (abnormal variation in RBC shape).

## Treatment:

1. Removal of toxic agent
2. Pyridoxine (vitamin B-6) trial in all cases of sideroblastic anemia as many acquired and certain congenital forms of sideroblastic anemia respond to this relatively safe drug, pyridoxine (usually 50-200 mg/d)
3. Thiamine (vitamin B-1) works by an understood mechanism to correct sideroblastic anemia in DIDMOAD syndrome
4. Folic acid has been reported to reverse sideroblastic changes by itself in some patients

5) Management of iron overload: Iron chelating agents

1. Deferoxamine (desferrioxamine; Desferal) used for iron overload due to repeated blood transfusions , it is given by subcutaneous pump for several hours a day
2. Deferasirox (Exjade) is a relatively new oral iron chelator given as once-daily oral tablet.

6) Chloroquine has been successfully used to treat pyridoxine-resistant sideroblastic anemia

7) Transfusion is the mainstay of treatment for those whose sideroblastic anemia does not respond to pyridoxine therapy ,but should be avoided if in asymptomatic patient with mild to moderate anemia

## Summary of sideroblastic anemia

- SA develops when entry of iron into mitochondria of developing RBCs is blocked
- Iron accumulates in mitochondria in deposits around nucleus, called ringed sideroblasts
- Iron studies – elevated total iron, variable iron binding capacity, normal to decreased transferrin saturation, and increased ferritin

## Anaemia in CKD

- Anaemia is common in patients with chronic kidney disease and contributes to many of the non-specific symptoms, including fatigue and SOB
- Haemoglobin can be as low as 5–7 g/dL in CKD stage 5, although it is often less severe or absent in patients with polycystic kidney disease

- Anaemia is more prevalent in those on haemodialysis as a result of haemolysis in the dialysis circuit
- Hence many patients require iron supplements, which may be given intravenously for those with iron intolerance or in situations where adherence may be difficult

# Causes of anaemia in CKD

1) Deficiency of erythropoietin
2) Toxic effects of uraemia on marrow precursor cells
3) Reduced red cell survival
4) Blood loss due to capillary fragility and poor platelet function
5) Reduced intake, absorption and utilisation of dietary iron

# Management:

- Exclusion of other causes of anaemia
- Recombinant human erythropoietin is very effective in correcting the anaemia of CKD and improving symptoms

➢ Erythropoietin treatment does not influence mortality, however, and correcting the Hb to normal levels may carry some extra risk ex: hypertension and thrombosis

- The target Hb is usually between 100 and 120 g/L

- Erythropoietin is less effective in the presence of iron deficiency, active inflammation or malignancy, in particular myeloma

## Parenteral iron therapy

IV iron can be given to patients :

- unable to tolerate oral iron
- whose needs are relatively acute
- who need an ongoing iron due to persistent GI blood loss or malabsorption

- Iron dextran has high-molecular-Wt that is why carry risk of serious anaphylactic reaction
- Fortunately, newer iron complexes are available in the such as sodium ferric gluconate (Ferrlecit), iron sucrose (Venofer), and ferric carboxymaltose (Injectafer), that have much lower rates of adverse effects

## Parenteral iron is used in two ways:

1) administer the total dose of iron required to correct the Hb deficit and provide the patient with at least 500 mg of iron stores
2) the second is to give repeated small doses of parenteral iron over a prolong period

- The amount of iron needed by an individual patient is calculated by the following formula =

**Body Wt. (kg) × 2.3 × (15 – patient's Hb g/dL)+ 500 or 1000 mg (for stores)**

- If a large dose of iron dextran is to be given (>100 mg), the iron preparation should be diluted in 5% dextrose or 0.9% NaCl solution then be infused over a **60-90** min

- Early in the infusion of iron, if chest pain, wheezing, a fall in blood pressure, or other systemic symptoms occur, the infusion of iron should be stopped immediately

- **Which of the following is *not* true about sideroblastic anemia?**
  a. Maybe inherited
  b. It may respond to pyridoxine
  c. Maybe caused by folate deficiency
  d. Most frequently caused by myelodysplasia
- **Which of the following organ is not damaged by transfusional iron overload?**
  a. Kidneys
  b. Parathyroid
  c. Heart
  d. Liver
  e. Pituitary

Thank you