Anaemia of Chronic Illness: Causes and Pathophysiology

Anemia of chronic disease (ACD) is the **second most common cause of anemia** after iron deficiency anemia (IDA). It is typically **mild to moderate** in severity and is associated with **chronic infections, inflammatory conditions, malignancies, and chronic kidney disease (CKD)** .

Etiology & Associated Conditions

- **Chronic infections** : e.g., HIV/AIDS, tuberculosis, osteomyelitis
- **Chronic inflammatory disorders** : rheumatoid arthritis, systemic lupus erythematosus (SLE), inflammatory bowel disease (IBD), vasculitis, sarcoidosis
- **Malignancies** : both hematologic and solid tumors
- **Chronic kidney disease**
- **Organ transplantation** : chronic graft rejection

Pathophysiology

Inflammation leads to multiple disturbances in iron metabolism and erythropoiesis:

1. **Hepcidin-Mediated Iron Sequestration**

   - **IL-6** ? ? Hepcidin (liver)
   - Hepcidin inhibits **ferroportin** (iron exporter in macrophages & enterocytes) ? ? iron release to plasma
   - Iron is trapped in macrophages of the reticuloendothelial system ? **functional iron deficiency**

2. **Reduced Erythropoiesis**

   - Inflammatory cytokines (IL-1, IL-6, TNF-?, IFN-?) suppress erythroid progenitor cells
   - Shortened RBC survival

3. **Erythropoietin Resistance**

   - Blunted or inadequate erythropoietin (EPO) response relative to anemia severity
   - In CKD, EPO production is intrinsically reduced

Laboratory Findings

Test	ACD	Iron Deficiency Anemia (IDA)
Serum Iron	?	???
TIBC	? or normal	?
Ferritin	? or normal	?
Transferrin Saturation	?	???
RDW	Normal or mildly ?	?

Test	ACD	Iron Deficiency Anemia (IDA)
MCV	Normocytic or microcytic	Microcytic
Bone Marrow Iron	Normal or ?	Absent

Ferritin is an acute phase reactant and is typically elevated in ACD, helping distinguish it from IDA.

Diagnosis

- **Clinical context** : Known chronic inflammatory or malignant condition
- **Iron studies** : Low serum iron, low TIBC, normal or high ferritin
- **Rule out iron deficiency anemia** : Consider checking **soluble transferrin receptor (sTfR)** or **bone marrow biopsy** if diagnosis is unclear
- **CKD-specific** : Measure **serum erythropoietin levels** if indicated

Differential Diagnosis

- Iron deficiency anemia
- Thalassemias
- Myelodysplastic syndromes
- Sideroblastic anemia
- Anemia of critical illness

Treatment

1. **Treat Underlying Condition**

   - Management of infection, autoimmune disease, or malignancy

2. **Erythropoiesis-Stimulating Agents (ESAs)**

   - **Epoetin alfa** or **darbepoetin alfa**
   - Primarily used in:
     - CKD-associated anemia
     - Cancer-related anemia (with caution)

   Use with **iron supplementation** if iron-restricted erythropoiesis is present.

3. **Iron Therapy**

   - Only if concurrent **true iron deficiency** is documented
   - **IV iron** preferred in patients on dialysis or those with inflammation-induced impaired oral absorption

4. **Blood Transfusion**

- Reserved for **severe symptomatic anemia** or hemodynamically unstable patients
- Avoid routine transfusion in **critically ill** unless Hb < 7–8 g/dL

Anemia of Critical Illness

- Common in ICU patients by day 3 of admission
- Caused by:
  - Suppressed EPO response
  - Cytokine-induced bone marrow suppression
  - Frequent phlebotomy
- Managed with restrictive transfusion strategy

High-Yield Pearls

- ACD is **not due to iron deficiency** , but rather **iron trapping** and impaired utilization.
- **Hepcidin** is the key mediator of iron dysregulation.
- **Normocytic, normochromic anemia** is typical, but microcytosis may occur with chronicity.
- **Ferritin helps differentiate ACD from IDA** : it is **elevated in ACD** , **low in IDA** .
- Always assess for **co-existing iron deficiency** in patients with ACD.