

Anemia of chronic disease
=Anemia of chronic disorders
(ACD)

Anemia of chronic disease (ACD)

- definition

ACD is a common type of anemia that occurs in patients with infectious, inflammatory, or neoplastic diseases that persist for more than 1 or 2 months.

It does not include anemias caused by marrow replacement, blood loss, hemolysis, renal insufficiency, hepatic disease, or endocrinopathy, even when these disorders are chronic.

Anemia of chronic disease (ACD) - epidemiology

The ACD is extremely common

- ACD is more common than any anemia syndrome other than blood loss with consequent iron deficiency
- ACD is the most common cause of anemia in hospitalized patients
- After patients with bleeding, hemolysis, or known hematologic malignancy were excluded, 52% of anemic patients met laboratory criteria for the anemia of chronic disorders
- ACD is observed in 27% of outpatients with rheumatoid arthritis and in 58% of new admissions to hospital rheumatology units

Disorders Associated with the Anemia of Chronic Disease ACD(1)

- Chronic infections
 - Pulmonary infections: abscesses, emphysema, tuberculosis, pneumonia
 - Subacute bacterial endocarditis
 - Pelvic inflammatory disease
 - Chronic urinary tract infections
 - Chronic fungal disease
 - HIV infections
 - Osteomyelitis
- Chronic, noninfectious inflammations
 - Rheumatoid arthritis
 - LES (Systemic lupus erythematosus)
 - Severe trauma, thermal injury
 - Vasculitis

Disorders Associated with the Anemia of Chronic Disease ACD(2)

- Malignant diseases
 - Cancer
 - Hodgkin's disease and Non-Hodgkin's Lymphomas
 - Leukemias
 - Multiple myeloma
- Miscellaneous
 - Alcoholic liver disease
 - Thrombophlebitis
 - Ischemic heart disease
- Idiopathic ACD

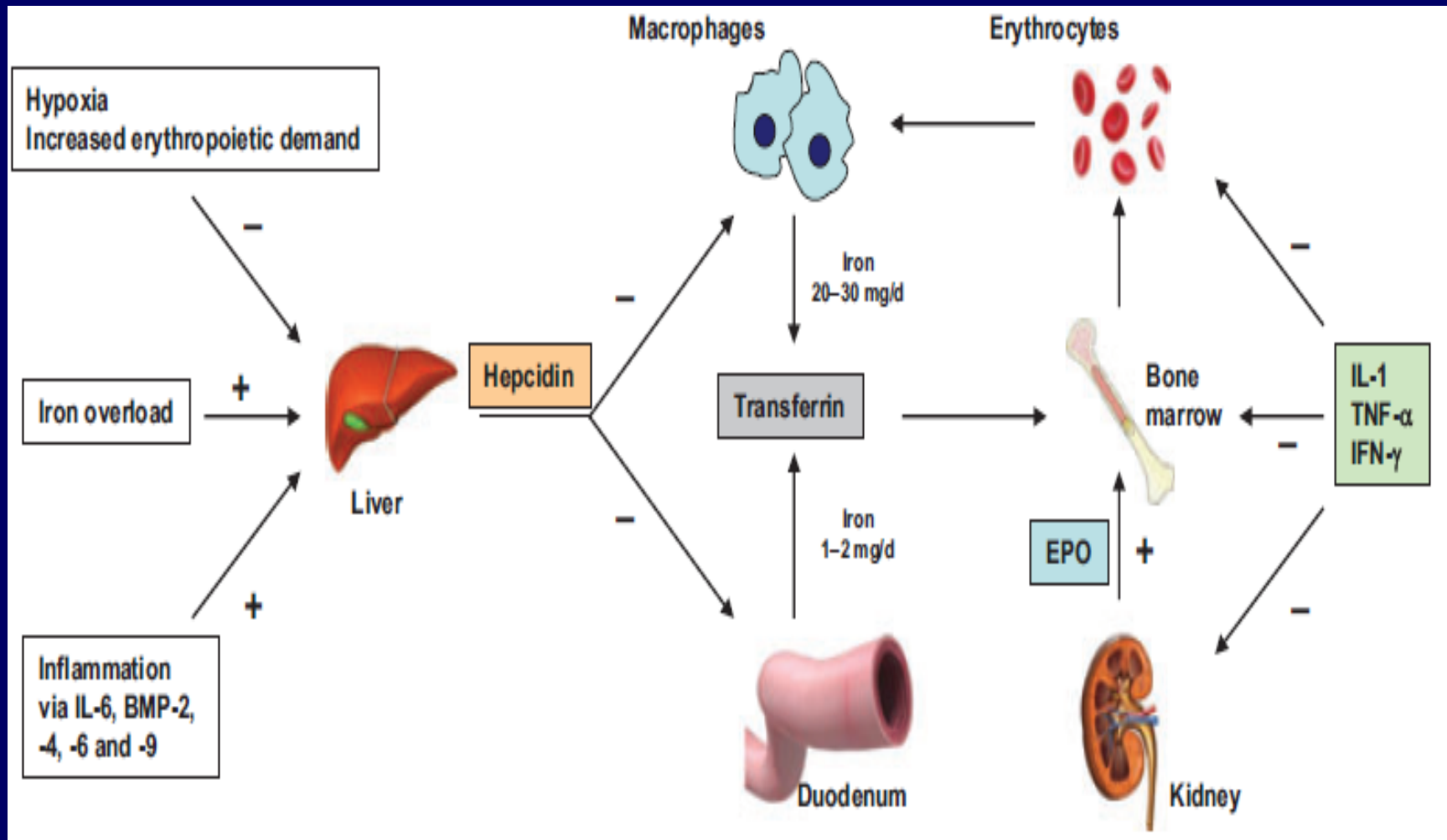
Anemia of chronic disease (ACD) - pathogenesis (1)

- Shortened red cell life span, moderately 20-30% (from 120 to 60-90 days)
- Relative bone marrow(erythropoiesis) failure
 - Cytokines released from inflammatory cells (TNF- α , IL-1, IFN- γ , hepcidin) affects erythropoiesis by inhibiting the growth of erythroid progenitors
 - Serum erythropoietin levels in patients with ACD are normal when compared to healthy subjects but much lower than levels in non-ACD anemic patients

Anemia of chronic disease (ACD) - pathogenesis (2)

- Heparin — One acute phase protein that appears to be most directly involved in iron metabolism is hepcidin, which appears to be a component of the innate immune response to acute infection. Heparin is the predominant negative regulator of iron absorption in the small intestine, iron transport across the placenta, as well as iron release from macrophages, secondary to its effect on internalization and degradation of the iron export protein ferroportin.

Anemia of chronic disease (ACD) - pathogenesis (3)



Anemia of chronic disease (ACD) - pathogenesis (4)

ABNORMAL IRON METABOLISM

- Activation of the reticuloendothelial system with increased iron retention and storage within it
- impaired release of iron from macrophages to circulating transferrin (impaired reutilization of iron)
- Reduced concentration of transferrin
(decreased production, increase sequestration in the spleen and in the foci of inflammation, increase loss)

Anemia of chronic disease (ACD) - symptoms

- Symptoms of the underlying disease
(malignancy or chronic inflammatory
disease)
- Symptoms of the anemia

Anemia of chronic disease (ACD) - laboratory features(1)

- The anemia is usually mild or moderate (Hb 7-11g/dl)
 - lower values are observed in 20-30% of patients
- The anemia is most often normochromic and normocytic (MCHC and MCV are normal)
 - MCV 70-80 fl in 5-40% of patients with ACD
 - MCHC 26-32 g/dl in 40-70%
- Erythrocyte sedimentation rate (ESR) - usually rapid
- Retikulocytes - most often normal or slightly decreased number, increased count is rarely

Anemia of chronic disease (ACD) - laboratory features(2)

- Iron metabolism

1. Serum Iron - decreased (it is necessary for the diagnosis of ACD)
2. TIBC - reduced or low-normal (N)
3. Transferrin saturation(TS) - moderately decreased (higher than in iron-deficiency anemia), usually $> 10\%$
4. Serum Ferritin-increased or normal
5. Serum Transferrin Receptor (sTR)-Normal
6. Sideroblasts in the bone marrow-reduced (5-20%)

Anemia of chronic disease (ACD) - differential diagnosis

Laboratory features	Iron deficiency	ACD
		without iron deficiency
sFe	↓↓	↓
TS	↓<10%	↓>10%
TIBC	↑	↓, N
sFerritin	↓<10μg/L	↑>200μg/L, N
Sideroblasts	<10%	10-20%
sTR	↑	N

Advantages of ACD for patients(?!)

- - Withdrawal of iron by increased storage of the metal within the reticuloendothelial system acts to limit the availability of iron to microorganisms or tumor cells and thereby inhibit their growth and proliferation
 - Decreased hemoglobin reduces the oxygen transport capacity of the blood and decreases the overall oxygen supply, which may primarily affect rapid proliferating (malignant) tissues and micro-organism
 - Retention and storage of iron in retuendothelial system directly and indirectly via cytokines strongly affects cell mediated immune function

Anemia of chronic disease (ACD) - therapy (1)

1. Treatment of the underlying disorder

2. Iron supplementation (IS)

- for patients with ACD with chronic infection or malignancy IS should be strictly avoided

- IS benefit patients with ACD associated with auto-immune or rheumatic disorders.

- when ACD is complicated by iron deficiency (about 27% patients)

Anemia of chronic disease (ACD) - therapy (2)

3. Transfusion demand (about 30%)patients who have low Hb and are symptomatic
4. Recombinant erythropoietin 10.000 units 3 times a week i.v. or s.c. 2-3tg, in the absence of response 20000u., If there is still no response, the treatment should be discontinued. (in 40% of patients it reduces number of transfusions)
Darbopoietin (erythropoietin analog with modified glycosylation permitting a longer half-life)-2,25µg/kg/2 week
5. Sequential administration of erythropoietin and iron (48h later)
5. Iron chelation with deferoxamine - in some patients therapy was associated with a rise in hemoglobin level
6. In future anti-TNF-antibodies