]Anemia of chronic disease (ACD):

This anemia is designated as *anemia of chronic disease* or *anemia of inflammation*. Commonly known “locally in Iraq” as “Secondary anemia”.

It is a common type of anemia, mild to moderate, characterized by being normochromic normocytic and if advanced become mildly hypochromic and even microcytic anemia.

Most patients suffer from a systemic disease; chronic infection, chronic inflammation, or some malignancies.

Patients in this defined subset typically have an elevated Erythrocyte sedimentation rate (ESR) and/or elevated C-reactive protein (CRP).

It is *characterized by* inadequate erythrocyte production in the setting of a low serum iron level, low to normal transferrin level (total iron binding capacity, TIBC), and normal to elevated ferritin level with adequate or even increased iron stores in the bone marrow macrophages. The defining feature of this condition is the sequestration of iron in macrophages.

The anemia is caused by the inhibitory effects of inflammatory cytokines on erythrocyte production. Among the cytokines, interleukin-6 has a central role. Interleukin-6 increases the production of the negative iron regulatory protein hepcidin by hepatocytes. Hepcidin blocks the release of iron from macrophages and hepatocytes, causing the characteristic hypoferremia associated with this anemia and limiting the availability of iron to the developing erythrocytes, also hepcidin impair the flow of iron from intestinal mucosal cells to plasma.

The plasma erythropoietin (Epo) level in ACD remains inversely correlated with the hemoglobin level but compared with patients with other types of anemia and normal renal function, it is inappropriately low. The

plasma levels of TNF-α, IL-1 and IL-6 are raised which in turn reduce Epo production

Marrow Iron Stain: Important information obtained from marrow examination is the *content* and *distribution* of iron. Iron in a marrow preparation can be found as storage iron in the cytoplasm of macrophages and as functional iron in nucleated red cells.

In normal individuals, a few Prussian blue–staining particles can be found inside or adjacent to many macrophages. Approximately one third of nucleated red cells contain one to four fine blue inclusion bodies, and such cells are called *sideroblasts*.

In iron deficiency anemia both sideroblasts and macrophage iron are absent.

The marrow morphology is normal in ACD, while sideroblasts are decreased or absent but macrophage iron is increased.

The increase in storage iron in association with a decreased level of circulating iron and a decreased number of sideroblasts is characteristic of ACD.

Management of ACD:

1. Effective treatment of the underlying disease restores normal erythropoiesis.

2. ACD requires diagnostic studies to rule out reversible causes, such as occult hemorrhage; iron, B_{12}, and folate deficiency; hemolysis; and drug reaction.
3. If treatment of the underlying disease is not effective and the patient has symptoms or medical complications attributable to anemia, one or more of the available anemia-specific treatment modalities should be considered (Blood transfusion, Iron treatment and Erythropoietin). ACD often responds to pharmacologic doses of erythropoietin.

Hematological indices to differentiate between hypochromic anemias:

Hematological indices	**IDA**	**ACD**	**Thalassemia trait**
MCV/MCH	↓	↓ or N	Very low for the degree of anemia
Serum Iron	↓	↓	N
TIBC	↑	↓ or N	N
Transferrin saturation	↓	↓	N
Serum ferritin	↓	N or ↑	N
Serum TfR	↑	N	N
Bone marrow Iron stores	↓	N or ↑	N
Erythroblast Iron	↓	↓	N

IDA: Iron deficiency anemia