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# ELDER CARE

A Resource for Interprofessional Providers



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## Anemia of Chronic Disease

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Anemia is common in older adults, and its prevalence rises with age. The National Health and Nutrition Examination Survey (NHANES III) reports that just over one of every ten adults  $\geq 65$  years is anemic. For individuals age 85 and older, the rate is 20% in women and 25% in men. Of the many types of anemia that can affect older adults, anemia of chronic disease, with or without chronic kidney disease, is the most common (Table 1).

The most common inflammatory processes resulting in ACD are infections, cancers, autoimmune disorders, and chronic kidney disease. In many patients, however, the nature of the inflammatory process is never determined.

### Diagnosis

ACD is typically mild (Hgb level 8-10) and normocytic, though microcytosis sometimes occurs. The serum iron level is low in ACD, and this leads some clinicians to misdiagnose it as iron deficiency. But, in ACD the low iron level reflects inability to mobilize adequate iron stores from the reticuloendothelial system into the blood, rather than a deficiency of iron. Body iron stores are actually adequate.

A distinguishing feature between iron deficiency and ACS is that in ACD, low serum iron levels are accompanied by low or low-normal iron binding capacity (ie, low transferrin level). In iron deficiency, on the other hand, low serum iron levels are accompanied by high iron binding capacity (Figure 1).

Further confirmation of the diagnosis can be obtained with a ferritin level. Ferritin is a measure of iron stores, but it also is an acute-phase reactant whose concentration in the blood increases during acute and chronic inflammation. Thus, in iron deficiency, the ferritin level is typically low, whereas in ACD, the ferritin level is often high.

Difficulty in diagnosis occurs when a patient has a mixed anemia – usually ACD co-existing with iron deficiency. If the patient's iron studies don't match the patterns shown in the figure, the two diagnoses can often be sorted out by ordering a test called "soluble transferrin receptor" and then calculating the ratio of soluble transferrin receptor to the log of the ferritin level. In patients with ACD alone, the ratio is  $< 1$ . With both iron deficiency and ACD, the ratio will be  $> 2$  (Table 2).

| Type of Anemia  | Prevalence |
|---|------------|
| <b>Isolated Causes</b>                                |            |
| Anemia of chronic disease                             | 19.7%      |
| Iron deficiency                                       | 16.6%      |
| Anemia of chronic kidney disease                      | 8.2%       |
| B12 deficiency  | 5.9%       |
| <b>Mixed Causes</b>                                   |            |
| Iron deficiency plus folate and/or B12 deficiency     | 3.4%       |
| Folate and B12 deficiency                             | 2.0%       |
| Anemia of chronic disease with chronic kidney disease | 4.3%       |
| Unknown or other                                      | 33.6%      |

Data from Guralnik and the National Health and Nutrition Examination Survey III.

Anemia of chronic disease (ACD), sometimes called anemia of inflammation, is due to the effects of chronic inflammation, which result in release of mediators like interleukins and tumor necrosis factor. These inflammatory mediators cause dysregulation of iron usage – the result being retention of iron in storage cells of the reticuloendothelial system. This limits iron availability for production of red blood cells, and the end result is anemia.

### TIPS FOR DEALING WITH ANEMIA OF CHRONIC DISEASE (ACD)

- Don't make the mistake of diagnosing iron deficiency just because serum iron levels are low. They are low in ACD, too, even though patients with ACD have adequate iron stores.
- Distinguish ACD from iron deficiency with the combination of iron, transferrin, and ferritin levels (Figure 1), supplemented by soluble transferrin receptor levels when needed.
- Don't treat anemia of ACD with iron unless concomitant true iron deficiency is present.

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## Treatment

**Treat the Chronic Disease** Optimal therapy of ACD is treatment of the chronic disease responsible for inflammation and anemia. But, this is not always possible and other measures are often used.

**Transfusion** Patients with ACD sometimes present with severe anemia, in which case transfusion is needed to prevent hemodynamic compromise. Transfusions are typically considered when the hemoglobin level is < 8 mg/dl.

**Iron** Keep in mind that despite the low level of serum iron, body iron stores are not deficient in ACD. Thus, iron therapy has no benefit and is not indicated. In fact, studies suggest that iron therapy may be harmful in the presence of chronic inflammation by contributing to endothelial dysfunction and vascular events. The only situations in which iron therapy should be used for ACD are when (a) concomitant true iron deficiency is present or (b) patients are receiving, but not responding to, erythropoietin-like drugs.

**Erythropoetic Drugs** Several drugs with erythropoietin-like activity are available in the US, including epoetin alfa, epoetin beta, and darbopoetin. Studies indicate that patients with ACD respond to these drugs with an increase

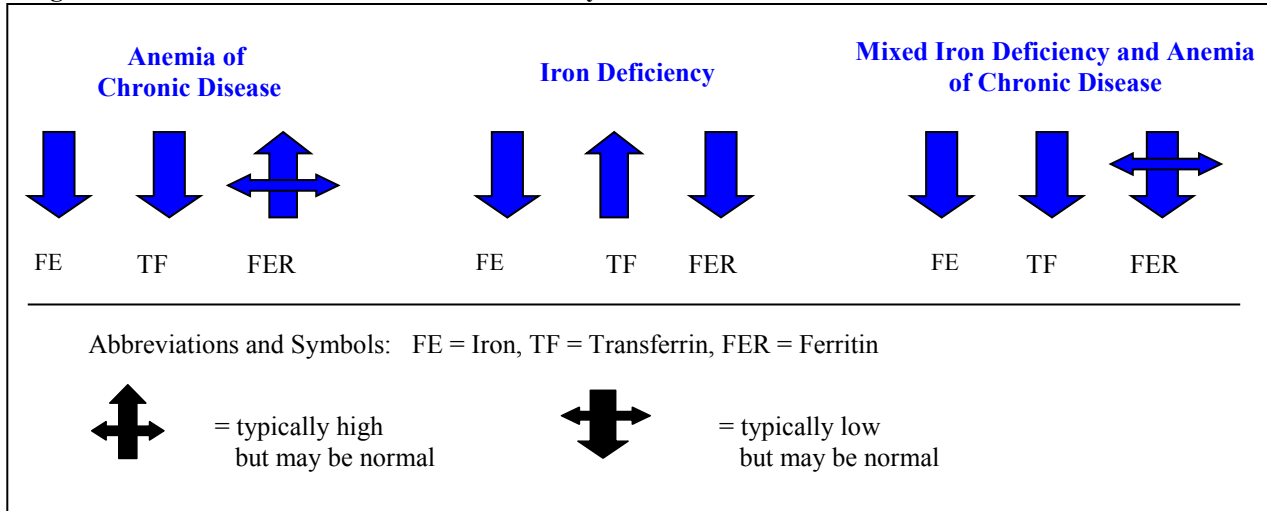
in hemoglobin levels, with the best responses occurring in patients who have connective tissue disorders or chronic kidney disease.

Use of erythropoetic drugs, however, is controversial. Their use – especially when used to raise hemoglobin levels to 11-12 gm/dl, which is the level recommended in some guidelines – has been linked to higher death rates from cardiovascular events, progression or recurrence of certain types of cancer, and an increased rate of venous thromboembolism in patients with cancer. Most experts now feel that if erythropoetic agents are used for ACD, goal hemoglobin levels should be lower than those specified in guidelines. The optimal role of these drugs for ACD is unclear.

| Condition             | Ratio of Soluble Transferrin Receptor to Log of Ferritin Level |
|-----------------------|--|
| ACD                   | <1   |
| ACD + Iron Deficiency | >2   |

ACD = Anemia of Chronic Disease  
Information from Weiss and Goodnough, NEJM, 2005

**Figure 1. Iron Studies in ACD and Iron Deficiency**



## References and Resources

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