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ELDER CARE

A Resource for Interprofessional Providers

Anemia of Chronic Disease

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Anemia, defined as a hemoglobin level <12 g/dL in women and <13 g/dL in men, is common in older adults, and its prevalence rises with age. The National Health and Nutrition Examination Survey reports that just over one of every 10 adults >65 years is anemic. For individuals >85 years the rate is 20% in women and 26% in men. It is even more prevalent in hospitalized older adults of whom 40-50% are anemic. Anemia in older adults is associated with reduced functional capacity, impaired quality of life, increased risk of falls, and is a risk factor for morbidity and mortality.

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 g/dL) 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 (i.e., 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 Figure 1, 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).

Table 1. Causes of Anemia in Adults Age ≥65 Years

Type of Anemia	Prevalence
Isolated Causes	
Anemia of chronic disease	19.7%
Iron deficiency	16.6%
Anemia of chronic kidney disease	8.2%
B12 deficiency	5.9%
Mixed Causes	
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	

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). Anemia of chronic disease (ACD) is due to the effects of chronic inflammation, which results in release of mediators like interleukins and tumor necrosis factor. These inflammatory mediators cause dysregulation of iron usage, resulting in retention of iron in storage cells of the reticulendothelial 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

ACD in advanced age is often multifactorial in etiology, and thus requires a multipronged treatment approach.

Treat the Chronic Disease Optimal therapy of ACD is treatment of the underlying chronic disease responsible for inflammation and anemia. But, this is not always possible which leaves limited options for treatment. Other measures are often used.

Optimize Nutritional Status ACD can be a manifestation of malnutrition in older adults.

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 Hgb level is < 8 mg/dl.

Iron Keep in mind that despite the low serum iron levels, 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, erythropoetic drugs.

Erythropoetic Drugs Several drugs with erythropoietin-like activity are available in the US, including epoetin alpha,

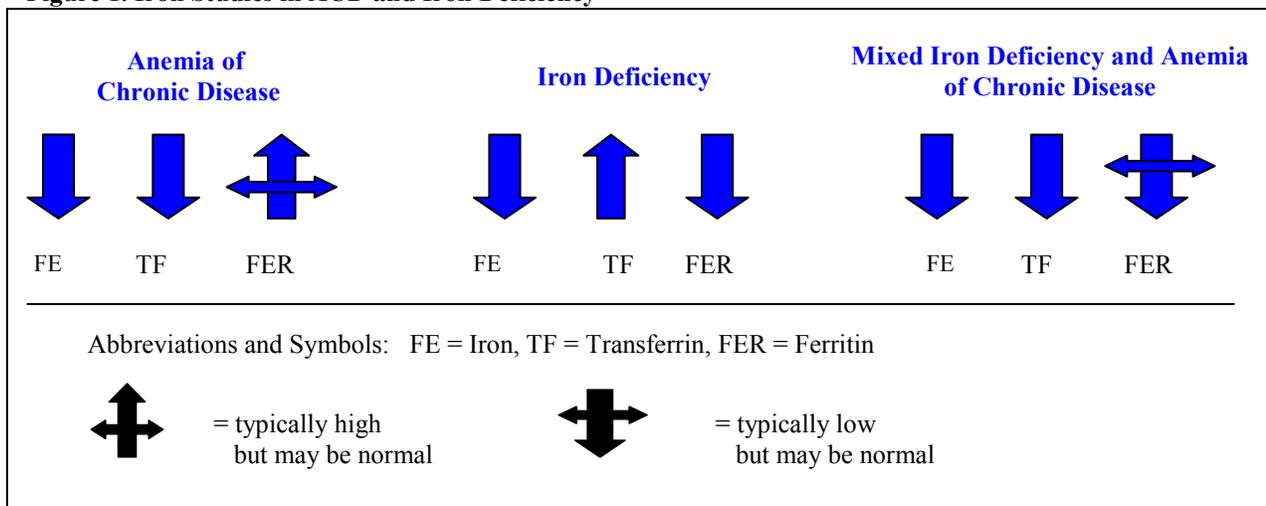
epoetin beta, and darbepoetin. Studies indicate that patients with ACD respond to these drugs with an increase in hemoglobin levels, with the best responses occurring in patients who have connective tissue disorders or chronic kidney disease.

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

- Guralnik JM, Eisenstaedt RS, Ferruci L, Klein HG, Woodman RC. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. *Blood*. 2004;104:2263-2268.
- Tabea Geisel, Julia Martin, Bettina Schulze, et al. An Etiologic Profile of Anemia in 405 Geriatric Patients. *Anemia*. 2014.
- Unger EF, Thompson AM, Blank MJ, Temple R. Erythropoiesis-stimulating agents — time for a reevaluation. *N Eng J Med*. 2010; 362: 189-192
- Weiss G, Goodnough LT. Anemia of chronic disease. *N Eng J Med*. 2005; 352:1011-23.

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