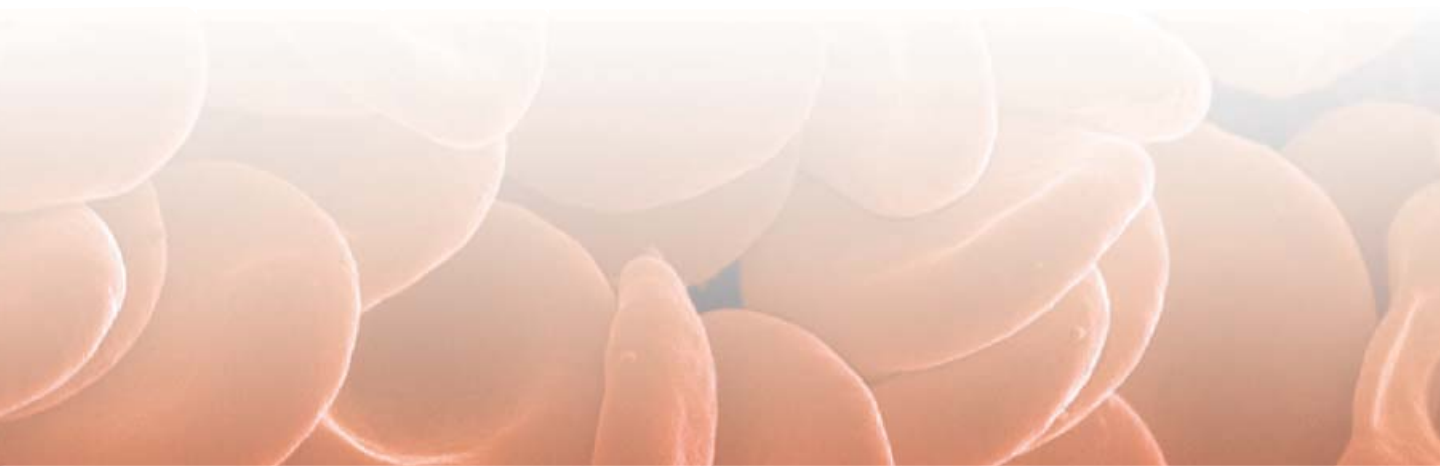


“Failure to evaluate anemia in the elderly could lead to delayed diagnosis of potentially treatable conditions.”

XI *Anemia* & Aging

Key Points

- Anemia is not a normal consequence of aging.
- Failure to evaluate anemia in the elderly could lead to delayed diagnosis of potentially treatable conditions.
- Untreated geriatric anemia is associated with increased mortality, increased prevalence of various comorbidities, and decreased function.
- Treatment of anemia in the elderly has been shown to improve outcomes.



Multifactorial Causes of Anemia in the Elderly

Anemia should not be accepted as an inevitable consequence of aging, as a cause is identified in about 80% of elderly patients.¹ In ambulatory elderly patients, the most common causes of anemia are chronic disease (kidney disease, infections, malignancies, and chronic inflammatory disorders), iron deficiency, and nutritional and metabolic disorders. Blood loss as a causal factor (from surgery, injuries, and gastrointestinal and genitourinary bleeding) is more common in hospitalized patients.^{1,5} Frequently, multiple factors contribute to the problem in the individual patient. Approximately 20% of geriatric anemias, however, do defy classification, and their pathogenesis remains speculative. Proposed mechanisms include the presence of inflammatory cytokines and abnormal cytokine modulation of erythropoiesis, due both to abnormal production of stimulatory cytokines and decreased responsiveness of the erythroid precursors.^{3,5-12} An increased amount of fatty marrow tissue, possibly related to atherosclerotic changes in the bone marrow feeding arteries, may also play a role.¹³

Anemia Prevalence Increases with Age

A recent review of studies of anemia in elderly patients found a wide variation in prevalence, ranging from 2.9% to 61% in men and 3.3% to 41% in women.¹⁴ As expected, higher rates are found in hospitalized patients than in community dwellers, and in the oldest patients. For example, a retrospective chart review of 151 elderly hospitalized patients by Sahadevan and colleagues found that

slightly more than a third of the patients were anemic. The prevalence of anemia was significantly higher in those ≥ 75 years old, 42.9%, compared to those 65 to 74 years old, 25% ($P < 0.05$).¹⁵ Similarly, a retrospective chart review of 183 hospitalized patients by Smieja and associates found 36% were anemic.¹⁶ In a study of 56 persons in good condition, aged 90 to 99 years, 29% were found to be anemic.¹⁷ Outpatient studies of more heterogeneous geriatric populations report prevalences of anemia between 5.2% and 13.6%.^{4,18,19}

Diagnosing Anemia in the Elderly

Although the prevalence of anemia does increase with age, successful aging is not usually associated with anemia. Therefore, failure to evaluate anemia in the elderly could lead to delayed diagnosis of potentially treatable conditions.

It is a common perception that Hb levels lower than reference values are acceptable in older individuals. However, most experts recommend using the same reference values for Hb as are used in younger individuals. Indeed, a review of 73 studies of mixed elderly populations indicates that the most frequently used anemia definition for men was Hb < 13 g/dL and Hb < 12 g/dL for women, the same values suggested by the World Health Organization for younger adults.²⁰

An accurate history and focused physical examination, together with a limited, noninvasive laboratory evaluation (complete blood count with reticulocyte count, tests of hepatic and renal function, serum ferritin, vitamin B₁₂ level, stools for occult blood), are frequently sufficient to determine the cause of geriatric anemia and to direct management.

The differentiation between anemia of chronic disease and iron deficiency may be more challenging in older individuals because the hallmarks of iron deficiency, microcytosis, and reduced serum ferritin level are somewhat less likely to be present.²¹ Microcytosis may be masked by coexistent conditions usually associated with macrocytosis (eg, folate and vitamin B₁₂ deficiency, hypothyroidism, HIV infections, and use of drugs such as phenytoin or methotrexate). Serum ferritin, in addition to being a marker for iron stores, is an acute phase reactant. Therefore, low levels due to iron deficiency could be masked by elevations due to the presence of other comorbidities. The clinical context helps in the interpretation of equivocal laboratory results.^{22,23} Determination of total iron binding capacity and measurement of the soluble transferrin receptor concentration²⁴ or the C-reactive protein concentration may contribute to the differential diagnosis.²⁵

Pernicious anemia affects approximately 2% of the population older than 60 years and could be present in the absence of macrocytosis.²⁶ The prevalence of anemia due to vitamin B₁₂ deficiency may be much higher than that of pernicious anemia. With aging, the most common cause of vitamin B₁₂ deficiency is achylia, which prevents proper digestion of food.²⁷

Consequences of Untreated Anemia in the Elderly

Untreated geriatric anemia has been associated with increased mortality, increased prevalence of various comorbid conditions, and decreased function. Low Hb concentration was found to predict early death in one study of 63 nurs-

ing home residents, aged 70 to 99 years.²⁸ In individuals aged 70 to 79 years, the 5-year survival rate was 67% in normal controls and 48% in anemic individuals. For those aged 80 to 89 years, the 5-year survival rate was 62% for normal controls and 41% for anemic patients. Those in the oldest group, 90 to 99 years, had 5-year survival rates of 25% for patients with normal Hb and 13% for anemic patients. Chaves and colleagues, who followed 1,002 disabled community-dwelling women, aged ≥ 65 years, found that women with a Hb of 12 g/dL had a significantly higher mortality risk than did women with a Hb of 13.9 g/dL (OR, 1.6; 95% CI, 1.1-2.4). The odds of dying decreased 24% (OR, 0.76; 95% CI, 0.62-0.93) for each 1-g/dL increase in Hb between 8.0 g/dL and 13.9 g/dL.²⁹

Several studies have addressed the impact of anemia on cognitive function. Argyriadou and colleagues found significant differences in cognitive impairment in anemic versus nonanemic patients. They reported cognitive impairment in anemic males of 55.6% compared to 34.4% in nonanemic males ($P = 0.016$). Similarly, the proportions were 47.5% in anemic females versus 40.1% in nonanemic females ($P = 0.016$).³⁰

Beard and colleagues, who compared 302 patients with Alzheimer's disease (AD) with healthy age- and gender-matched controls aged ≥ 65 years, found an almost twofold increase in the incidence of AD when anemia was present (OR, 1.88; 95% CI, 1.11-3.47). However, an associated retrospective cohort study by the same researchers of 618 community residents found no overall increase of AD risk.³¹ Milward and colleagues failed to confirm an association between

anemia and AD but noted a significant association between anemia and vascular dementia (VAD). Nearly 45% of VAD subjects were anemic compared with 17% of nonanemic controls enrolled in a community-based study of elderly individuals.³² In-hospital delirium was increased in older patients with postoperative anemia, according to findings of a study conducted by Marcantonio and colleagues. In the study group of 1,341 patients ≥ 50 years admitted for major elective noncardiac surgery, postoperative Hct $< 30\%$ was associated with a nearly twofold increased risk of death (OR, 1.7; 95% CI, 1.1-2.7).³³

Other researchers have noted the association between anemia and functional ability and common comorbidities found in the elderly. Kamenetz and colleagues, in an investigation of 48 elderly subjects, ages 65 to 90 years, found patients with mild anemia to be impaired on a test of functional independence.³⁴ Iron deficiency anemia and also iron deficiency without anemia have been associated with restless legs syndrome.³⁵ In their review of 94 cohort and 72 case-control studies, Espallargues and colleagues found pernicious anemia to be one of several important risk factors for osteoporotic fracture.³⁶

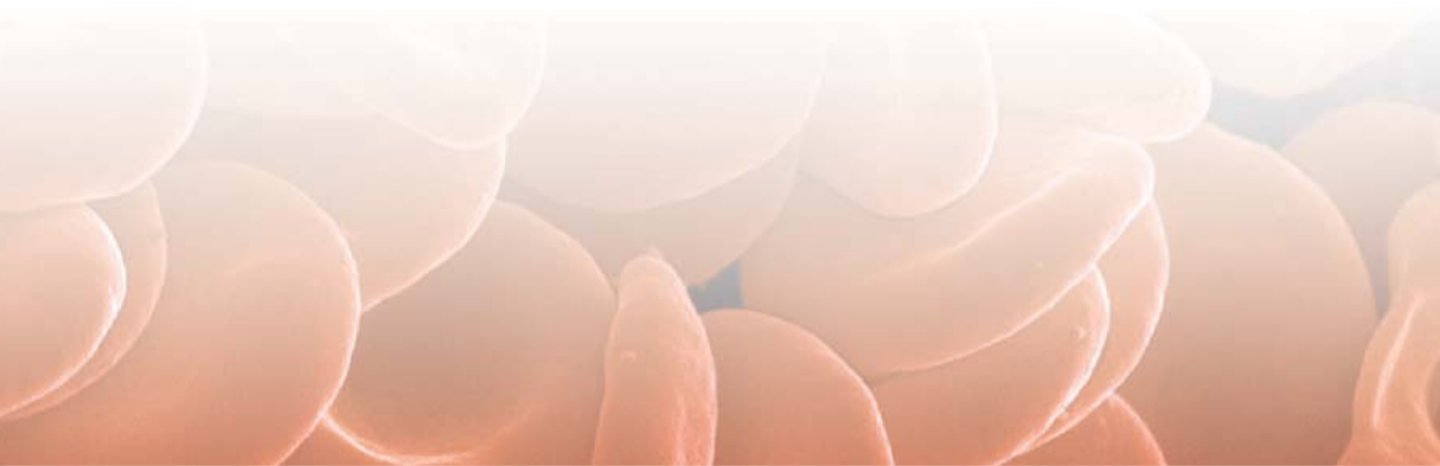
Beneficial Effects of Anemia Management

Treatment of anemia may improve outcomes in elderly patients with chronic dis-

eases as much as in younger patients. One study of 11 aged patients with chronic renal failure found that early correction of anemia with epoetin improved the quality of life, exercise performance, and cognitive function.³⁷ Treatment also reduced transfusion need. In most patients, partial regression of left ventricular hypertrophy occurred, and no congestive heart failure was documented. Moreno and colleagues reported that 23 elderly patients with end-stage renal disease who were on dialysis showed an increase of Hct from 21% to 29% in response to epoetin therapy. These patients improved in quality of life measures as much as did the younger patients included in the study.³⁸ Elderly cancer patients with cisplatin-associated anemia were found to respond to epoetin administration, with an increase in Hb levels and a need for blood transfusions comparable to that of younger individuals.³⁹

Wu and colleagues, in their retrospective study of nearly 79,000 acute myocardial infarction patients ≥ 65 years, found that the prevalence of anemia at admission was 43.4% and that a lower Hct was associated with a higher 30-day mortality rate. Mortality rates were highest among the patients with the lowest Hct values and decreased as Hct values increased. Blood transfusion lowered short-term mortality rates in patients with a Hct $\leq 30\%$ and might be effective in patients with a Hct as high as 33% at admission.⁴⁰

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