Anemia in older persons is commonly overlooked despite mounting evidence that low hemoglobin levels are a significant marker of physiologic decline. Using World Health Organization definition of anemia (hemoglobin level less than 13 g per dL [130 g per L] in men and less than 12 g per dL [120 g per L] in women), more than 10 percent of persons, except those at the end of life or who decline interventions. About one third of those at the end of life or who decline interventions. About one third of patients living in nursing homes.

Anemia in older persons is effectively treated with vitamin or iron replacement. Iron deficiency anemia often is caused by gastrointestinal bleeding and requires further investigation in most patients. Anemia may be caused by less common but potentially serious conditions, such as autoimmune hemolytic anemia, malignancy, or myelodysplastic syndrome.

Occasionally, anemia may be caused by unexplained conditions, such as autoimmune hemolytic anemia, malignancy, or myelodysplastic syndrome. Anemia in older persons is difficult, and there is little evidence that treatment decreases morbidity and mortality, or improves quality of life. Occasionally, anemia may be caused by less treatable conditions, such as autoimmune hemolytic anemia, malignancy, or myelodysplastic syndrome.

Anemia in older persons is a common problem with serious consequences in older persons. Using World Health Organization definition of anemia (hemoglobin level less than 13 g per dL [130 g per L] in men and less than 12 g per dL [120 g per L] in women), a large cohort study found that the incidence of anemia increased steadily with age. From 65 to 69 years of age, the incidence was 6 percent in men and 4 percent in women. In persons 85 years and older,
to 14 percent in men and 13 percent in women. In one study, approximately 50 percent of patients living in nursing homes had anemia.

### SORT: KEY RECOMMENDATIONS FOR PRACTICE

<table>
<thead>
<tr>
<th>Clinical recommendation</th>
<th>Evidence rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia is an independent risk factor for increased morbidity and mortality, and decreased quality of life in community-dwelling older persons.</td>
<td>B</td>
</tr>
<tr>
<td>Most older persons with iron deficiency anemia should be evaluated for gastrointestinal bleeding.</td>
<td>C</td>
</tr>
<tr>
<td>Normal levels of homocysteine and methylmalonic acid virtually exclude folate and vitamin B\textsubscript{12} deficiencies.</td>
<td>C</td>
</tr>
<tr>
<td>High-dose oral vitamin B\textsubscript{12} replacement for vitamin B\textsubscript{12} deficiency is effective and well tolerated.</td>
<td>B</td>
</tr>
</tbody>
</table>

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion information about the SORT evidence rating system, go to [http://www.aafp.org/afpsort.xml](http://www.aafp.org/afpsort.xml)

Anemia is often overlooked in older persons despite considerable evidence that low hemoglobin levels indicate physiologic decline in these patients. Multiple studies demonstrate that anemia is an independent risk factor for increased morbidity and mortality, and decreased quality of life in community-dwelling older persons ([Table 1]). Increasing functional deterioration is associated with decreasing hemoglobin concentration in an inverse and linear manner.

For example, one study of community-dwelling older persons found that women with borderline anemia (13 g per dL) perform worse than women with a hemoglobin level of 13 to 15 g per dL (130 to 150 g per L) on tests of walking speed, balance, and ability to rise from a chair.

### TABLE 1.

**Risks Associated with Anemia in Older Persons**

**Increased morbidity**
- Decreased mobility in community-dwelling older persons
- Decreased quality of life
- Increased risk of fatigue, depression, dementia, and delirium (in hospitalized)

**Increased mortality**
- Community-dwelling older persons
- Nursing home residents
- Persons with preexisting heart or kidney disease
- Persons undergoing noncardiac surgery

Information from references through 17.

These implications of anemia should lead physicians to investigate for causes that can be readily addressed, with treatments that have the potential to improve quality of life and benefits of treating anemia in older adults who are frail or who are at the end of life.
medical tests and interventions may exceed the benefits when disease burden severe. Limited overall benefits, the risk of false-positive test results, and patient reasons to defer evaluation. This article outlines potential causes of anemia and beneficial in older persons.

**Etiologies**

The Third National Health and Nutrition Examination Survey studied the prevalence anemia in a large national sample of community-dwelling persons. Most cases of anemia were mild, with only 2.8 percent of women and 1.6 percent of men having a hemoglobin dL (110 g per L). Approximately one third of persons with anemia had a nutritional deficiency; one third had anemia of chronic inflammation, chronic kidney disease, or both; and one third anemia. A breakdown of specific etiologies are found in Table 2.

**TABLE 2.**

**Etiologies of Anemia in Noninstitutionalized Persons 65 Years and Older**

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutritional</td>
<td>Iron deficiency</td>
</tr>
<tr>
<td></td>
<td>Folate deficiency</td>
</tr>
<tr>
<td></td>
<td>Vitamin B₁₂ deficiency</td>
</tr>
<tr>
<td></td>
<td>Iron deficiency plus folate or vitamin B₁₂ deficiency, or all three</td>
</tr>
<tr>
<td></td>
<td>Folate and vitamin B₁₂ deficiencies</td>
</tr>
<tr>
<td>Chronic</td>
<td>Anemia of chronic inflammation</td>
</tr>
<tr>
<td>disease</td>
<td>Renal insufficiency</td>
</tr>
<tr>
<td></td>
<td>Renal insufficiency and anemia of chronic inflammation</td>
</tr>
<tr>
<td>Unexplained</td>
<td>—</td>
</tr>
</tbody>
</table>


**Clinical Diagnosis**

Anemia often has an insidious onset in older persons. Although an acute drop symptoms of volume depletion, such as dizziness and increased falls, slower tolerated, with symptoms developing as compensatory mechanisms fail. Older heart rate and cardiac output as readily as younger persons, with dyspnea, fatiguing more common as anemia worsens. Preexisting cardiac diseases, such as disease and congestive heart failure, often become more symptomatic as hemoglobin levels drop.

There are few signs on physical examination that are specific for mild or moderate anemia. Conjunctiva are usually noted when the hemoglobin level drops below 9 g per L. In persons with multiple chronic illnesses, physicians may overlook anemia or attribute its symptoms to the underlying disease process. Thus, it is important to have a high index of suspicion present with even subtle symptoms of decline. A complete blood count or point measurement will quickly confirm the diagnosis of anemia.
Additional history and physical examination findings often clarify the etiology of anemia. It should address signs and symptoms associated with blood loss, such as chronic gastrointestinal bleeding, dark urine suggestive of hematuria, or history is important, with strict vegan diets increasing the risk of vitamin B₁₂ deficiency. Consumption increases the risk of folate deficiency and bleeding from peptic ulcer disease.

Chronic inflammatory diseases and chronic kidney disease are associated with anemia. Long-standing anemia warrants consideration of familial disorders, such as thalassemias and hereditary spherocytosis.

Medications should be reviewed, with attention to those that increase the risk of nonsteroidal anti-inflammatory drugs, warfarin (Coumadin). A careful review should identify alarming signs such as recent immobility, anorexia, and night sweats. Weight loss, lymphadenopathy, and localized bony pain are signs of serious illness and warrant consideration and chronic infection.

**Laboratory Testing and Evaluation**

Once anemia is confirmed, a complete blood count is helpful. If bleeding or iron deficiency is clinically suspected, measurement of serum ferritin is also warranted. The red blood cell size or mean corpuscular volume (MCV) is used to distinguish microcytic, normocytic, and macrocytic anemias. Many patients have a previously documented complete blood count that can be compared for changes in the baseline MCV. Three algorithms (Figures 1–30, 23–33, and 31–34) are presented to understand etiology or etiologies for anemia. The algorithms are based on probabilities, with the understanding that many anemias are multifactorial, and that it is difficult to conclusively identify the underlying causes.

**MICROCYTIC ANEMIA**

Microcytic anemias (Figure 1–20) are usually caused by iron deficiency. Ferritin storage, and a ferritin level below 35 ng per mL (78.64 pmol per L) is highly suggestive of deficiency anemia. It is important to note that ferritin levels increase with acute illness and inflammation, and in some persons with iron deficiency anemia and an acute inflammatory process, ferritin levels may be spuriously elevated. A cutoff of 45 ng per mL (101.11 pmol per L) has a higher sensitivity in older adults.

**Diagnosis of Microcytic Anemia**
Figure 1.
Algorithm for the diagnosis of microcytic anemia.
Information from references 23 through 30.

TABLE 3.
Ferritin Testing in Older Persons with Anemia

<table>
<thead>
<tr>
<th>Serum ferritin level (ng per mL)</th>
<th>Likelihood ratio</th>
<th>Probability of iron deficiency anemia (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 19 (42.69 pmol per L)</td>
<td>41</td>
<td>95</td>
</tr>
<tr>
<td>19 to 45 (42.69 to 101.11 pmol per L)</td>
<td>3.1</td>
<td>61</td>
</tr>
<tr>
<td>46 to 100 (103.36 to 224.70 pmol per L)</td>
<td>0.46</td>
<td>18</td>
</tr>
<tr>
<td>&gt; 100 (224.70 pmol per L)</td>
<td>0.13</td>
<td>6</td>
</tr>
</tbody>
</table>

*—Transferrin receptor-ferritin index is calculated by dividing the soluble transferrin receptor level (mg per L) by the log of the ferritin level (ng per mL).

*—Based on an estimated 33 percent prevalence of iron deficiency anemia.

Information from reference 24.

Iron deficiency anemia often is caused by gastrointestinal bleeding and requires most older persons.35,36 The presence of iron deficiency anemia markedly increases the likelihood of gastrointestinal malignancy, especially in persons 65 years and older.35 Even in asymptomatic patients, more than one half are found to have a bleeding-related lesion on endoscopic esophagogastroduodenoscopy and colonoscopy. Advanced age, low MCV (60
fecal occult blood test results are associated with higher rates of gastrointestinal bleeding. Potential benefits of diagnosing malignancies and other pathologies, it is important to remember that the risks of perforation with colonoscopy increase with age, significant comorbid invasive interventions. Invasive diagnostic interventions are best used when disease management and improve prognosis.

NORMOCYTIC ANEMIA

Normocytic anemias (Figure 2) have a wide differential diagnosis. Although anemias are secondary to chronic disease, including chronic kidney disease, it important to exclude early nutritional deficiencies and hemolysis. A peripheral blood smear, reticulocyte B12 and folate levels should be ordered. Many patients with vitamin B12 or fol normal MCV. If the reticulocyte index (reticulocyte count times hematocrit hematocrit level) is greater than 2 percent, hemolysis and subsequent confirm considered. A positive direct Coombs test result strongly supports autoimmune hemolytic anemia, both warm and cold antibody types, is life-th has good outcomes with immunosuppression. Other causes of reticulocytosis and hypersplenism. Most persons with anemia have a low reticulocyte count, bone marrow is not producing adequate red blood cells. If vitamin B12 and fol these patients should be evaluated for iron deficiency anemia and kidney dise have a mixed anemia with more than one etiology. The soluble transferrin rec increased to 2.5 mg per L (29.5 nmol per L) or greater with iron deficiency ar soluble transferrin receptor level by the log of the ferritin level, a value of 1.5 chronic disease and a value greater than 1.5 supports iron deficiency with chr

Diagnosis of Normocytic Anemia
MACROCYTIC ANEMIA

Macrocytic anemias (Figure 3) may be caused by drug therapy, alcoholism, hypothyroidism, vitamin B₁₂ deficiency, or folate deficiency. An elevated reticulocyte count suggests hemolysis, hypersplenism, or recent blood loss. When the reticulocyte count is elevated, obtain serum vitamin B₁₂ and folate levels. If the vitamin B₁₂ or folate level is borderline low, serum homocysteine level (to confirm folate deficiency) and methylmalonic acid level (to confirm vitamin B₁₂ deficiency) should be obtained. Normal levels of homocysteine and methylmalonic acid virtually exclude folate and vitamin B₁₂ deficiencies.
An abnormal peripheral blood smear result in patients with anemia warrants a myelodysplastic syndrome and malignancies, especially multiple myeloma. Macrocytic anemia is associated with myelodysplastic syndrome and myeloproliferative conditions. In such cases, bone marrow biopsy should be considered if the findings would potentially affect treatment.

**Treatment**

Almost all older persons with nutritional anemia should be treated, because treatment and cost-effective. The only exceptions may be very ill patients at the end of life and those who decline interventions. For iron deficiency anemia, the usual replacement dose is ferrous sulfate, 325 mg (65 mg of elemental iron) per day, or ferrous gluconate, 325 mg (38 mg of elemental iron) therapy, with 15 mg of elemental iron per day as liquid ferrous gluconate, hemoglobin and ferritin concentrations with fewer gastrointestinal adverse effects than higher iron doses. Treatment is usually continued for six months to replete iron stores. I respond to oral iron therapy, parenteral treatment with iron dextran or iron sucrose. High-dose oral therapy (cyanocobalamin, 1 to 2 mg per day) to treat vitamin B12 deficiency is noted by reticulocytosis within one week, followed by a more gradual increase in hemoglobin level.
Treatment of anemia of chronic disease, chronic kidney disease anemia, and unexplained anemia is difficult. The initial and preferred treatment is to correct the underlying disorder. Optimal management of chronic diseases will minimize inflammation and lessen bone marrow suppression. Most anemias in older persons are mild and do not require further intervention. When anemia is severe (less than 10 g per dL [100 g per L]), symptoms that warrant additional treatment often develop. Two options to treat severe anemia are blood transfusions and erythropoiesis-stimulating agents, both of which have significant limitations. Blood transfusions provide immediate relief of common symptoms including dyspnea, fatigue, and dizziness. Risks of transfusions include volume overload, iron overload, infections, and acute reactions.

Erythropoiesis-stimulating agents have been approved for the treatment of anemia of chronic disease in limited situations (Table 4), but their use remains controversial. Erythropoietin, produced mainly by the kidneys, stimulates the production of red blood cells in the bone marrow. Two recent randomized trials of the use of erythropoiesis-stimulating agents in persons with chronic kidney disease and anemia found that increasing the hemoglobin level to a target of 13.5 g per dL resulted in an increased rate of death and cardiovascular events. Goal hemoglobin levels for chronic kidney disease are avoiding transfusions and maintaining a hemoglobin level significantly below 12 g per dL. Although some studies have shown modest benefits of erythropoiesis-stimulating agents in persons with cancer and anemia, several have found decreased survival with these agents. For selected chemotherapy-associated anemias, erythropoiesis-stimulating agents are recommended as the hemoglobin level approaches or falls below 10 g per dL.

**TABLE 4. Guidelines for Use of Erythropoiesis-Stimulating Agents in Anemia**

**Indications approved by the U.S. Food and Drug Administration**

- Persons with anemia of chronic kidney disease undergoing dialysis to maintain a hemoglobin level of 10 to 12 g per dL (100 to 120 g per L)
- Persons with a hemoglobin level less than 10 g per dL who currently are on chemotherapy for cancer
- Persons with human immunodeficiency virus infection and anemia secondary to zidovudine (Retrovir) therapy
- Persons with anemia scheduled for surgery who are at risk of needing a transfusion (epoetin alfa [Epogen] only)

**Other indications covered by Medicare**

- Certain persons with myelodysplastic syndrome
- Persons undergoing treatment for hepatitis C
- Inflammatory bowel disease
- Rheumatoid arthritis
- Systemic lupus erythematosus

Information from references 44 through 47.

For most persons with anemia of chronic disease or unexplained anemia, there is little evidence that correcting the hemoglobin level decreases morbidity and mortality, or improves quality of life. Anemia may be a marker of frailty and physiologic decline. Therefore, it is prudent to limit the focus on increasing the hemoglobin level.
erythropoiesis-stimulating agents to the treatment of severe anemia associated with chronic kidney disease and other approved indications, unless patients are part of clinical trials evaluating erythropoiesis-stimulating agents.

Newer treatment modalities for myelodysplastic syndrome and multiple myeloma may prove effective regardless of patient age.\(^{52,53}\) Hematology consultation should be obtained if indicated.

The Authors

MICHAEL H. BROSS, MD, is an associate professor in the Department of Family Medicine at the University of Colorado Denver School of Medicine in Denver.

KATHLEEN SOCH, MD, is an associate professor of family medicine at the Texas A&M College of Medicine in College Station, and the director of geriatric training in the Christus Spohn Family Medicine Residency Program in Corpus Christi, Tex.

TERESA SMITH-KNUPPEL, MD, is a geriatric fellow in the Christus Spohn Family Medicine Residency Program in Corpus Christi.

Address correspondence to Michael H. Bross, MD, University of Colorado Denver School of Medicine, 1860 Grant St., Ste. 100, Denver, CO 80238 (e-mail: michael.bross@ucdenver.edu). Reprints are not available from the authors.

Author disclosure: Nothing to disclose.

The authors thank Sally P. Stabler, MD, professor of medicine and co-head of the Division of Hematology at the University of Colorado Denver, for her review of the manuscript.

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