Anemia in the Long-Term Care Setting

CLINICAL PRACTICE GUIDELINE

PALTmed
POST-ACUTE AND LONG-TERM CARE MEDICAL ASSOCIATION

Panel Members:
* Charles A. Cefalu, MD, MS— Chair
* William Simonson, PharmD, FASCP, CGP—Co-chair
Lowell Anthony, MD
Mary Balaskas, Pharm.D
T.S. Dharmarajan, MD, FACP
Deborah Heath, RN, BSN
William Hovland, MD
Pamela Long, CNA, Certified Preceptor, Geriatric Care Specialist
Kathleen Niedert, MBA, RD, LD, FADA, NHA
Carolyn Philpot, GNP
Jacqueline Shellington, LCSW
Vashu Thakur, MD
David Thomas, MD, CMD

* Steering Committee Member

Technical Writer:
Eleanor Mayfield

PALTmed Staff:

Jacqueline Vance, RNC. CDONA/LTC, CPG Project Manager, Director of Clinical Affairs
Nancy Robinson, MS, RN, Associate Director, Clinical Affairs

For more information about the PALTmed guidelines or to order copies of these clinical practice guidelines, call 800/876-2632 or 410/740-9743 or visit our web site at https://paltmed.org.

For guideline updates visit www.CPGNews.org.

Preface

This clinical practice guideline (CPG) has been developed under a project conducted by the Post-Acute and Long-Term Care Medical Association (PALTmed), the national professional organization representing attending physicians and medical directors who care for patients in the long-term care setting. This is one of a number of guidelines undertaken as part of the association's mission to improve the quality of care delivered to patients in these settings.

Original guidelines are developed by interdisciplinary workgroups, using a process that combines evidence and consensus-based approaches. Workgroups include practitioners and others involved in patient care in long-term care facilities. Beginning with a general guideline developed by an agency, association, or organization such as the Agency for Healthcare Research and Quality (AHRQ), pertinent articles and information, and a draft outline, each group works to make a concise, usable guideline that is tailored to the long-term care setting. Because scientific research in the long-term care population is limited, many recommendations are based on the expert opinion of practitioners in the field. A bibliography is provided for individuals who desire more detailed information.

Guideline revisions are completed under the direction of the Clinical Practice Guideline Steering Committee. The committee incorporates information published in peer-reviewed journals after the original guidelines appeared as well as comments and recommendations not only from experts in the field addressed by the guideline but also from "hands-on" long-term care practitioners and staff.

Purpose

PALTmed seeks to develop and revise guidelines that focus on specific concerns and common problems in the long-term care setting. Although AHRQ and other agencies, organizations, and associations have developed a number of guidelines for condi-tions that occur in elderly and chronically ill individuals, many of these guidelines limit or omit considerations that are unique to the long-term care population.

PALTmed guidelines emphasize key care processes and are organized for ready incorporation into facility-specific policies and procedures to guide staff and practi-tioner practices and performance. They are meant to be used in a manner appropri-ate to the population and practice of a particular facility. Guideline implementation will be affected by resources available in the facility, including staffing, and will require the involvement of all those in the facility who have a role in patient care.

Audience

This guideline is intended for the members of the interdisciplinary team in long-term care facilities, including the medical director, director of nursing, physicians, nursing staff, consultant pharmacist, and other professionals such as therapists, social workers, dietitians, and nursing assistants who care for residents of long-term care facilities.

PALTmed CPGs include many functions and tasks related to recognizing, clarifying, managing, and monitoring various conditions and situations. But the guidelines only sometimes specify who should do these tasks. For example, many disciplines includ-ing nursing assistants, licensed nurses, dieticians, and social workers may make and document observations (e.g., that someone does not sleep at night, is more with-drawn, or has a change in usual eating patterns). But only some of them may be qual-ified to determine the significance of those observations (e.g., what is causing the sleeplessness or change in eating patterns). In contrast, physicians and nurse practi-tioners may not be present to make observations, but are trained to analyze the sig-nificance and causes of symptoms. Thus, each facility should ensure that tasks are done correctly and by appropriate interdisciplinary team members. It is important for observers to make and document findings effectively, but they should get appropri-ate support for interpreting the findings when this is not within the scope of their training or practice.

Assumptions

Guidelines in the long-term care setting should be consistent with fundamental goals of desirable long-term care practice. Operationally, this requirement means that the nursing facility care team systematically addresses (1) each individual's risk factors for a number of diseases and conditions and (2) the adverse consequences of the diseases and conditions on the patient's functioning and quality of life.

However, when nursing facility patients are at or near the end of life, care goals will shift from functional improvement or physical stability to palliation or comfort care. PALTmed guidelines address this transition and provide suggestions for appropri-ate modification of the patient's care plan.

Long-term care facilities care for a variety of individuals, including younger patients with chronic diseases and disabilities, short-stay patients needing postacute care, and very old and frail individuals suffering from multiple comorbidities. When a workup or treatment is suggested, it is crucial to consider if such a step is appropriate for a specific individual. A workup may not be indicated if the patient has a terminal or end-stage condition, if it would not change the management course, if the burden of the workup is greater than the potential benefit, or if the patient or his or her proxy would refuse treatment. It is important to carefully document in the patient's medical record the reasons for decisions not to treat or perform a workup or for choosing one treatment approach over another.

How to Use These Guidelines

Each guideline includes a narrative portion that covers definition, recognition, assessment, treatment, and monitoring of the condition being addressed. "Recognition" means identifying the presence of a risk or condition. "Assessment" means clarifying the nature and causes of a condition or situation and identifying its impact on the individual. "Treatment" means selecting and providing appropriate interventions for that individual. "Monitoring" means reviewing the course of a condition or situation as the basis for deciding to continue, change, or stop interventions.

Each guideline also includes an algorithm that summarizes the steps involved in addressing the condition. In the algorithm, rectangles signify points where action is to be taken; diamonds indicate points where a decision must be made.

Terminology

We recognize that people who reside in long-term care facilities are "residents". However, we have used the term "patient(s)" throughout these guidelines because we are addressing individuals within the context of treating a medical condition. In addition, these guidelines apply substantially to individuals who come to long-term care facilities for short-term care. "We have also used the term "family," which is intended to include other decision-makers and proxies who may advocate for the patient or act on the patient's behalf." When referring to pharmaceutical products, we have avoided the use of brand names and refer to classes of drugs whenever possible.

Anemia
in the Long-Term Care Setting

DEFINITION

Anemia is a condition of low hemoglobin concentration caused by decreased production, increased loss, or destruction of red blood cells (erythrocytes). The World Health Organization defines anemia as hemoglobin of less than 12 g/dL in women and less than 13 g/dL in men.[1] Although other definitions exist for anemia, the WHO definition has been adopted for practical purposes.

INTRODUCTION

Anemia is common in the longterm care setting, with a prevalence ranging from 34.4 percent to 60 percent.[2, 3] The prevalence of anemia increases with each decade of life over age 70.[4] Causes of anemia include blood loss, increased red-cell destruction, decreased red-cell production, and decreased erythropoietin production.

Anemia is a marker for increased morbidity, hospitalizations, mortality, and health care costs. It is associated with both frailty[5] and mobility impairment[6] in older patients. Associative data suggest that anemia may be a risk factor for falls and related fractures[7–9] and for increased mortality over 5 years.[5] Anemia is associated with loss of muscle density[10, 11] and decreased muscle strength. In addition, anemia is associated with an increase in cardiac adverse events such as myocardial infarction, with subsequent poor outcomes.[12] The mortality risk for patients with congestive heart failure is 34 percent higher for those who also have anemia.[13] Prolonged anemia has been cited as a contributing factor for the development of left ventricular hypertrophy and other comorbidities.[14–16] In a population-based study, an almost two-fold increase in the occurrence of Alzheimer's disease was observed in patients with anemia compared with those who did not have anemia.[17] Much of these data are derived from studies of community-dwelling older adults. Specific data on anemia in long-term care patients are scarce. Preliminary data suggest that caring for patients with anemia in the long-term care setting may be more costly than caring for patients without anemia.[3]

Anemia presents a challenge in long-term care facilities. Despite its prevalence, it

often goes unevaluated or is inadequately evaluated in frail elderly patients. Practitioners may attribute anemia to the aging process rather than to a clinical condition that requires evaluation and management. Laboratory assessments to diagnose anemia are not commonly performed in long-term care facilities. Anemia may develop slowly and may exhibit few specific symptoms or signs until it is more advanced.[9,11, 18–25] Caregivers and health care professionals may not relate nonspecific symptoms such as fatigue, weakness, and lack of stamina to anemia. Patients may become less active to compensate for the effects of anemia. Table 1 lists other barriers to effective recognition and treatment of anemia in the long-term care setting.

TABLE 1
Barriers to Effective Recognition and Treatment of Anemia in the Long-Term Care Setting

- Lack of a consistent definition of anemia in the elderly
- Knowledge deficits concerning best practices in the assessment and management of anemia
- Lack of data on the outcomes of anemia treatment in the frail elderly
- Lack of research on anemia in the elderly long-term care population

Studies suggest the importance of treating anemia to improve patients' overall health and prevent certain comorbid conditions or complications.[2, 9, 26–29] Table 2 lists several complications associated with anemia.

TABLE 2
Complications Associated With Anemia

- Cardiac complications (e.g., congestive heart failure, left ventricular hypertrophy,[30] myocardial infarction[22, 23])
- Cognitive impairment[17,19,24]
- Depression[31]
- Falls[7, 9, 23, 25]
- Frailty[32, 33]
- Impaired physical performance[11, 32]
- Increased mortality[6]

Outcomes That May Be Expected From Implementation of This Clinical Practice Guideline

The following outcomes may be expected from implementation of this clinical practice guideline:

- Better recognition and more appropriate management of anemia.
- Comprehensive evaluation of the causes of anemia when appropriate.

- Adequate assessment and monitoring of anemia.
- Improvement in patients' functional status, cognitive function, exercise performance, and quality of life.
- Reduced morbidity and mortality.
- Reduced medical care costs as a result of treatment of identifiable causes of anemia.

RECOGNITION

STEP 1

Assess the patient's medical history and current hematologic status. The admission history and physical examination may indicate a history of anemia, the presence of a chronic disease that may be associated with anemia, or symptoms that could be caused by anemia. Document any history of anemia in the patient's record. Perform a complete blood count (CBC) on admission if a recent one (i.e., performed within the last 6 months) is not available, if the patient has had a significant change in cognition or physical function, or if the patient has had recent or suspected bleeding.

Unlike anemia that is caused by acute bleeding, anemia that develops slowly (i.e., over a period of time long enough to allow compensatory mechanisms to operate) will produce nonspecific symptoms. Table 3 lists nonspecific signs and symptoms that may indicate anemia.

TABLE 3
Nonspecific Signs and Symptoms That May Indicate Anemia

- Bleeding gums
- Chest pain
- Dizziness
- Decreased ability to participate in exercise
- Decreased activity level
- Decreased appetite
- Dyspnea
- Fatigue
- Impairment in physical performance
- Increase in falls
- Increased confusion
- Jaundice
- Melena (dark tarry stool)
- Microscopic hematuria
- Pallor

Because anemia can have a substantial impact on elderly patients' health and quality of life, it is important that staff of long-term care facilities are trained to recognize signs and symptoms that may suggest anemia and to identify patients at risk for the condition. (See "Be an Anemia Detective," in PALTmed's 2005 Physician Information Tool Kit, *Anemia in the Long-Term Care Setting*.[a]) It is also important for caregivers to communicate observations and concerns to the interdisciplinary team. Table 4 des-cribes the potential roles of selected members of the interdisciplinary care team in rec-ognizing anemia.

TABLE 4
Responsibilities of Selected Interdisciplinary Team Members in Recognizing Anemia

Discipline	Responsibilities	Possible Observations
Dietitian	◆ Take nutrition history on admission ◆ Review patient's dietary intake for possible iron and vitamin deficiencies	◆ Lack of foods rich in iron, B_{12}, or folate in the patient's diet ◆ Anorexia, nausea, weight loss
Nurse	◆ Evaluate patient's function and ability to perform ADLs ◆ Report signs and symptoms that may suggest anemia to the practitioner for further evaluation ◆ Discuss with practitioner the need for a CBC to screen for anemia, stool for occult blood, or other tests to evaluate whether anemia is present	◆ Hematochezia (bloody stools) ◆ Melena (dark, tarry stools) ◆ Pale mucous membranes, skin, or nailbeds ◆ Evidence of heart failure despite medical treatments ◆ Complaints of lightheadedness or dizziness upon standing ◆ Complaints of fatigue ◆ Vital signs show hypotension or above-normal heart rate
Nursing assistant	◆ Report decline in nutritional intake and changes in patient's ability to perform ADLs	◆ Inability to perform ADLs that the patient previously could perform
Pharmacist	◆ Review laboratory results ◆ Review patient's medication history and current medication regimen for possible ADEs and interactions between medications or between medications and foods that may be causing or contributing to anemia ◆ Monitor effects of pharmacological treatment and ADEs related to treatment ◆ Look for presence of conditions that can contribute to anemia (CHF, CKD, rheumatoid arthritis, peptic ulcer disease, cancer, etc.)	◆ Use of medications that can cause or contribute to anemia (e.g., chemotherapy, NSAIDs, phenytoin, proton pump inhibitors) ◆ Laboratory test results indicating abnormal hematological status or renal function
Physical therapist	◆ Monitor patient's response to exercise ◆ Report declines in patient's exercise capacity to practitioner	◆ Lack of progression, inability to follow physical therapy plan ◆ Poor endurance during therapy

ADLs: activities of daily living; ADEs: adverse drug events; CBC: complete blood count; CHF: congestive heart failure; CKD: chronic kidney disease; NSAIDs: nonsteroidal anti-inflammatory drugs.

[a] Post-Acute and Long-Term Care Medical Association. LTC Physician Information Took Kit: Anemia in the Long-Term Care Setting. 2005. Columbia, MD.

STEP 2

Does the patient have anemia? Confirm the patient's anemia by checking a CBC with differential. If the patient has anemia, skip to Step 4 to consider possible additional evaluation of the condition. If the patient does not have anemia, or the results are borderline, skip to Step 3 to assess for risk factors that subsequently could cause anemia.

STEP 3

Assess the patient for anemia risk factors. The presence of certain comorbid conditions may predispose patients to anemia (Table 5). As previously noted, anemia may be asymptomatic, especially in the early stages, or may present with very nonspecific signs and symptoms. It is therefore important for the practitioner to assess patients' risk for anemia. If one or more risk factors are present, further evaluation may be necessary.

TABLE 5

Conditions That May Predispose to Anemia

- Cancer
- Chronic inflammation
- Gastrointestinal bleeding (e.g., Crohn's disease, ulcerative colitis, peptic ulcer disease)
- Endocrine disorders (e.g., diabetes, thyroid disease)
- History of anemia
- Low dietary intake of iron, vitamin B_{12} (e.g., strict vegetarianism), or folate
- Recent blood loss (e.g., due to accident, surgery)
- Renal disease (e.g., chronic kidney disease)
- Use of drugs that can cause anemia (see Step 6, Table 11)

Nursing staff who are aware that a patient has underlying conditions that can contribute to anemia should report this to the practitioner, document their findings in the patient's record, and update the Minimum Data Set (MDS). Table 6 provides examples of elements in the MDS 2.0 that may be relevant to anemia.

TABLE 6

Elements of MDS–Version 2.0* That May Be Relevant to Anemia

- Changes in cognitive status (B6)
- Change in mood (E3)
- Chronic infections (I2) (e.g. osteomyelitis, Helicobacter pylori)
- Decline in ADL function (G9)
- Falls (J4)
- Nutritional problems (K4)
- Skin conditions (M1, M4)
- Weight loss, anorexia (K3)

** Questions and/or section numbers may change in future revised versions of the MDS.*

ASSESSMENT

STEP 4

Determine whether an additional diagnostic workup of anemia is appropriate. The practitioner should use a clearly defined process to assess patients who have anemia. However, not all such patients are candidates for a complete diagnostic evaluation. Assessment should be individualized, taking into consideration the patient's wishes as well as cognitive and other co-morbid factors that may influence life expectancy or quality of life. Considerations that may affect the type and extent of diagnostic evaluation for anemia include:

- Is the patient symptomatic due to anemia?
- Does the patient have conditions that may exacerbate anemia over time and lead to adverse outcomes?
- Has the patient been evaluated for anemia in the past?
- What are the goals of treatment?

As always, consider the patient's decision-making capacity, religious beliefs, advance directives, and care goals when determining whether a diagnostic evaluation for anemia is appropriate. Document in the patient's record the rationale for the decision to perform or not perform a workup for anemia.

STEP 5

Perform appropriate laboratory evaluation. Determining the etiology of the patient's anemia as specifically as possible will guide both treatment decisions and monitoring. In some cases (e.g., iron deficiency), etiology is easy to identify; in others (e.g., aplastic anemia), it may be more difficult.

Table 7 lists suggested components of a noninvasive laboratory evaluation of anemia. The choice of tests will depend on the suspected cause of anemia or the patient's comorbidities. Tests can be performed simultaneously or sequentially (e.g., order a CBC, then a reticulocyte count, then a test of stool for occult blood). Table 8 presents common causes and diagnostic criteria for anemia due to iron or vitamin deficiencies, chronic inflammation (including chronic kidney disease), and hemolysis.

TABLE 7

Suggested Components of a Noninvasive Laboratory Evaluation of Anemia

- Complete blood count with reticulocyte count
- Examination of morphology by peripheral smear
- Ferritin, serum iron, total iron-binding capacity
- Serum folate and vitamin B_{12}
- Hepatic and renal function
- Sedimentation rate
- Serum protein electrophoresis
- Stool for occult blood
- Thyroid-stimulating hormone

TABLE 8

Common Causes and Diagnostic Criteria for Specific Types of Anemia

Type of Anemia	Possible Causes	Diagnostic Criteria
Iron-deficiency anemia	◆ Hemorrhage ◆ Hemosiderinuria, hemoglobinuria, and pulmonary hemosiderosis	◆ Low serum ferritin ◆ High total iron-binding capacity and transferrin ◆ Low serum iron ◆ Low transferrin saturation
Vitamin B_{12}–deficiency anemia	◆ Inadequate dietary intake of vitamin B_{12} ◆ Decreased vitamin B_{12} absorption due to reduced intestinal absorption or deficient intrinsic factor	◆ Low serum vitamin B_{12} ◆ Elevated methylmalonic acid and homocysteine
Folate-deficiency anemia	◆ Inadequate dietary intake (most common cause) ◆ Alcoholism ◆ Dialysis ◆ Liver disease ◆ Malabsorption disorders ◆ Medications	◆ Decreased serum folate
Anemia of chronic disease/chronic inflammation	◆ Failure of bone marrow to produce red-blood cells due to erythropoietin resistance (e.g., as seen in cancer, arthritis, other chronic inflammatory conditions) ◆ Age-associated alterations in cytokine levels	◆ Elevated sedimentation rate ◆ Elevated C-reactive protein ◆ Low reticulocyte count ◆ Normocytic, normochromic anemia with normal or elevated iron stores
Anemia associated with chronic kidney disease[34,35]	Presence of chronic kidney disease	◆ Decreased GFR as estimated by an appropriate formula (e.g., Cockroft-Gault, MDRD) ◆ ≥Stage 3 chronic kidney disease ◆ Hemoglobin <12 g/dL in women, <13.5 g/dL in men[36]
Unexplained anemia	◆ Contributing factors may include shortened RBC survival, occult blood loss, and nutrient deficiency ◆ A diagnosis of exclusion when other etiologies cannot explain the cause of anemia	N/A
Hemolytic anemia	◆ Hypersplenism ◆ Autoimmunity ◆ Artificial heart valves ◆ DIC ◆ Hemoglobinopathy	◆ Elevated reticulocyte count ◆ Elevated bilirubin (unconjugated) ◆ Elevated LDH ◆ Positive Coomb's test ◆ Decreased haptoglobin

DIC: disseminated intravascular coagulation; GFR: glomerular filtration rate; LDH: lactate dehydrogenase; MDRD: Modification of Diet in Renal Disease.

A useful approach to the diagnosis of anemia is to use red-cell morphology (mean corpuscular volume, mean corpuscular hemoglobin concentration) and the peripheral smear when pertinent, to determine the course of laboratory evaluation. For further assistance in determining the etiology of anemia see Appendix 1, an algorithm for the diagnosis of anemia using red-cell morphology.

It is sometimes difficult to differentiate iron-deficiency anemia from anemia of chronic disease and in some cases the two may coexist. Table 9 illustrates how to differentiate iron-deficiency anemia from anemia of chronic disease on the basis of lab values. After the practitioner has conducted a preliminary evaluation, consultation with a relevant specialist may be appropriate if the cause of anemia is not clear or if further evaluation or treatment is necessary. Consideration of the risks and benefits of treatment and discussion with the patient or family is recommended.

TABLE 9
Differentiating Iron-Deficiency Anemia From Anemia of Chronic Disease on the Basis of Lab Values

Blood Test	ACD	IDA	ACD + IDA
Iron	↓	↓	↓
TIBC	↓	↑	LN or ↓↑
% Transferrin saturation	↓ or N	↓	↓
Ferritin	↑ or N	↓	↓ or N
Soluble transferrin receptor	N	↑	↑ or N

ACD: anemia of chronic disease; IDA: iron-deficiency anemia; N: normal; LN: low normal; TIBC: total iron-binding capacity.

Adapted from Weiss[37]

STEP 6

Identify or clarify specific characteristics and causes of the patient's anemia. Anemia may be multifactorial. Table 10 identifies common causes of anemia. Table 11 lists commonly used drugs and alternative remedies that may cause or contribute to anemia. An accurate history and physical examination and a noninvasive laboratory evaluation (Step 5) are often enough to determine the cause of anemia in elderly long-term care patients. However, in one-third of adults aged 65 or older, the cause of anemia is unknown.[43]

TABLE 10
Common Causes of Anemia

- Acute or chronic blood loss (e.g., due to diverticular disease, excessive phlebotomy, gastrointestinal ulcers, postoperative complications)
- Increased red-cell destruction (hemolysis) (e.g., due to autoimmune disease, acquired cardiac valvular disease, disseminated intravascular coagulopathy, hemoglobinopathies)
- Decreased red-cell production as a result of:
  - Chronic disease (e.g., inflammation, malignancy, chronic liver disease, hyperparathyroidism, hypothyroidism)
  - Decreased erythropoietin production (e.g., due to chronic kidney disease)
  - Hemoglobinopathies (e.g., heterozygous thalassemia)
  - Marrow aplasia (hereditary or acquired)
  - Marrow dysfunction (e.g., tumor cells, fibrous tissue, granulomas)
  - Nutritional deficiencies
    - Iron deficiency (due to chronic bleeding, iron-deficient diet, or impaired iron absorption)
    - Deficiency of vitamin B_{12} or folate
    - Undernutrition
  - Suppression of DNA synthesis (e.g., long-term maintenance chemotherapy)

TABLE 11

Commonly Used Drugs and Alternative Remedies That May Cause or Contribute to Anemia[38–42]

Drugs That Can Cause GI Bleeding

- Anticoagulants
- Antiplatelet agents
- Bisphosphonates
- Corticosteroids
- Nonsteroidal anti-inflammatory drugs (including COX-2 inhibitors)

Drugs That Affect Folate Levels and Utilization

Drugs that can decrease folate absorption:

- Alcohol
- Phenobarbital
- Phenytoin
- Sulfasalazine

Drugs that interfere with folate metabolism:

- Lamotrigine
- Methotrexate
- Pentamidine
- Phenobarbital
- Primidone
- Triamterene
- Sulfasalazine
- Trimethoprim/sulfamethoxazole

Drugs That Decrease Vitamin B_{12} Absorption

- Colchicine
- H_2 blockers
- Metformin
- Proton pump inhibitors

Drugs That Can Cause Myelosuppression

- 6-Mercaptopurine
- Azathioprine
- Azidouridine
- Busulfan
- Cyclophosphamide
- Daunorubicin
- Doxorubicin
- Fluorouracil
- Hydroxyurea
- Methotrexate
- Thioguanine
- Zidovudine

Alternative Remedies That May Contribute to Anemia

- Black cohosh
- Ginkgo (may cause bleeding)
- Green tea
- Yohimbine (may cause renal failure)

TREATMENT

STEP 7

Manage anemia, including its symptoms and underlying causes. To the extent possible, identify and manage the underlying causes of anemia, when doing so will help to stabilize or improve the patient's hematologic status.

Once the cause of the patient's anemia has been determined, the decision about whether and how to treat it may require discussion with the patient and family. Issues for discussion may include:

- The cause of the patient's anemia, if known.
- Treatment options and expected outcomes.
- The patient's care goals and prognosis.

Before initiating treatment, weigh the potential benefits of the intervention against its potential risks. Some anemias (e.g., iron-deficiency anemia, folate-deficiency anemia) are relatively easy to treat. No specific treatment exists for anemia of chronic disease or inflammation, although symptoms can be managed. Table 12 summarizes treatment options for specific types of anemia.

TABLE 12
Summary of Treatment Options for Specific Types of Anemia

Type of Anemia	Treatment Options
Iron-deficiency anemia	◆ Ferrous sulfate 325 mg once daily[44] (avoid most drug interactions by administering 2 hrs after calcium supplements, tetracycline, or other interacting medications) ◆ Dietary interventions ◆ Consume iron-rich foods
Vitamin B_{12}–deficiency anemia	◆ Vitamin B_{12} 1,000 μg /mL deep SC or IM if needed, weekly x 1 month, then monthly ◆ Dietary interventions ◆ Consume foods that are good sources of vitamin B_{12} (liver, other meats, fish, poultry, eggs, fortified products—e.g., soy milk)
Folate-deficiency anemia	◆ Folate l mg orally, daily for 2-3 weeks, then re-evaluate the need for continued therapy ◆ Dietary intervention ◆ Consume folic acid–rich foods (e.g., leafy vegetables, nuts, whole grains)
Anemia of chronic disease/ chronic inflammation	◆ Treat or stabilize the underlying disease
Anemia associated with chronic kidney disease	◆ Epoetin alfa or darbepoetin alfa SC
Hemolytic anemia	◆ Identify underlying cause ◆ Discontinue any contributing medications

IM: intramuscular; SC: subcutaneous.

Iron-Deficiency Anemia

Iron can be given orally by means of iron salts (e.g., ferrous sulfate, gluconate, fumarate). Elemental-iron content varies according to the type of iron salt. For example, 325 mg of ferrous sulfate contains 97.5 mg of elemental iron; 240 mg of ferrous gluconate contains 27 mg of elemental iron.

Between 10 percent and 30 percent of patients will experience unpleasant gastrointestinal side effects from oral iron. Common side effects include abdominal cramps, constipation, diarrhea, black stool, and epigastric discomfort. As a means of reducing gastrointestinal side effects, once-daily dosing is preferred in older adults. Side effects are dose related; low-dose iron therapy is effective in elderly patients.[45] A daily dose of ferrous sulfate greater than 325 mg may increase the incidence of constipation.[44]

Oral iron supplements are usually best absorbed on an empty stomach. However, because iron can cause gastric irritation, administration with food may be necessary. The addition of ascorbic acid (500 mg) may enhance iron absorption without increasing gastric distress. Absorption of iron in enteric-coated capsules is no better than that of standard iron preparations.

Many oral iron products are available in a wide variety of dosage forms, including tablets, capsules, extended-release tablets and capsules, and chewable tablets, as well as oral solution, suspension, and elixir. When choosing a dosage form, consider its elemental iron content and acceptability for the patient. To avoid unnecessary accumulation of iron, verify that the patient's anemia is caused by iron deficiency before administering iron therapy and check serum iron and ferritin concentrations periodically.

Parenteral iron, administered either intramuscularly or intravenously, may be an option for patients who do not respond to or cannot tolerate oral iron. However, the safety and efficacy of parenterally administered iron in the elderly long-term care population have been insufficiently studied. It is important to be aware that not all iron formulations are approved for parenteral administration.

The use of parenteral iron in the long-term care population is limited by difficulties associated with administration (e.g., insufficient muscle mass) and concerns for adverse effects (e.g., pain at injection site, skin discoloration). Exercise caution when administering intravenous iron because of the possibility of anaphylactic or anaphylactoid reactions. These reactions, which are rare but potentially lethal, typically occur within several minutes of administration.[46] Clinicians must closely follow the manufacturer's recommendations for proper administration of parenteral iron, including giving a test dose and ensuring that persons trained to provide emergency treatment for severe allergic or anaphylactic reactions are available in the event of such an emergency.

The patient's response to iron therapy may be verified by an increase in the reticulocyte count, which usually occurs 7–10 days after iron replacement begins. A subnormal response to treatment may occur because of continued bleeding, insufficient dietary iron intake, hemoglobinopathy, insufficient supplementation, malignancy, underlying infection, or (rarely) malabsorption of oral iron.

Therapy may need to continue for up to 6 months to fully replenish the body's stored iron. The duration of therapy should be determined by factors including the severity and causes of anemia, the severity of any related symptoms, and the patient's hematologic response. Discontinue therapy when treatment goals are reached or if it is concluded that therapy has not helped and is unlikely to help attain the desired results (e.g., because the patient's anemia is caused by chronic disease).[47]

Vitamin B_{12}–Deficiency Anemia

Anemia caused by a deficiency of vitamin B_{12} is typically treated by either oral or parenteral supplementation.[48–50] When absorption through the gastrointestinal tract is deficient (as in pernicious anemia and other malabsorption disorders), vitamin B_{12} must be administered by deep subcutaneous or intramuscular injection.

Vitamin B_{12} is also available commercially as an intranasal gel and as a sublingual preparation. These formulations may offer advantages for patients with cognitive impairment or dysphagia,[51] but they are more costly. Table 13 lists options for maintenance dosing of vitamin B_{12} deficiency. When B_{12} deficiency is caused by pernicious anemia, treatment is usually lifelong; discontinuation of therapy is associated with a risk of recurrence of the deficiency.[51]

TABLE 13
Options for Treating Vitamin B_{12} Deficiency

Preparation	Geriatric Maintenance Dose
Deep subcutaneous/ intramuscular injection	100-1,000 μg Q 1-3 months
Oral dosing	500-2,000 μg/d
Sublingual forms	2,000 μg/d
Intranasal administration	500 μg weekly

Adapted from Dharmarajan[51]

Folate-Deficiency Anemia

Folate-deficiency anemia should be treated with oral folic acid (1 mg daily). It is important to check for the presence of a concurrent vitamin B_{12} deficiency before ordering folate therapy because giving folate will worsen a co-existing B_{12} deficiency and may allow progression of neurological features of the co-existing B_{12} deficiency. If a B_{12} deficiency is present, treat it and the folate deficiency simultaneously.

As with the treatment of iron-deficiency anemia, the duration of therapy should be determined by factors including the severity and causes of anemia, the severity of any related symptoms, and the patient's hematologic response. Discontinue therapy when treatment goals are reached or if it is concluded that therapy has not helped and is unlikely to help attain the desired results.

Anemia of Chronic Disease/Chronic Inflammation

Anemia of chronic disease (ACD) is the second most common type of anemia among older adults.[52] It presents as a normocytic anemia that is typically secondary to chronic kidney disease or to a chronic inflammatory disease or process. ACD is sometimes referred to as anemia of chronic inflammation because it is often associated with chronic infections and other inflammatory diseases such as rheumatoid arthritis.

ACD is usually not severe enough to produce symptoms. When symptoms do occur, they usually result from the underlying disease rather than from the anemia itself. Laboratory results alone are insufficient to make a diagnosis of ACD; the diagnosis is typically made by excluding other causes[47] and by identifying an underlying chronic disease or infection. ACD improves if a treatable cause is identified and corrected. Iron and vitamin supplements generally do not help.[47]

Anemia associated with chronic kidney disease. Anemia associated with chronic kidney disease (CKD) was redefined in 2006 by the National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (K/DOQI) as hemoglobin of less than 12 g/dL in women and less than 13.5 g/dL in men in the presence of renal dysfunction.[36]

Anemia is common in patients with CKD. In the third National Health and Nutrition Examination Survey, the prevalence of anemia in the population as a whole was 5.2% in patients with stage 3 CKD (glomerular filtration rate [GFR] 30–59 mL/min) and 44.1% in those with stage 4 CKD (GFR 15–29 mL/min); at stage 5 CKD (GFR <15 and/or on dialysis), almost all patients were anemic.[53] (See Table 14 for the stages of CKD.)

TABLE 14
Stages of Chronic Kidney Disease[36]

Stage	Description	GFR (mL/min/1.73 m²)
1	Kidney damage with normal or elevated ↑ GFR	≥ 90
2	Kidney damage with mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney failure	<15 (or dialysis)

Chronic kidney disease is defined as either kidney damage or GFR <60 mL/min/1.73 m² for ≥ 3 months. Kidney damage is defined as pathological abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

GFR: glomerular filtration rate.

Deficiency of the hormone erythropoietin is the primary but may not be the sole cause of anemia associated with CKD.[53] Erythropoietin, produced in the kidneys, normally stimulates erythrocyte production by the bone marrow. Patients with CKD often have impaired erythropoietin production. Anemia associated with CKD may have other causes, including bleeding, hemolysis, and nutritional deficiencies.

Anemia associated with CKD can be severe and may lead to cardiovascular complications and death.[54,55] It is typically not responsive to iron, vitamin B_{12}, or folate supplementation. Synthetic erythropoietin-stimulating agents (ESAs) are available to treat this type of anemia.* In a study of 11 patients aged 66–85 with anemia associated with chronic kidney disease, early correction of anemia with ESAs improved quality of life, exercise performance, and cognitive function. Treatment also reduced the need for blood transfusions.[56] In 23 elderly patients with end-stage renal disease who were on dialysis, ESA therapy increased hematocrit values by eight percentage points on average. Improvements in quality-of-life measures were comparable in elderly and younger patients.[57]

The use of ESAs to treat anemia associated with CKD should be carefully evaluated in frail elderly patients in the long-term care setting. In this setting, ESA therapy should be reserved for patients who are likely to obtain important clinical benefit. Initiation of ESA therapy is not recommended in patients with limited life expectancy, significantly impaired function due to comorbid conditions unrelated to CKD or anemia, significant dementia, or other conditions that make clinical benefit unlikely.[58]

ESA therapy may increase the risk of both fatal and nonfatal thrombotic events, especially if hemoglobin levels rise to greater than 12 g/dL. In a recent study, patients with anemia associated with CKD who were treated with ESAs to a target hemoglobin of 13.5 g/dL experienced more cardiovascular complications than those treated to a target hemoglobin of 11.3 g/dL. These complications included heart attacks, hospitalization for congestive heart failure, stroke, and death.[59]

The U.S. Food and Drug Administration currently advises practitioners to follow dosing recommendations in the labeling for ESAs and ensure that hemoglobin is maintained in a range between 10 g/dL and 12 g/dL. The FDA further advises that after initiation of an ESA or adjustment of the dose, the practitioner should measure the patient's hemoglobin twice a week for 2–6 weeks to ensure that it has stabilized. The ESA dose should be decreased if the patient's hemoglobin increases by more than 1 g/dL in any 2-week period.[60] Practitioners should be aware that it may take between 2 and 6 weeks after a dosage adjustment for a significant change in hemoglobin to be observed.

Administer ESA therapy subcutaneously or intravenously; rotate the injection site with each administration. Evaluate the patient's iron status before and during ESA therapy. Almost all patients will eventually require supplemental iron to allow the

*Iron-, vitamin B_{12}-,or folate-deficiency anemia may coexist with anemia associated with chronic kidney disease. ESA therapy may not be effective if any of these coexisting deficiencies are not corrected.

stimulated bone marrow to produce erythrocytes. Blood pressure must be closely monitored and controlled in patients receiving ESAs. Patients with uncontrolled hypertension should not receive ESAs. Table 15 summarizes the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF K/DOQI) guidelines on the use of ESAs to treat anemia associated with CKD.

TABLE 15

Summary of NKF K/DOQI Guidelines on Using ESAs* to Treat Anemia Associated With CKD

Dosing

- In determining initial ESA dose and dose adjustments, consider patient's hemoglobin level, target hemoglobin, observed rate of increase in hemoglobin, and clinical circumstances
- The approved dose of epoetin alfa is 50–100 U/kg 3x per week
- The approved dose of darbepoetin alfa is 0.45 mcg/kg once weekly
- Decrease ESA dose by 25%, but do not necessarily withhold it, when downward adjustment of hemoglobin is necessary
- Replace missed ESA doses as soon as possible
- In ESA-dependent patients, continue ESA dosing during hospitalization
- Hypertension, vascular access occlusion, inadequate dialysis, history of seizures, and compromised nutritional status are not contraindications to ESA therapy

Route of administration

- In determining route of administration, consider CKD stage, treatment setting, efficacy, safety, and class of ESA used
- Convenience favors SC administration in CKD patients who are not on hemodialysis
- Convenience favors IV administration in CKD patients who are on hemodialysis

Frequency of administration

- In determining frequency of administration, consider CKD stage, treatment setting, efficacy considerations, and class of ESA
- Convenience favors administration of ESAs that are longer acting and can be given less frequently, particularly in CKD patients who are not on hemodialysis

Frequency of monitoring

- Monitor hemoglobin once or twice a week during initiation or changes in therapy. When hemoglobin stability is achieved, monitor monthly

CKD: chronic kidney disease; ESA: erythropoietin-stimulating agents; IV: intravenous; K/DOQI: Kidney Disease Outcomes Quality Initiative; NKF: National Kidney Foundation; SC: subcutaneous.

Adapted from NKF[36]

*On March 9th, 2007 the FDA issued a new boxed warning to physicians related to the off label and above recommended dosage use of ESAs.

Some patients with anemia associated with CKD may not respond to ESA therapy. Resistance to ESA therapy most commonly arises from iron deficiency (real or functional) or from the presence of inflammation or infection from any underlying cause. Other causes of resistance to ESA therapy include multiple myeloma, hemoglobinopathies, vitamin B_{12} or folate deficiency, malnutrition, hemolysis, aluminum toxicity, ostitis fibrosa, and (rarely) pure red-cell aplasia.[61,62] Lack of response or an inadequate response to ESA therapy should trigger an evaluation for these conditions and interventions to correct the underlying condition when possible.

ESAs have also been approved to increase hemoglobin concentrations in patients who have anemia associated with cancer chemotherapy or zidovudine therapy for treatment of HIV. Administration of ESAs less frequently than recommended in the product labeling has been used successfully.[58]

Blood transfusions. Generally, blood transfusions should be used as a last-resort treatment for anemia, usually for chronic asymptomatic anemia, when the hemoglobin level drops to 7 g/dL63 and the hematocrit value to 21 percent. In high risk patients with significant cardiovascular or respiratory disease and clinically significant symptoms, (e.g., chest pain, dizziness, shortness of breath, tachycardia, hypotension) consider transfusion if hemoglobin is less than 8 g/dL. Immediate transfusion is often required in the presence of acute blood loss producing hypotension with associated tachycardia and tachypnea.

When evaluating the risks and benefits of transfusion in the long-term care setting, consider the quality of life that would be achieved for the patient; the wishes of the patient and family; and the benefits and burdens to the patient of a hospital transfer. It is important to remember that a blood transfusion may invalidate the results of subsequent laboratory tests for anemia.

MONITORING

The monitoring of patients with anemia requires attention to patient symptoms and consistent follow-up of hematologic status, underlying causes, and laboratory values.

STEP 8

Monitor the patient's response to interventions and adjust as necessary. Monitor the patient's response to treatment by reassessing symptoms and ordering follow-up laboratory tests as indicated (Table 16) and individual tests relevant to the underlying causes of the patient's anemia (e.g., nutritional deficiency, gastrointestinal bleeding). Also monitor the patient for adverse consequences of anemia treatment (Table 17). Reassess the treatment approach if the patient experiences adverse effects or does not respond to treatment.

The appropriate time to stop treatment will vary according to the cause of the patient's anemia and the stabilization of any related symptoms. In general, stop or modify therapy when treatment goals have been reached or when it is apparent that the patient is not responding to therapy.

TABLE 16

Suggested Laboratory Tests for Monitoring Response to Anemia Treatment

Patients taking iron supplements	Quarterly or as-indicated measurement of hemoglobin, serum iron, total iron-binding capacity, ferritin
Patients taking vitamin B_{12} or folate supplements	Measurement of serum B_{12}, serum folate, and hemoglobin every 6–8 weeks until stable, then every 6–12 months or as indicated (**Exception:** Generally, serum B_{12} is not measured during therapy if the deficiency is caused by an absorption disorder)
Patients taking ESAs	Weekly or twice weekly measurement of hemoglobin until stable, then monthly

TABLE 17

Common Adverse Effects of Anemia Treatments

Oral iron

- Abdominal cramps
- Constipation
- Diarrhea
- Dyspepsia
- Iron overload
- Nausea and vomiting

Parenteral iron**[64]

- Allergic reactions
- Backache
- Chest pain
- Chills
- Dizziness
- Fever with increased sweating
- Flank, groin, or muscle pain
- Flushing or redness of skin
- Headache
- Hypotension
- Iron overload
- Metallic taste
- Nausea or vomiting
- Numbness, pain, or tingling in hands or feet
- Pain, redness, or sores at injection site
- Tachycardia

* These adverse effects may be more applicable to older parenteral iron formulations.

Erythropoietin-stimulating agents[65]

- May cause or worsen hypertension
- Excessive dose or duration can lead to polycythemia and dangerous thrombotic events, including myocardial infarction and stroke

Blood Transfusion

- Anaphylaxis
- Chills
- Fever
- Bloodborne infection
- Transfusion reaction

Iron-deficiency anemia. Stop treatment when hemoglobin and serum ferritin values are normalized. After a patient has been receiving iron for 6 months, iron stores should be replenished and therapy should be discontinued unless there is ongoing blood loss or an uncorrectable underlying cause.

Folate-deficiency anemia. Stop treatment when hemoglobin is normalized, assuming the cause of the folate deficiency (e.g., dietary deficiency, adverse drug interaction) is resolved.

Vitamin B_{12}-deficiency anemia. Vitamin B_{12}-deficiency anemia due to absorption disorders requires lifelong treatment. For other causes of B_{12} deficiency, consider stopping treatment when the B_{12} level is normalized.

Anemia of chronic disease. If the anemia has an underlying cause that is treatable, treat that condition to help to normalize hemoglobin. If the underlying cause is untreatable, monitor the CBC periodically. If a patient with ACD develops worsening anemia due to another cause (e.g., bleeding, hemolysis), treat the new condition.

Anemia associated with chronic kidney disease. Monitor patients receiving ESAs to ensure that hemoglobin does not exceed 12 g/dL. Monitor hemoglobin once or twice weekly until it has stabilized and a maintenance dose has been established. If the patient's hemoglobin is above the target level, decrease the ESA dose but do not necessarily withhold it. Long-term therapy may be necessary.

STEP 9

Monitor the impact of anemia on the patient. Review the treatment goals specified in the patient's plan of care. Consider outcomes in light of the patient's overall prognosis and personal preferences. Subjective outcomes, such as improved quality of life, increased engagement in activities, improved stamina, and decreased fatigue may be important. Expect individual patients' responses to treatments to vary. Continue to monitor the patient's nutrition, where nutritional factors play a role in the etiology of the patient's anemia.

STEP 10

Monitor the facility's management of anemia. Review the management of patients with anemia through the facility's quality improvement processes. Table 18 suggests indicators that a facility may wish to use to measure the success of interventions to manage anemia.

TABLE 18
Sample Performance Measurement Indicators

Process Indicators

- Systematic follow-up of abnormal CBCs
- Systematic evaluation for the causes of anemia when appropriate
- Appropriate use of medications to treat anemia
- Systematic laboratory monitoring of patients with anemia

Outcome Indicators

- Improvement in physical, social, and cognitive function of patients with anemia
- Increase in hemoglobin concentrations in patients with treatable anemia
- Reduction in hospitalizations for anemia-related complications

SUMMARY

Anemia is a common condition in the frail elderly population. In many cases a cause for the patient's anemia can be identified when a systematic evaluation process is followed. Nutritional deficiencies that may be contributing to anemia should be treated to the extent possible. Pharmacologic treatment options are available for specific disorders and deficiency states that contribute to anemia. However, these therapies and blood transfusions should not substitute for a systematic evaluation of the patient's anemia. Treatment of chronic diseases that contribute to anemia should be optimized. It is advisable to monitor both treatment effects and the patient's clinical and functional status.

REFERENCES

1. World Health Organization. Nutritional Anaemias: Report of a WHO Scientific Group. 1968. Geneva, Switzerland.
2. Artz AS, Fergusson D, Drinka PJ, et al. Prevalence of anemia in skilled-nursing home residents. Arch Gerontol Geriatr 2004; 39: 201–206.
3. Van Vleet J, Narayanan S, O'Quigley M, et al. Costs associated with anemia in the nursing home: Results from the Resource Utilization and Treatment of Anemia in Long-term-care Residents (RESTORE) Study. Poster presented at the American Geriatrics Society Annual Meeting. Orlando, FL, May 13–15, 2005.
4. Morley JE, Thomas DR, Geronemus RP, et al. Diagnosis and management of anemia in long-term care. Accredited continuing medical education program sponsored by Medical Education Resources, Inc. Supplement to Annals of Long-Term Care, August 2003.
5. Kamenetz Y, Beloosesky Y, Zelter C, et al. Relationship between routine hematological parameters, serum IL-3, IL-6 and erythropoietin and mild anemia and degree of function in the elderly. Aging Clin Exp Res 1998; 10: 32–38.
6. Chaves P, Ashar T, Guralnik JM, et al. Looking at the relationship between hemo-

globin concentration and previous mobility difficulty in older women: Should the criteria used to define anemia in older people be changed? J Am Geriatr Soc 2002; 50: 1257–1264.
7. Dharmarajan TS, Avula S, Norkus EP. Anemia increases risk for falls in hospitalized older adults: An evaluation of falls in 362 hospitalized, ambulatory, long term care and community patients. J Am Med Dir Assoc 2006; 7: 287–293.
8. Penninx BW, Pluijm SM, Lips P, et al. Late-life anemia is associated with increased risk of recurrent falls. J Am Geriatr Soc 2005; 53(12): 2106–2111.
9. Dharmarajan TS, Norkus EP. Mild anemia and the risk of falls in older adults from nursing homes and the community. J Am Med Dir Assoc 2004; 5: 395–400.
10. Cesari M, Penninx BWJH, Lauretani F, et al. Hemoglobin levels and skeletal muscle: Results from the InCHIANTI Study. J Gerontol A Biol Sci Med Sci 2004; 59: 249–254.
11. Penninx BW, Pehor M, Cesari M, et al. Anemia is associated with disability and decreased physical performance and muscle strength in the elderly. J Am Geriatr Soc 2004; 52(5): 719–724.
12. Wu WC, Rathore SS, Wang Y, et al. Blood transfusion in elderly patients with acute myocardial infarction. N Engl J Med 2001; 345: 1230–1236.
13. Ezekowitz JA, McAlister FA, Armstrong PW. Anemia is common in heart failure and is associated with poor outcomes; insights from a cohort of 12,065 patients with new-onset heart failure. Circulation 2003; 107: 223–225.
14. Levin A. The role of anaemia in the genesis of cardiac abnormalities in patients with chronic kidney disease. Nephrol Dial Transplant 2002; 17: 207–210.
15. Metivier F, Marchais SJ, Guerin AP, et al. Pathophysiology of anaemia: Focus on the heart and blood vessels. Nephrol Dial Transplant 2000; 15(suppl 3): 14–18.
16. Levin A, Singer J, Thompson CR, et al. Prevalent left ventricular hypertrophy in the predialysis population: identifying opportunities for intervention. Am Journal Kidney Disease 1996; 27: 347–354.
17. Beard CM, Kokmer E, O'Brien PC, et al. Risk of Alzheimer's disease among elderly patients with anemia: Population based investigations in Olmstead County, Minnesota. Ann Epidemiol 1997; 7(3): 219–224.
18. Van Dijk PT, Mehr DR, Ooms ME, et al. Comorbidity and 1-year mortality risks in nursing home residents. J Am Geriatr Soc 2005; 53: 660–665.
19. Zuccala G, Marzetti E, Cesari M, et al. Correlates of cognitive impairment among patients with heart failure: Results of a multicenter survey. Am J Med 2005; 118: 496–502.
20. Li S, Foley RN, Collins AJ. Anemia, hospitalization, and mortality in patients receiving peritoneal dialysis in the United States. Kidney Int 2004; 65(5): 864–869
21. Zeidman A, Fradin Z, Blecher A, et al. Anemia as a risk factor for ischemic heart disease. Isr Med Assoc J 2004; 6(1): 16–18.
22. Felker GM, Gattis WA, Leimberger JD, et al. Usefulness of anemia as a predictor of death and rehospitalization in patients with decompensated heart failure. Am J Cardiol 2003; 92(5): 625–628.
23. Guse CE, Porinsky R. Risk factors associated with hospitalization for uninten-

tional falls: Wisconsin hospital discharge data for patients aged 65 and over. Wis Med J 2003; 102: 37–42.
24. Argyriadou S, Vlachonikolis I, Melisopoulou H, et al. In what extent anemia coexists with cognitive impairment in elderly: A cross-sectional study in Greece. BMC Fam Pract 2001; 2: 5. Epub 2001 Oct. 25.
25. Herndon JG, Helmick CG, Sattin RW, et al. Chronic medical conditions and risk of fall injury events at home in older adults. J Am Geriatr Soc 1997; 45: 739–743.
26. Balducci L. Epidemiology of anemia in the elderly: Information on diagnostic evaluation. J Am Geriatr Soc 2003; 51: S2–S9.
27. Penninx BWJH, Guralnik JM, Onder G, et al. Anemia and decline in physical performance among older persons. Am J Med 2003; 115: 104–110.
28. Gruson KI, Ahronoff GB, Egol KA, et al. The relationship between admission hemoglobin level and outcome after hip fracture. J Orthop Trauma 2002; 16: 39–44.
29. Guralnik JM, Ferrucci L, Pieper CF, et al. Lower extremity function and subsequent disability: Consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci 2000; 55: M221–M231.
30. Levin A, Singer J, Thompson CR, et al. Prevalent left ventricular hypertrophy in the predialysis population: Identifying opportunities for intervention. Am J Kidney Dis 1996; 27: 347–354.
31. Onder G, Penninx B, Cesari M, et al. Anemia is associated with depression in older adults: Results from the InCHIANTI study. J Gerontol A Biol Sci Med Sci 2005; 60: 1168–1172.
32. Chaves PH, Semba RD, Leng SX, et al. Impact of anemia and cardiovascular disease on frailty status of community-dwelling older women: The Women's Studies I and II. J Gerontol A Biol Sci Med Sci 2005; 60(6): 729–735.
33. Lango D. Closing in on a killer: Anemia in elderly people. J Gerontol A Biol Sci Med Sci 2005; 60: 727–728.
34. Strippoli GF, Navaneethan SD, Craig JC. Haemoglobin and haematocrit targets for the anaemia of chronic kidney disease. Cochrane Database Syst Rev 2006; 18;(4): CD003967.
35. Tangalos EG, Hoggard JG, Murray AM, Thomas DR. Treatment of kidney disease and anemia in elderly, long-term care residents. J Am Med Dir Assoc 2004; 5(4 Suppl): H1–H6.
36. National Kidney Foundation, Inc. Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease. New York: 2006. Available at http://www.kidney.org/professionals/kdoqi/guidelines_anemia/. Accessed 1/23/07.
37. Weiss G, Goodnough L. Anemia of chronic disease. N Engl J Med 2005; 352: 1011–1023.
38. Beers MH, Berkow R. Merck Manual of Diagnosis and Therapy, 17th ed. Merck & Co., 1999–2005. Available at http://www.merck.com/mrkshared/mmanual/home.jsp.

39. Clinical Pharmacology. Adverse events. www.cpip.gsm.com. Accessed 9/10/05.
40. Hutson PR. Hematology: Red and white blood cell tests. In: Lee M. Basic Skills in Interpreting Laboratory Data, 3rd ed. 2004. Bethesda, MD: American Society of Health-System Pharmacists.
41. Parr MD, Doukas M. Drug induced hematologic disorders. In: Dipiro JT et al. (eds.). Pharmacotherapy: A Pathophysiologic Approach, 3rd edition. 1997. Stamford, CT: Appleton and Lange, pp. 1915–1927.
42. Spruill WJ, Wade WE. Anemia. In: Dipiro JT et al. (eds.). Pharmacotherapy: A Pathophysiologic Approach, 3rd edition. 1997. Stamford, CT: Appleton and Lange, pp. 1857–1875.
43. Guralnik JM, Eisenstadt RS, Ferrucci L, et al. Prevalence of anemia in persons 65 and older in the United States: Evidence for a high rate of unexplained anemia. Blood 2004; 104: 2263–2268.
44. Fick DM, Cooper JW, Wade WE, et al. Updating the Beers criteria for potentially inappropriate medication use in older adults: Results of a US consensus panel of experts. Arch Intern Med 2003; 163(22): 2716–2724.
45. Rimon E, Kagansky N, Kagansky M, et al. Are we giving too much iron? Low dose iron therapy is effective in octogenarians. Am J Med 2005; 118: 1142–1147.
46. American Society of Health System Pharmacists [ASHP]. Anti-Anemia Drugs. 2006. Bethesda, MD: American Hospital Formulary Service Drug Information.
47. Beers MH, Fletcher AJ, Jones TV, et al. The Merck Manual of Medical Information – Second Home Edition, Online Version. Merck & Co., Inc., 2004–2005. http://www.merck.com/mmhe/sec14/ch172/ch172c.html. Accessed 8/28/06.
48. Vidal-Alaball J, Butler CC, Cannings-John R, et al. Oral vitamin B_{12} versus intramuscular vitamin B_{12} for vitamin B_{12} deficiency. The Cochrane Database Syst Rev 2005; 20(3): CD004655.
49. Eussen SJ, de Groot LC, Clarke R, et al Oral cyanocobalamin supplementation in older people with vitamin B_{12} deficiency: A dose-finding trial. Arch Intern Med 2005; 165(10): 1167–1172.
50. Bolaman Z, Kadikoylu G, Yukselen V, et al. Oral versus intramuscular cobalamin treatment in megaloblastic anemia: A single-center, prospective, randomized, open-label study. Clin Ther 2003; 25(12): 3124–3134.
51. Dharmarajan TS, Adiga GU, Norkus EP. Vitamin B_{12} deficiency. Recognizing subtle symptoms in older adults. Geriatrics 2003; 58(3): 30–38.
52. Thomas DR. Anemia in older persons. In: Pathy JMS, Sinclair AJ, Morley JE (eds.). Principles and Practice of Geriatric Medicine. 2006. West Sussex, England: John Wiley & Sons, Ltd.
53. Nurko S. Anemia in chronic kidney disease: Causes, diagnosis, treatment. Cleve Clin J Med 2006; 73(3): 289–297.
54. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004; 23: 1296–1305.
55. John R, Webb M, Young A, Stevens PE. Unreferred chronic kidney disease: A longitudinal study. Am J Kidney Dis 2004; 42: 825–835.
56. Bedani PL, Verzola A, Bergami M, et al. Erythropoietin and cardiocirculatory con-

dition in aged patients with chronic renal failure. Nephron 2001; 89: 350–353.
57. Moreno F, Aracil FJ, Perez R, et al. Controlled study on the improvement of quality of life in elderly hemodialysis patients after correcting end-stage renal disease-related anemia with erythropoietin. Am J Kidney Dis 1996; 27: 548–556.
58. Berns JS. Should all patients with chronic kidney disease receive an EPO-like drug? Cleve Clin J Med 2006; 73(3): 298–300.
59. Singh AK, Szczech L, Tang KL, et al. Correction of anemia with epoetin alfa in chronic kidney disease. N Engl J Med 2006; 355(20): 2085–2098.
60. U.S. Food and Drug Administration, Center for Drug Evaluation and Research. Information for Healthcare Professionals: Erythropoiesis Stimulating Agents (ESA). Available at http://www.fda.gov/cder/drug/InfoSheets/HCP/RHE_HCP.htm. Accessed 1/25/07.
61. Agarwal AK. Practical approaches to the diagnosis and treatment of anemia associated with CKD in elderly. J Am Dir Assoc. 2006; 7: S7–S12.
62. Denker BM. Erythropoietin: From bench to bedside. Nephrology Rounds 2004; 2 (3). Available at http://www.nephrologyrounds.org/cgi-bin/templates/framesets/nephrologyRoundsUSA/fs_snell.cfm. Accessed 1/25/07.
63. Menitove JE. Transfusion medicine. In: Goldman L, Ausiello D. Cecil Textbook of Medicine, 22nd ed. 2004. Philadelphia, PA: Saunders, p. 995.
64. USP DI Volume 1: Drug Information for the Health Care Professional, 26th ed, 2006. Greenwood Village, CO: Thompson Micromedex.
65. Centers for Medicare and Medicaid Services, F329, §483.25(l) Unnecessary Drugs. Rev. 9-20-2006. Available at http://www.cms.hhs.gov/SurveyCertificationGenInfo/PMSR/itemdetail.asp?filterType=none&filterByDID=0&sortByDID=4&sortOrder=descending&itemID=CMS1186880 [S&C-06-29-04-F329 REV.pdf]. Accessed 11/8/06.

BIBLIOGRAPHY

Dharmarajan et al. Vitamin B_{12} status in hospitalized elderly from nursing homes and the community. J Am Direct Assoc. 2000; 1: 21–72.

Guyatt GH, Patterson C, Ali M, et al. Diagnosis of iron-deficiency anemia in the elderly. Am J Med 1990; 88: 205–209.

Hertel JEW, Locay HR, Scarlata DS, et al. Darbepoetin alfa administration to achieve and maintain target hemoglobin levels for 1 year in patients with chronic kidney disease. Mayo Clin Proc 2006; 81(9): 1188–1194.

Josten E, Ghesquiere B, Linthoudt H, et al. Upper and lower gastrointestinal evaluation of elderly inpatients who are iron deficient. Am J Med 1999; 107: 24–29.

Kis AM, Carnes M. Detecting iron deficiency in anemic patients with concomitant medical problems. J Gen Intern Med 1998; 13: 455–461.

Iron deficiency. Revised May 15, 2003. Available at http://sickle.bwh.harvard.edu/fe-def.html. Accessed 1/23/07.

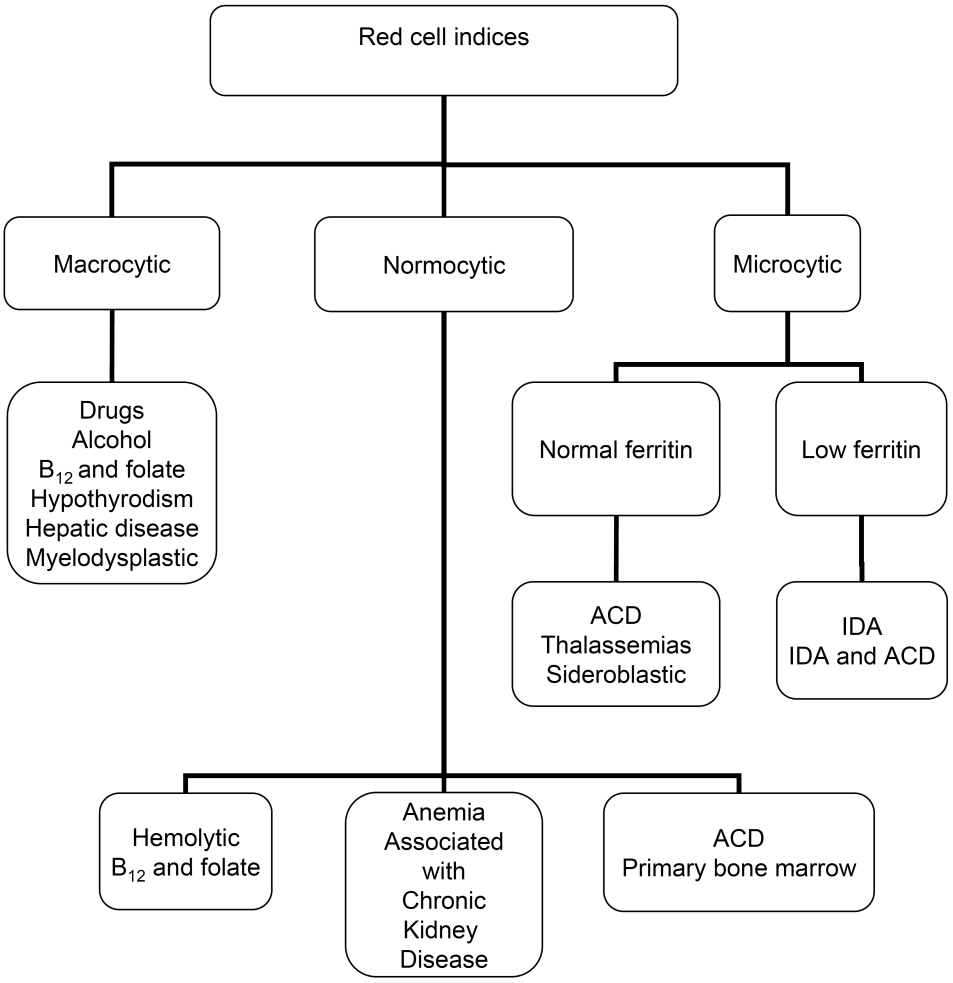
Oh RC, Brown DL. Vitamin B_{12} deficiency. Am Fam Physician 2003; 67: 979–986.

Patterson C, Turpie ID, Benger AM. Assessment of iron stores in anemic geriatric patients. J Am Geriatr Soc 1985; 33:764–767.

Spivak JL. Anemia in the elderly: Time for new blood in old vessels? Arch Intern Med 2005; 165(19): 2187–2189.
Wians Jr. FH, Urban JE, Keffer JH, Kroft SH. Discriminating between iron deficiency anemia and anemia of chronic disease using traditional indices of iron status versus transferrin receptor concentration. Am J Clin Pathol 2001; 115: 112–118.

APPENDIX 1.

Algorithm for Diagnosis of Anemia Using Red Cell Morphology

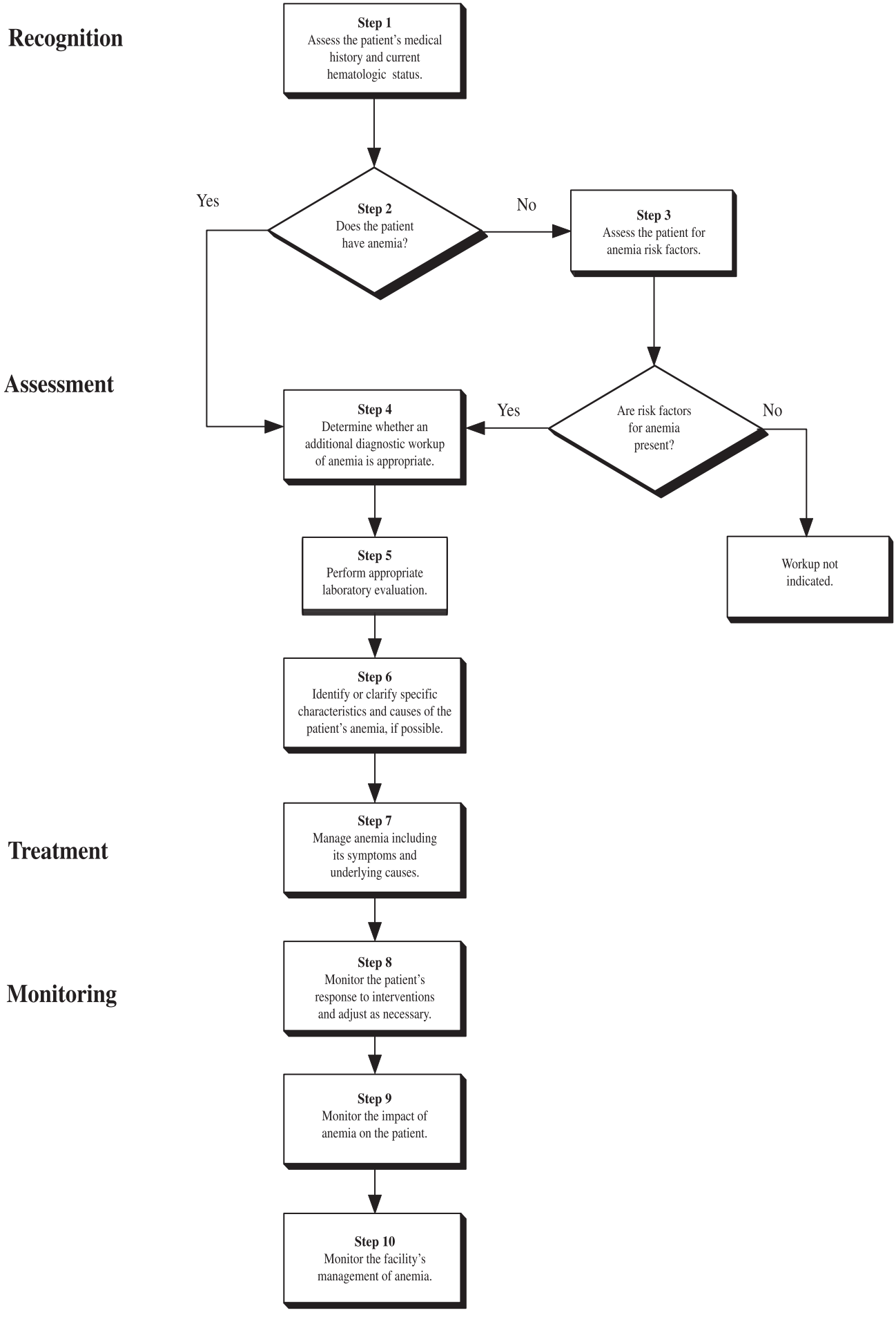


ACD: anemia of chronic disease
IDA: iron deficiency anemia
(Categories overlap when the morphology of the anemia may present in one of several ways.)

Adapted from:
Thomas, 2006. Copyright John Wiley & Sons Limited. Reproduced with permission.

NOTES

This is the anemia in the long-term care setting algorithm to be used in conjunction with the written text of this clinical practice guideline. The numbers next to the different components of the algorithm correspond with the steps in the text.


Recognition
Step 1
Assess the patient's medical history and current hematologic status.
Step 2
Does the patient have anemia?
Yes
No
Step 3
Assess the patient for anemia risk factors.
Assessment
Are risk factors for anemia present?
Yes
No
Step 4
Determine whether an additional diagnostic workup of anemia is appropriate.
Workup not indicated.
Step 5
Perform appropriate laboratory evaluation.
Step 6
Identify or clarify specific characteristics and causes of the patient's anemia, if possible.
Treatment
Step 7
Manage anemia including its symptoms and underlying causes.
Monitoring
Step 8
Monitor the patient's response to interventions and adjust as necessary.
Step 9
Monitor the impact of anemia on the patient.
Step 10
Monitor the facility's management of anemia.

The Post-Acute and Long-Term Care Medical Association developed this guideline with the support and cooperation of the following individuals and companies:

Naushira Pandya, MD, CMD, CPG Project Chair
Charles Cefalu, MD, MS, Clinical Practice Committee Chair

Steering Committee Members:

Marjorie Berleth, MSHA RNC FADONA
Lisa Cantrell, RN, C
Sandra Fitzler, RN
Joseph Gruber, RPh, FASCP, CGP
Hosam Kamel, MD, CMD
Susan M. Levy, MD, CMD
Harlan Martin, R.Ph., CCP, FASCP
Evvie F. Munley
Jonathan Musher, MD, CMD
Barbara Resnick, PhD, CRNP
William Simonson, Pharm.D., FASCP

Corporate Supporters:

Amgen
Merck & Co., Inc.
Ross Products Division of Abbott Laboratories
Sanofi-Aventis

Organizational Participants:

American Association of Homes and Services for the Aging
American College of Health Care Administrators
American Geriatrics Society
American Health Care Association
American Society of Consultant Pharmacists
National Association of Directors of Nursing Administration in Long-Term Care
National Association of Geriatric Nursing Assistants
National Conference of Gerontological Nurse Practitioners

PALTmed
POST-ACUTE AND LONG-TERM CARE MEDICAL ASSOCIATION