Anemias in the Elderly

A. Robert Turner, MD, FRCPC; and Emily H. Turner, BSc (Hons)
Presented at University of Alberta's Conference Program April 2006

The incidence of anemia rises with age and is particularly prevelent in those > 85 years. Anemia in the elderly can be associated with the following symptoms:

- weakness,
- fatigue,
- increased falls and/or
- depression.

Severe anemia can lead to significant changes in mentation, as well as heart or kidney failure. This article will review the common causes of anemia in the elderly and will discuss some therapeutic approaches.

Most of the causes of anemia in the elderly are common to all age groups, but others are specific to the older population, including:

- myelodysplasia,
- anemia of chronic disorders,
- iron deficiency related to chronic blood loss from the GI tract,
- renal failure, or
- folate/B12 deficiency due to inadequate intake or diminished absorption.

As many as 50% of anemia cases in the elderly have no obvious diagnosis. In many of these cases, several of the above-mentioned lesions may combine to cause the anemia.

As many as 50% of anemia cases in the elderly have no obvious diagnosis.

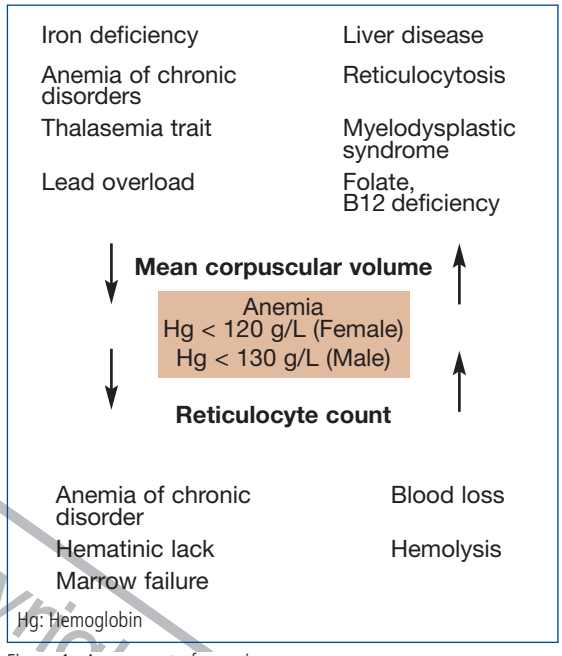


Figure 1. Assessment of anemia.

Definition of anemia

The World Health Organization has defined anemia as a hemoglobin level of < 120 g/L for women and < 130 g /L for men. The prevalence of anemia in the elderly ranges from 3% to 60% in elderly men and from 3% to 40% in elderly women.

Approach to the diagnosis of anemia

The use of two readily available assessments help to categorize the causes of anemia (Figure 1). Patients with a low mean corpuscular volume (MCV) (< 80 femtolitres) may have:

- iron deficiency,
- anemia of chronic disorders,
- thalassemia trait or
- lead poisoning.

Patients with an elevated MCV (> 100 femtolitres) may have reticulocytosis, which is a normal response to anemia caused by hemolysis or blood loss. Alternatively, they may:

- have liver disease,
- have a myelodysplastic disease,
- be responding to cytotoxic chemotherapy or
- have a B12/folate deficiency (generally patients with a B12/folate deficiency have a very elevated MCV).

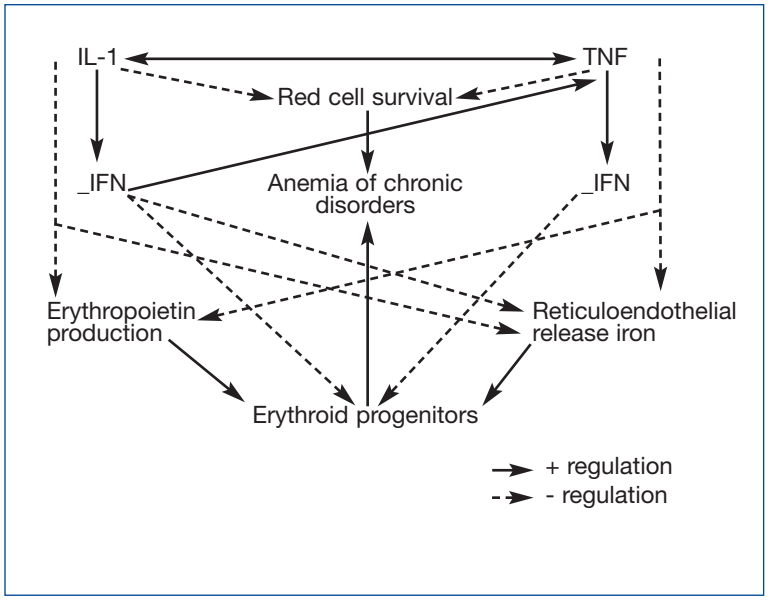


Figure 2. Cytokine effects in the pathogenesis of anemia.

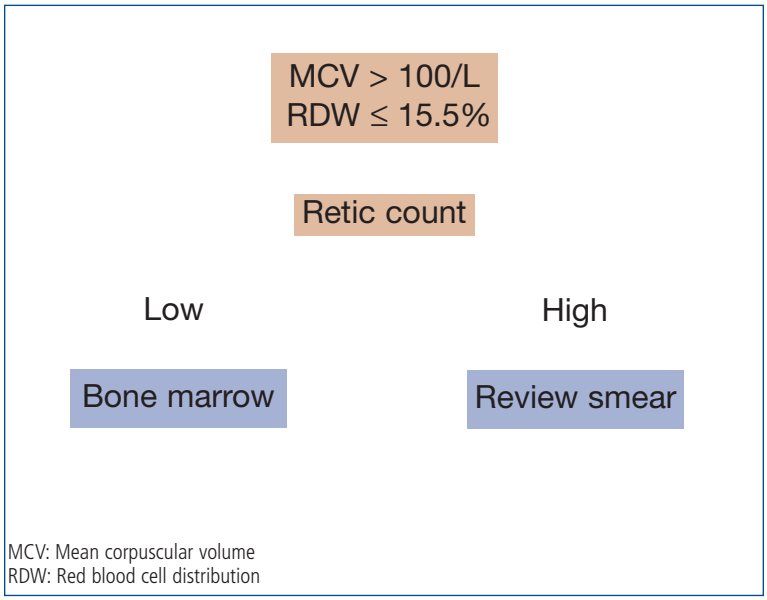
In the elderly, the differentiation between iron deficiency and anemia of chronic disorders is often difficult. Indeed, those two conditions may coexist. According to an article printed in the *New England Journal of Medicine* on the pathogenesis of anemia of chronic disorders, there are three groups of patients with biochemical or clinical evidence of inflammation and a reduced iron saturation. Patients whose ferritin is < 30 ng/mL have iron deficiency and need iron replacement. Patients whose ferritin is > 100 ng/mL have anemia of chronic disorders and do not need iron supplementation. Ferritins between 30 ng/mL and 100 ng/mL represent an indeterminate or combination of iron deficiency and anemia of chronic disorders. In this case, a trial of iron supplementation is recommended.[1]

The prevalence of anemia in the elderly ranges from 3% to 60% in elderly men and from 3% to 40% in elderly women.

The same article in the *New England Journal of Medicine* updates our understanding of the pathophysiology of anemia of chronic disorders. This is a disease where developing red blood cell precursors are starved of iron as a result of the effects of a variety of cytokines stimulated by the immune response, on the liver, GI tract and on the bone marrow. In addition, erythropoietin production is blunted and the

Dr. Robert Turner is a Clinical Hematologist and Medical Oncologist. He is a Professor of Medicine and Oncology at the University of Alberta, a Clinical Hematologist at the University of Alberta Hospital and a Senior Specialist in Medical Oncology at the Cross Cancer Institute in Edmonton, Alberta.

Emily Turner is a Graduate Student, Department of Chemistry, the University of Washington, Seattle, Washington.



MCV: Mean corpuscular volume
RDW: Red blood cell distribution

Figure 3. Approach to work-up of homogenous macrocytic anemia.

Table 1
Macrocytic anemia investigations

Causes	Diagnostic tests
Liver disease	GGTP
Myelodysplasia	Bone marrow
Decreased folate	Red cell folate
Decreased B12	Serum B12

GGTP: γ-glutamyl transpeptidase

Table 2
Reticulocytosis investigations

Causes of anemia	Diagnostic aids
Blood loss	• Patient history • Stool for occult blood
Hemolysis	• Haptoglobin • Plasma hemoglobin • Lactate dehydrogenase • Direct/indirect bilirubin • Peripheral blood smear

splenic destruction of red blood cells is stimulated. In order to bypass this pathophysiology, patients may need to be treated with parenteral iron or with erythropoietin. Both treatments can be associated with an improvement in the quality of life (Figure 2).[1]

Chronic GI loss of iron is an important issue in anemia in the elderly. Angiodysplastic lesions can lead to chronic GI losses. Many women will have become iron deficient during their fertile years and will still lack the adequate iron stores needed to deal with blood losses that might arise from GI sources, or from operations.

Low serum testosterone, chronic elevation of serum creatinine, or alterations in thyroid function should also be considered in the work-up of mild and chronic anemias in the elderly.

Macrocytic anemias

Patients with macrocytic anemia who have a low red blood cell distribution usually have chronic liver disease, or are in a state of chronic bone marrow failure. If the reticulocyte count is elevated, the patient may be responding to chronic hemolysis. Clues for the etiology may come from the peripheral blood smear (Figure 3).

The peripheral blood and the MCV should not be relied upon to rule out a B12 deficiency. Pernicious anemia is a protean disorder that can produce significant cognition changes without anemia. Every geriatric patient

deserves at least one serum B12. The downsides of B12 supplementation are limited and this therapy should be used whenever a B12 deficiency is suspected. Nowadays folate deficiency is exceedingly unusual given the supplements that are found in food stuffs (Table 1).

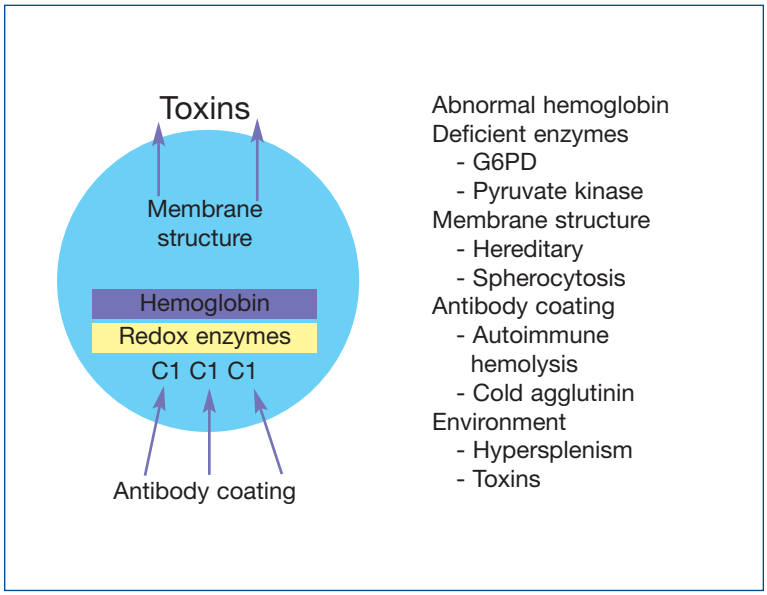


Figure 4. Types of hemolysis.

Myelodysplastic syndrome

Myelodysplastic syndrome is a common cause of macrocytic anemia in the elderly. Myelodysplasia can be translated into *a marrow that does not work*. The etiology of this marrow failure is not known. Only a small fraction of patients will transform to an acute leukemia, but this condition should be suspected whenever there is an anemia associated with abnormal white cell counts and/or platelet counts. To diagnose myelodysplasia, a bone marrow aspirate and bone biopsy is necessary. This is an uncomfortable procedure which should be ordered judiciously. Unfortunately, there is no evidence-based therapy for myelodysplasia beyond transfusion support. Unless one is contemplating putting the patient on a clinical trial, a bone marrow aspirate is not likely necessary.

Reticulocytosis

Reticulocytes are young red blood cells that have recently lost their nucleus. An elevated reticulocyte count indicates that the patient's bone marrow is producing more red blood cells in response to erythropoietin. Erythropoietin is produced when the kidney senses hypoxia and is the result of either blood loss or hemolysis (Table 2).

If a patient's stool is positive for occult blood, a GI investigation is appropriate. Hemolysis can be indicated by the presence of a low haptoglobin or an elevated indirect bilirubin and/or lactate dehydrogenase. The cause of the hemolysis is most often cold or warm hemolytic anemia. Other causes of hemolysis (Figure 4) are very unusual.

Cold and warm hemolytic anemia in the elderly are most often associated with an under-

Table 3

TPRBC transfusions

- 1 unit of packed cells = 10 g hemoglobin
- Avoid single transfusion
- Even though blood is free, there are costs to the patient. These include:
  - Transfusion reaction
  - Iron overload (clinically important > 50-75 units)
  - Congestive heart failure
  - Hepatitis
  - AIDS

lying lymphoma or chronic lymphocytic leukemia.

Transfusion therapy

There is no magic number for the initiation of red blood cell transfusions. The symptoms of anemia are the most important. These symptoms include:

- headache,
- angina,
- postural hypotension and
- edema.

One unit of packed red blood cells raises the hemoglobin by 10 g per litre. Generally, two units to three units is prescribed with each transfusion episode. While viral infections, such as hepatitis B, hepatitis C and HIV, are of great concern to patients and physicians, the risk of these infections is exceedingly low. A more important concern is the possibility of bacterial contamination of the red cell units or of misidentification of the patient. Other complications include iron overload if > 50 units of red blood cells is administered. Congestive heart failure is common is elderly patients and can be exacerbated by the administration of two units to three units of packed red blood cells without diuresis (Table 3).

Minimal assessment of anemia in the elderly includes:

- Comple blood cell count with reticulocyte count and differential
- Peripheral blood smear
- Stools for occult blood
- Serum protein electropheresis looking for paraproteinemia
- Thyroid stimulating hormone
- Ferritin
- Serum B12
- Testosterone (in males)

A decrease in the hemoglobin level in elderly patients is not physiological. Anemia is associated with functional impairments, including mobility disorders and cognitive defects. It behooves us to pay attention to anemia in the elderly. Many of the causes listed above are amenable to therapy.

cme

Reference

1. Weiss G, Goodnough L: Anemia of Chronic Disease. N Engl J Med 2005; 352:1011-23.

Resources

2. Steensma DP, Bennett JM: The Myelodysplastic syndromes: Diagnosis and treatment. Mayo Clin Proc 2006; 81(1):104-30.
3. Turner, AR, Anglin P, Burkes R, et al: Epoietin Alfa in cancer patients: Evidence-based guidelines. J Pain Symptom Manage 2001; 22(5): 954-64.