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## Focus on:

# Anemia in the Elderly

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Anemia is a common finding in elderly patients. The World Health Organization (WHO) criteria for anemia are a hemoglobin of < 120 g/L for women and < 130 g/L for men. Using these values, the prevalence of anemia ranges from as low as 8% for 70-year-olds, to more than 40% for those over age 85.<sup>1-4</sup>

## What are the symptoms?

Fatigue, dyspnea, and other typical symptoms often occur with less severe anemia in elderly patients than would be expected with younger adults. The symptoms of other diseases may be exacerbated if anemia is also present. Therefore, anemia should be considered when patients present with worsening of heart or lung disease. Anemia can also contribute to problems, such as decreased mobility, dizziness, cognitive impairment, and even depression. These medical conditions, or the aging process itself, are often blamed

### Karen's case

Karen, 68, has a long history of rheumatoid arthritis. For several years, her disease has been inactive and has not required treatment. However, for the past six months, she has experienced worsening joint pain and stiffness, especially in the mornings, along with progressive fatigue. In addition to active arthritis on physical exam, she is noted to be pale and tachycardic.



- What is the most likely cause of her anemia?
- What treatment approach is recommended?
- Is iron replacement therapy required?
- Is colonoscopy/endoscopy or bone marrow biopsy indicated?

**For more on Karen, go to page 86.**

### Laboratory investigations

- Rheumatoid factor: Reactive, 640 IU/mL
- White blood cells: 14.2 x10<sup>9</sup>/L (4.8-10.8 x10<sup>9</sup>/L)
- Hemoglobin: 98 g/L (120-160 g/L)
- MCV: 76 g/L (81-97 g/L)
- Platelets: 390 x10<sup>9</sup>/L (150-400 x10<sup>9</sup>/L)
- ESR: 71 mm/h (0-20 mm/h)
- Ferritin: 426 g/L (11-307 g/L)

MCV: Mean corpuscular volume  
ESR: Erythrocyte sedimentation rate

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## Anemia in the Elderly

Table 1

### Common causes of anemia

- Anemia of chronic disease
- Iron deficiency anemia
- Vitamin B<sub>12</sub> deficiency
- Folate deficiency
- Myelodysplasia
- Bleeding
- Chronic leukemia, lymphoma, or myeloma

Table 2

### Indications for investigating anemia

- Hemoglobin < 110-120 g/L
- Progressive anemia
- Leukopenia or leukocytosis
- Thrombocytopenia
- High or low MCV
- Other clinical or laboratory abnormalities

MCV: Mean corpuscular value

for patients' complaints, causing the presence of anemia to be overlooked.

There are many possible causes of anemia (Table 1). Among hospitalized patients, anemia of chronic disease (ACD) and iron deficiency anemia (IDA) are the most common findings.<sup>5</sup> In about 20% of patients, no underlying cause of anemia can be found.<sup>3,5</sup>

Renal failure is an important cause of anemia for patients of all ages. Although renal function shows a steady decline with age, the overall magnitude of this decline is small without underlying renal disease.<sup>6</sup> Since anemia from renal impairment is not seen until more significant renal dysfunction is present, this age-related change alone is probably not responsible for significant anemia in the elderly.

## What investigations can be done?

The decision to investigate anemia will depend on the severity of anemia and the presence of other laboratory and clinical findings. It would be reasonable to consider a hemoglobin value of 110 g/L to 120 g/L as a threshold for investigating anemia. (Above these values, anemia is unlikely to affect quality of life.) However, the decision to investigate any patient at any level of hemoglobin must be based on the individual case and clinician's judgement. Observation can be considered if there are no other blood abnormalities (Table 2).

The mean corpuscular value (MCV) is useful for differentiating between common causes of anemia and deciding on a course of investigation (Figure 1). In most cases, elderly patients

# Anemia in the Elderly

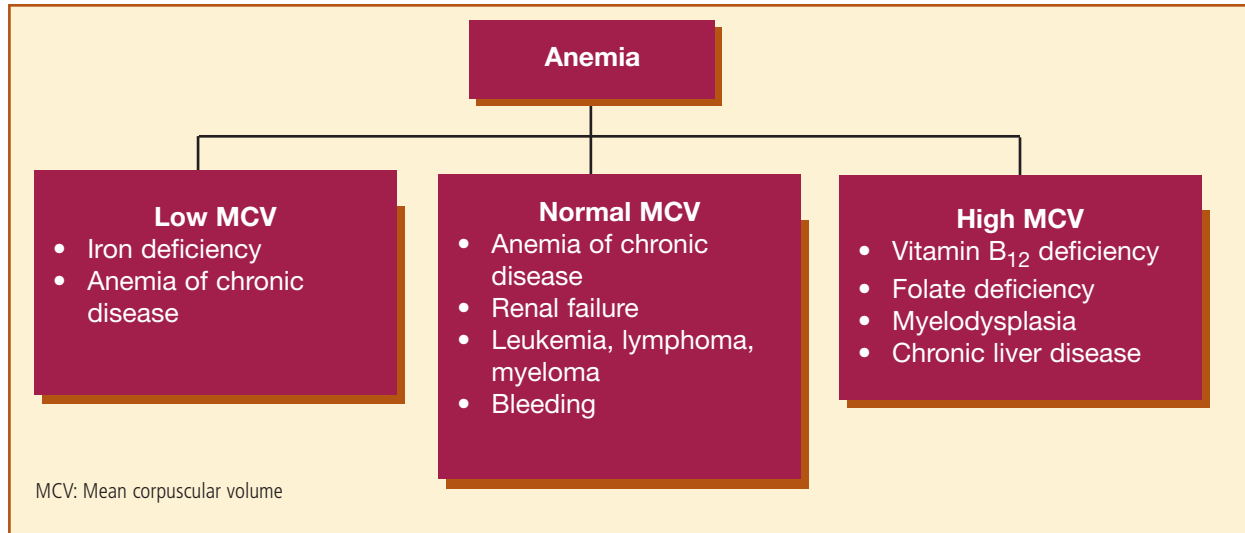


Figure 1. Common causes of anemia according to MCV.

Table 3

## Useful investigations

- Complete blood cell count
- Peripheral blood smear
- Reticulocyte count
- Serum ferritin (if low MCV)
- B<sub>12</sub>, folate (if high MCV)
- Creatinine
- Serum protein electrophoresis

MCV: Mean corpuscular value

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## Anemia in the Elderly

Table 4

### Sources for GI blood loss

- Esophagitis
- Varices
- Peptic ulcer disease
- NSAID use
- Gastric cancer
- Inflammatory bowel disease
- Angiodysplasia
- Colorectal cancer
- Benign polyps

NSAID: Non-steroidal anti-inflammatory drug  
GI: Gastrointestinal

### A followup on Karen

The patient likely has anemia of chronic disease, a common finding with active rheumatologic diseases.

Iron deficiency is very unlikely, as the serum ferritin is not low. Iron replacement would not be helpful, and investigation of the gastrointestinal tract is not indicated.

The best therapy for anemia of chronic disease is to treat the underlying cause, in this case the patient's rheumatoid arthritis. Bone marrow biopsy would not be needed at this time, but would be considered if the anemia does not improve with arthritis treatment.

will present with normochromic, normocytic anemia. Occasionally anemia of iron, B<sub>12</sub>, or folate deficiency can present before changes in the MCV are seen, so that the actual diagnosis is not initially suspected. Tests that may be useful in the initial investigation of patients are listed in Table 3.

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## What are the different types of anemia?

### IDA

The serum ferritin is the most accurate test for diagnosing IDA. Ferritin is often low before the MCV becomes abnormal, especially early in the development of IDA. As the iron deficiency worsens, the MCV falls along with hemoglobin. Iron deficiency is almost always present when the serum ferritin is < 15 g/L. It is less likely, but may still be present, with serum ferritin as high as 100 g/L. Serum iron is usually low in IDA, but the total iron binding capacity (TIBC) is elevated.

Iron deficiency is the cause of anemia in 10% to 15% of elderly patients. It is rarely caused by nutritional deficiency and is usually due to blood loss through the gastrointestinal (GI) tract. GI blood loss is often occult and is not ruled out by negative fecal blood tests. Therefore, investigation of the GI tract should usually be undertaken when IDA occurs in the elderly, especially to rule out malignancy. Numerous lesions can be responsible (Table 4). Upper GI tract lesions are most common, accounting for IDA in 40% to 50% of elderly patients. For as many as 40% of patients with IDA, no source of blood loss can be found despite extensive investigation. Fortunately these patients do well with iron replacement, and repeat investigation is not often needed.<sup>7,8</sup>

## Anemia in the Elderly

Treatment of IDA anemia includes treating the source of blood loss once it is identified. Oral iron replacement three times daily is usually effective. This measure often results in constipation and other GI side-effects, which can be reduced by lowering the dose to once or twice daily. If oral iron is not effective or not tolerated, intramuscular and intravenous iron preparations are available.

### ACD

ACD is caused by inflammatory cytokines produced in response to many acute and chronic conditions

Unlike IDA, the TIBC is usually normal or low in ACD. The serum ferritin is the most useful test for differentiating the two. Ferritin will increase with inflammation as an acute phase reactant and, as a result, is often high in ACD. A serum ferritin > 100 g/L is unlikely to occur in IDA and is more in keeping with ACD. In a minority of cases, iron studies cannot distinguish between IDA and ACD as the cause of microcytic anemia. In these situations, a bone marrow aspirate may be required for diagnosis.

ACD is unlikely to resolve without treatment of the underlying disorder. Iron replacement is not helpful unless iron deficiency is also present.

### Vitamin B<sub>12</sub> and folate deficiency

Both vitamin B<sub>12</sub> and folate deficiency are common among the elderly, each occurring in 5% to 10% of patients. These deficiencies

will usually produce macrocytic anemia. Vitamin B<sub>12</sub> and folic acid levels should be checked when anemia is associated with a high MCV. Occasionally the MCV will be normal, and vitamin deficiencies should be considered in cases of normocytic anemia in which no cause can be found. Because neurologic side-effects of B<sub>12</sub> deficiency can occur without anemia, some experts recommend screening all elderly patients at least once for occult B<sub>12</sub> deficiency. False positive and false negative results are possible with vitamin B<sub>12</sub> testing, especially with results in the low normal range, which may not accurately reflect true tissue levels. Serum methylmalonic

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## Anemia in the Elderly

### Frequently Asked Questions

#### 1. When is GI tract workup indicated?

A GI tract cause for anemia should be suspected in any elderly patient presenting with iron deficiency. Iron deficiency should first be confirmed with serum ferritin testing. A GI tract lesion should also be considered if there is evidence of GI blood loss or unexplained abdominal symptoms.

#### 2. Do anemic elderly patients have a poorer quality of life?

Anemia does seem to predict poorer quality of life and survival in the elderly. Anemia can worsen the outcome of heart and lung disease, as well as other medical problems and the cause of anemia itself can be associated with poor prognosis.

#### 3. What is the role for erythropoietin therapy in anemic elderly patients?

Erythropoietin is very effective in treating anemia associated with chronic renal failure and can be helpful in treating anemia in cancer patients and HIV-infected patients. High doses of erythropoietin may benefit some patients with ACD or myelodysplasia.

#### 4. Are bone marrow biopsy and aspirate helpful in finding the cause for anemia in the elderly?


Most anemic elderly patients will not need bone marrow biopsy and aspirate, as the cause of anemia can usually be determined using less invasive investigations. Bone marrow biopsy and aspirate should probably be performed if there is pancytopenia or other abnormalities of the white blood cells or platelets, or if a monoclonal gammopathy is present.

acid (MMA) levels can be very helpful in this setting, as an elevation of serum MMA is very specific for vitamin B<sub>12</sub> deficiency.

Treatment of vitamin B<sub>12</sub> deficiency usually involves intramuscular injection of vitamin B<sub>12</sub>, 100 g to 1000 g daily for three to seven days, followed by maintenance injections every one to three months. Oral preparations are also available. Folate deficiency is treated with oral folic acid, 1 mg daily.

### Myelodysplastic syndromes

Myelodysplastic syndromes (MDS) usually presents with anemia, along with abnormalities of white blood cells and platelets. MDS is rare before age 50, but much more common in the elderly, occurring in up to 5 % of those over 65. MDS should be suspected in cases of unexplained or unresponsive anemia, or anemia with abnormalities of the other blood cells. Bone marrow aspiration and biopsy are required for diagnosis.

Numerous therapeutic options exist, including chemotherapy, immunosuppression, and growth factors, such as granulocyte colony-stimulating hormone and erythropoietin. The response to most therapies is limited, however, and treatments have not been shown to improve survival. For this reason, treatment is limited to transfusion and other supportive care measures for most elderly patients. 

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### Take-home message

- Some causes of anemia include chronic disease, iron deficiency, vitamin B<sub>12</sub> deficiency, folate deficiency, and myelodysplasia.
- MCV is a useful tool to determine the cause of anemia.
- Treatment differs depending on the cause, ranging from iron replacement to supportive care measures.

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