# Anemia for the Primary Care Physician



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#### **KEYWORDS**

- Anemia Iron deficiency Anemia of inflammation Anemia of chronic disease
- Hemolytic anemia

#### **KEY POINTS**

- Anemia is always a sign of an underlying disease or deficiency. Pay attention to identifying
  the cause. A focused history, physical examination, complete blood cell count, reticulocyte count, and peripheral smear examination are the first steps in a work-up of anemia.
- Iron deficiency is the most common cause of anemia. Repletion of iron stores should be accompanied by identification of the cause of iron deficiency.
- The hallmark of cobalamin deficiency is the presence of neurologic symptoms. Treatment
  of CNS symptoms should be prompt and parenteral to prevent irreversible damage.
- Anemia of inflammation (AI) is caused by hepcidin-induced alterations of iron metabolism.
   Besides treating the underlying cause, erythropoietin (EPO)-stimulating agents (ESAs) and intravenous iron are effective in management.
- Hemolytic anemias, whether hereditary or acquired, are frequently chronic problems that require intermittent treatment, at least, and lifelong surveillance. A hematologist is best involved in the management.

#### INTRODUCTION

The World Health Organization defines anemia as a hemoglobin level of less than 13 g/dL in men and less than 12 g/dL in women. This is based on the average hemoglobin of healthy individuals. **Table 1** shows the World Health Organization limits for anemia defined as mild, moderate, and severe. Unless considered severe, anemia is often overlooked by primary care physicians. It is crucial to appreciate that even mild anemia may be an indication of a serious underlying condition. This article presents anemia and its management as they pertain to the primary care setting.

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Table 1 Anemia severity classification (hemoglobin values in grams per deciliter)			
	Anemia		
Population	Mild	Moderate	Severe
Pregnant women	10.0–10.9	7.0–9.9	<7.0
Nonpregnant women (≥15 y of age)	11.0–11.9	8.0-10.9	<8.0
Men (≥15 y of age)	11.0–12.9	8.0–10.9	<8.0

Data from WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and mineral nutrition information system. Geneva: World Health Organization; 2011. (WHO/NMH/NHD/MNM/11.1). Available at: http://www.who.int/vmnis/indicators/haemoglobin.pdf. Accessed June 7, 2016.

A broad classification is presented of anemia and details provided for the more common causes of anemia. The rarer diagnoses are touched on briefly and are best referred to a hematologist.

#### **ERYTHROPOIESIS**

To understand the etiology of anemia, a basic understanding of erythropoiesis, the process by which red blood cells (RBCs) are produced, is necessary. The primary regulatory hormone involved in erythropoiesis is EPO. This hormone is mostly produced by the kidney (small amounts are produced in the liver) and its release is contingent on the availability of oxygen for tissue metabolic needs. Once released, EPO stimulates both the production and maturation of erythroid precursor cells in the bone marrow. The availability of key nutrients—iron, vitamin B<sub>12</sub>, and folate—is essential for normal erythropoiesis. Other critical elements of erythropoiesis include a healthy bone marrow and a normal hemoglobin type.

#### Evaluation of a Patient with Anemia

#### History

Obtaining a good history is important. Key questions to address in the history include the following:

- Has there been any blood loss?
- What is the duration of the anemia? Is this genetic or acquired?
- Are there associated features? And, therefore, are they due to infection or malignancy?
- Are there comorbidities known to cause anemia (eg, renal failure, rheumatoid arthritis, and inflammatory bowel disease)?
- Does the patient's ethnicity influence the differential?

A thorough medication history, including use of aspirin and nonsteroidal antiinflammatory drugs, may be useful.<sup>1</sup>

#### Physical examination

The physical examination helps both confirm the presence of anemia (particularly in low resource settings) and determine the cause. Pallor of the conjunctiva has a sensitivity and specificity of 70% to 100%, respectively. Jaundice in the presence of anemia provides a clue to an etiology of hemolysis.<sup>2</sup>

Other important findings are accompanying lymphadenopathy, hepatosplenomegaly, bone tenderness, petechiae, and ecchymoses.

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