

The Evidence-Based Evaluation of Iron Deficiency Anemia



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KEYWORDS

• Iron deficiency anemia • Microcytic anemia • Occult gastrointestinal bleed

KEY POINTS

- The identification of iron deficiency anemia and any underlying contributing comorbidities is necessary to initiate the appropriate treatment.
- In the United States, iron deficiency anemia is most prevalent in young women due to menorrhagia. In this population, a focused history, a complete blood count and a ferritin level are sufficient to confirm the diagnosis of iron deficiency anemia.
- Profoundly low mean corpuscular volume in the setting of mild anemia and a normal red cell distribution width are more suggestive of thalassemia than iron deficiency anemia and necessitate hemoglobin electrophoresis for confirmation.
- In many chronic disease states, it can be difficult to distinguish between iron deficiency anemia and anemia of chronic disease. Transferrin receptor assays and the transferrin receptor-ferritin index will help to distinguish between the two.
- Iron deficiency anemia in the elderly, even in the absence of overt gastrointestinal bleeding, necessitates endoscopic evaluation for underlying gastrointestinal malignancy.

INTRODUCTION

Anemia is of interest to the general internist, as it results in significant morbidity and mortality in a variety of patient populations. It is associated with impaired cognitive function and development in young women,¹ perinatal complications in pregnancy,² an increased risk of falls in the elderly^{3,4} and a variety of other symptoms that affect patients' daily lives. Iron deficiency anemia (IDA) is a common cause of anemia and accounts for 50% of all cases of anemia worldwide. In the United States, IDA affects 1% to 2% of the population and is most prevalent in reproductive-aged women, affecting up to 12% of women aged 20 to 49.⁵ Sufficient iron stores are required for multiple processes, including oxygen transport as part of the hemoglobin molecule, enzymatic reactions as part of the cytochrome system, and electron transport and

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energy metabolism throughout the body.⁶ Early diagnosis of IDA can prevent multiple complications and improve quality of life. However, despite the multiple complications associated with IDA, routine screening for anemia in the asymptomatic, nonpregnant population is not recommended by the US Preventive Services Task Force.^{7,8}

Although iron deficiency is a common cause of anemia, there are additional potential etiologies for a reduction in the number of red blood cells or quantity of hemoglobin. Thus, on initial diagnosis of anemia, an internist must perform the appropriate evaluation to identify the cause of the anemia and subsequently select the appropriate treatment regimen. However, the process of evaluation can result in significant cost. In a nation suffering from rising health care expenditures, it is the responsibility of all physicians to do their part in decreasing this burden. Therefore, whereas identifying the underlying etiology of anemia is important, it is equally critical that we perform the evaluation in a cost-conscious manner. The purpose of this review is to suggest the most cost-effective, evidence-based assessment of IDA.

To fully understand the evaluation of IDA, we must first review the physiology of iron storage. Iron is absorbed from the diet, mainly in the small intestine, and released from stores when necessary. Free iron can be toxic to cells; therefore, it is bound to transferrin while in circulation. The transferrin-iron complex is taken up by erythroid marrow or liver parenchymal cells that express transferrin receptors. Once released from the transferrin receptor complex, iron becomes available for heme synthesis and other processes. Excess iron is bound to ferritin for storage. Hepcidin, another protein produced by the liver, is also integral in the regulation of iron stores. The physiology of hepcidin and its function in iron regulation is discussed later in this article, but it is important to note that hepcidin is increased in the setting of inflammation or iron overload and decreased in the setting of IDA.⁹ It also should be noted that given the multiple mechanisms for maintenance of physiologic iron stores, true iron depletion develops over time.¹⁰

Case 1 Presentation

A young, otherwise healthy woman presents to the clinic with complaints of fatigue. If you were concerned for anemia as the underlying cause of her fatigue, what further information would you obtain from the patient?

As discussed previously, women of reproductive age are most commonly affected by IDA. In these and all the cases detailed later in this article, the first and most cost-conscious tool in a physician's diagnostic arsenal is the history and physical examination.

The first step in obtaining the history from this patient is to identify any other symptoms potentially attributable to IDA. A list of symptoms that occur in IDA can be seen in **Box 1**.^{10,11} Next, further inquiry regarding possible etiologies of iron deficiency is warranted. These causes of IDA can be categorized into insufficient intake, malabsorption, and blood loss.

Chronic blood loss is commonly associated with menstruation and conditions involving the gastrointestinal tract. Therefore, a detailed gynecologic history as well as questions directed at symptoms of dyspepsia, melena, or hematochezia are essential. In consideration of an underlying malabsorptive state, the patient must be questioned specifically regarding symptoms related to or a personal history of inflammatory bowel disease, celiac disease, and gastrointestinal surgery.¹²

Insufficient intake of iron is rare in the United States; however, it can still occur in a variety of patients, including those with eating disorders or in individuals who follow a restricted diet, as in vegetarians and vegans. Therefore, a careful diet history can also prove useful.

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