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Patient information: Iron deficiency anemia

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IRON DEFICIENCY ANEMIA OVERVIEW

Anemia is a disorder that can be caused by a number of different conditions, including heavy menstrual periods, cancer, bleeding in the digestive tract, and sickle cell disease, just to name a few. Iron deficiency anemia is a specific type of anemia that is usually caused by blood loss or decreased absorption of iron from foods.

Iron deficiency anemia can be mild or severe, and can be temporary or chronic. The condition is common in the United States, affecting 1 to 2 percent of adults. It is even more common in developing countries, primarily due to differences in diet.

This topic will review the signs and symptoms, potential causes, diagnostic tests, and treatment of iron deficiency anemia in adults.

WHAT IS ANEMIA?

Anemia is defined as a decreased number of red blood cells, as measured by one of the following blood tests:

- Hemoglobin (Hgb) is a pigment that carries oxygen in the red blood cells. Iron is a critical component of hemoglobin; without iron, hemoglobin cannot carry or release oxygen. Normal Hgb ranges are described here ([table 1](#)).
- Hematocrit is the percent of a sample of whole blood occupied by intact red blood cells (RBCs). Normal hematocrit ranges are described here ([table 1](#)).
- RBC count is the number of red blood cells in a certain amount of whole blood (usually one microliter). Normal RBC ranges are described here ([table 1](#)).

Iron deficiency anemia occurs when there is an insufficient amount of iron in the body to make hemoglobin. When the quantity of hemoglobin is reduced, red blood cells carry less oxygen throughout the body. However, a person may not have signs or symptoms of anemia until their hemoglobin level is reduced by 20 percent or more.

ANEMIA SIGNS AND SYMPTOMS

Many people with iron deficiency anemia have no symptoms at all. Of those who do, the most common symptoms include:

- Weakness
- Headache
- Irritability
- Fatigue
- Difficulty exercising (due to shortness of breath, rapid heart beat)

Less common symptoms of iron deficiency include brittle nails, sore tongue, restless legs syndrome, pica, and pagophagia. Pica is an abnormal craving to eat non-food items, such as clay or dirt, paper products, or starch (eg, cornstarch). Pagophagia is an abnormal craving to eat ice.

ANEMIA CAUSES

Two common causes of iron deficiency anemia are blood loss (most common) and decreased absorption of iron from food.

Blood loss — The source of blood loss may be obvious, such as repeated blood donations, trauma, surgery, or in women who have heavy menstrual bleeding. In other cases, the source of the blood loss is not visible, as in someone who has bleeding in their digestive tract.

Decreased iron absorption — Normally, the body absorbs iron from food through the gastrointestinal tract. If the GI tract is not functioning correctly, as in people with certain conditions (eg, celiac disease, gastritis), an inadequate amount of iron may be absorbed, leading to iron deficiency anemia. This is a much less common cause of iron deficiency anemia than blood loss.

Other causes — A common cause of iron deficiency anemia in developing countries is a lack of foods that contain iron. However, this is a rare problem in adults in developed countries such as the United States because many foods have added iron (eg, breakfast cereal, bread, pasta).

Vegetarians are at increased risk for developing iron deficiency anemia because iron from plant sources is not absorbed as readily as iron from meat sources. Vegetarian sources of iron are discussed below. (See ['Iron and diet'](#) below.)

Pregnant women often develop iron deficiency anemia because of the increased iron requirements of the growing fetus and placenta, and the increased volume of blood circulating in the woman's body during pregnancy.

ANEMIA DIAGNOSIS

A person may be diagnosed with iron deficiency anemia after blood testing done to evaluate symptoms or after testing done for another, unrelated reason. The initial workup generally involves a medical history, physical examination, and blood tests.

Complete blood count — A complete blood count (CBC) is a group of tests that includes a red blood cell count, Hgb, and Hct. It also includes the mean corpuscular volume (MCV, referring to the cell size), mean corpuscular hemoglobin (MCH, referring to the cell color), and others. Normal values for these tests are listed here ([table 1](#)).

In people with iron deficiency anemia, the RBC count, Hgb, and Hct are lower than normal. The MCV and MCH are also usually lower than normal, indicating that the RBCs are smaller (called microcytic) and paler (hypochromic) than normal RBCs.

As part of the complete blood count, a small amount of blood is examined under a microscope. The shape, color, and size of the RBCs can help to determine the type of anemia ([picture 1](#)).

Other blood tests — In many cases, iron deficiency anemia is suspected based upon the results of the medical history, the CBC, and the blood smear. In other cases, further testing may be done to confirm the diagnosis.

- Serum iron — Measures how much iron is circulating in the blood
- Total iron binding capacity (TIBC or transferrin) — Measures the amount of a protein (transferrin) in the blood that is capable of transporting iron to RBCs or body stores)
- Transferrin saturation — Measures the percentage of iron-binding sites on transferrin that are occupied by iron.
- Ferritin — Measures ferritin, a protein that stores iron in the liver and spleen. Ferritin is a more accurate measure of the body's iron reserves than the other blood tests listed above.

In a person with iron deficiency anemia, the serum iron, transferrin saturation, and ferritin are often lower than normal and the TIBC may be higher than normal. The normal values for these tests are listed here ([table 2](#)).

Search for source of blood and iron loss — Once the diagnosis of iron deficiency anemia is made, the next step is to try to identify the cause of blood or iron loss. The healthcare provider may ask questions about the following situations, which can increase the risk of developing iron deficiency anemia:

- For women, history of menstrual bleeding, pregnancy, delivery, breastfeeding
- Multiple blood donations
- GI problems such as ulcer, H. pylori infection, celiac disease
- Family or personal history of bleeding disorders
- Family or personal history of colon cancer

Depending upon the answers to these questions, further testing may be recommended. As an example, if bleeding is suspected in the digestive tract, a stool test (eg, Hemoccult) may be performed. If the stool test is positive for blood, the gastrointestinal tract should be examined to determine the source of the bleeding. (See "[Patient information: Colon cancer screening](#)".)

ANEMIA TREATMENT

The treatment for iron deficiency anemia is an iron supplement, which may be taken by mouth or given as an injection (called parenteral iron). This iron is needed to increase production of hemoglobin and also to rebuild the body's iron reserves.

Oral iron tablets are recommended in most people with iron deficiency anemia. Injections of iron are usually reserved for people whose digestive tract is unable to adequately absorb iron or in those who are unable to tolerate oral iron.

A blood transfusion may be given if a person is actively bleeding and/or the person's hemoglobin or hematocrit levels are very low.

Oral iron — Oral iron tablets are usually a safe, inexpensive, and effective treatment for people with iron deficiency. The following tips are recommended:

- Enteric coated (EC) iron tablets are not recommended because iron is best absorbed from the duodenum and jejunum (the first and middle parts of the small intestine). EC iron releases iron further down in the intestinal tract, where it is not as easily absorbed. In some cases, the EC iron tablet passes through the entire intestinal tract with the coating intact, meaning that none of the iron was absorbed.
- Certain foods and medicines can reduce the effectiveness of iron tablets. Iron tablets should not be taken with food, certain antibiotics, tea, coffee, calcium supplements, or milk. Iron should be taken 1 hour before or 2 hours after these items. Iron should be taken 2 hours before or 4 hours after antacids.
- Iron tablets are best absorbed in an acidic environment; taking iron with one 250 mg vitamin C tablet or orange juice can enhance iron absorption.

Types of oral iron — There are several types of oral iron. The primary difference between the types is the amount of elemental iron each contains. There is no evidence that one form of iron is more effective than another.

- Ferrous fumarate — 106 mg elemental iron/tablet
- Ferrous sulfate — 65 mg elemental iron/tablet
- Ferrous sulfate liquid — 44 mg elemental iron/teaspoon (5 mL)
- Ferrous gluconate — 28 to 36 mg iron/tablet

The recommended daily dose of elemental iron for adults with iron deficiency in adults is 150 to 200 mg/day. The least expensive form of iron is iron sulfate. As an example, one 325 mg iron sulfate tablet taken three times per day supplies 195 mg of elemental iron per day. A healthcare provider can help to determine what dose and type of iron is most appropriate.

Side effects — Some people experience nausea, constipation, stomach upset, and/or vomiting after taking oral iron. Options for dealing with these side effects include:

- Take a smaller dose

- Use a formulation with a lower elemental iron content (eg, ferrous gluconate instead of ferrous sulfate)
- Take the liquid form of ferrous sulfate and adjust the dose until symptoms are tolerable.

Taking iron tablets will turn the stool a dark, almost black color. This is to be expected, and does NOT mean that the iron tablets are causing intestinal bleeding.

Children under 6 years are at particular risk of iron poisoning, making it very important to store iron tablets out of the reach of children.

Duration of treatment — Treatment with oral iron is recommended for as long as it takes the hemoglobin and hematocrit to return to normal. A blood count is often repeated one to two months after starting iron to determine if the treatment has been effective.

When the Hgb has returned to normal, treatment with iron may be discontinued. However, some clinicians recommend continuing the iron for at least six months after the Hgb normalizes in order to replenish the body's iron stores.

If oral iron does not increase hemoglobin — On occasion, a person's hemoglobin will not improve despite treatment with oral iron. There are several possible reasons for this, as listed in the table ([table 3](#)). The next step in this situation depends upon why the person did not respond.

Parenteral iron — Iron may be given by injection in certain situations, such as in people who cannot tolerate oral iron tablets or whose gastrointestinal tract cannot absorb an adequate amount of iron from pills (eg, due to inflammatory bowel disease or in patients undergoing dialysis or treatment for cancer). Parenteral iron is usually given in a healthcare provider's office or hospital. The medication is infused into a vein slowly, over the course of an hour or more.

Side effects — Side effects, such as itching, heart palpitations, and dizziness, can occur with parenteral iron. One form of parenteral iron, iron dextran, can cause serious or even life-threatening allergic reactions in some people. Other forms of parenteral iron, including iron sucrose and ferric gluconate complex, have much lower risks of life-threatening side effects. As a result, most clinicians recommend non-dextran forms of parenteral iron.

Blood transfusion — Blood transfusion is a term that may be used to describe the use of packed red blood cells (PRBCs) in a person with anemia. PRBCs are prepared from whole blood by eliminating most of the plasma (the liquid part of blood) and virtually all of the white blood cells and platelets.

In people with iron deficiency anemia, a blood transfusion usually involves giving one or more units of packed red blood cells into a vein. Each unit of PRBCs contains approximately 200 mg of iron and will raise the hemoglobin by about 1 gm/dL.

Blood transfusions are generally reserved for people who have a low or unstable blood pressure due to bleeding, and/or if the person's organs (brain, heart) are being deprived of oxygen as a result of severe anemia. A transfusion may also be recommended in select cases if the person is not actively bleeding and has a stable blood pressure but their hemoglobin or hematocrit level is very low (eg, hemoglobin less than 7 g/dL or hematocrit less than 20 percent).

Blood transfusion is described in detail in a separate topic. (See "[Patient information: Blood donation and transfusion](#)".)

Side effects — There can be side effects of blood transfusion, with the most common being fever, chills, and mild shortness of breath. However, this only occurs in 0.15 to 0.19 percent of transfusions. More serious or even life-threatening allergic reactions can occur, although this is not common.

The risk of infection with the hepatitis C virus or the virus causing AIDS is extremely low because of better screening of blood donors as well as improved laboratory testing. These infections occur only once for every 2 million transfusions.

Iron and diet — Although dietary iron is important in preventing iron deficiency, people with iron deficiency anemia need more iron than they can consume through their diet alone. In a 2000 calorie diet, there is only about 10 mg of elemental iron (compared to 65 mg in one 325 mg iron sulfate tablet). Therefore, increasing dietary iron alone is not usually recommended as a treatment for iron deficiency anemia, although it may be recommended in combination with iron therapy.

Dietary sources of iron are found in meat, grains, fruits, and vegetables ([table 4](#)). For people who do not eat meat, good plant sources of iron include whole or enriched breads or grains, iron-fortified cereals, legumes, green leafy vegetables, dried fruits, soy products, blackstrap molasses, bulgur, and wheat germ. To maximize absorption, iron-rich foods should not be consumed with coffee or tea. Taking vitamin C or drinking orange juice with high iron foods can further enhance absorption.

ANEMIA PREVENTION

People who have had iron deficiency anemia once may be at increased risk for developing it again, depending upon why they developed anemia originally. In these people, a daily multivitamin or iron supplement may be recommended to maintain the body's iron stores.

However, iron supplements and multivitamins that contain iron should not be taken without consulting a healthcare provider due to the potential risk of iron overdose. Most men and postmenopausal women do not need supplemental iron unless they have an underlying illness that reduces iron absorption or causes bleeding.

Increasing dietary iron can also help to maintain iron stores. (See '[Iron and diet](#)' above.)

WHERE TO GET MORE INFORMATION

Your healthcare provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed every four months on our web site (www.uptodate.com/patients).

The following organizations also provide reliable health information.

- National Library of Medicine

(www.nlm.nih.gov/medlineplus/ency/article/000584.htm)

- National Heart, Lung, and Blood Institute

(www.nhlbi.nih.gov/health/dci/Diseases/ida/ida_diagnosis.html)

- Center for Disease Control and Prevention

(www.cdc.gov/nccdphp/dnpha/nutrition/nutrition_for_everyone/basics/iron.htm)

[1-3]

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GRAPHICS

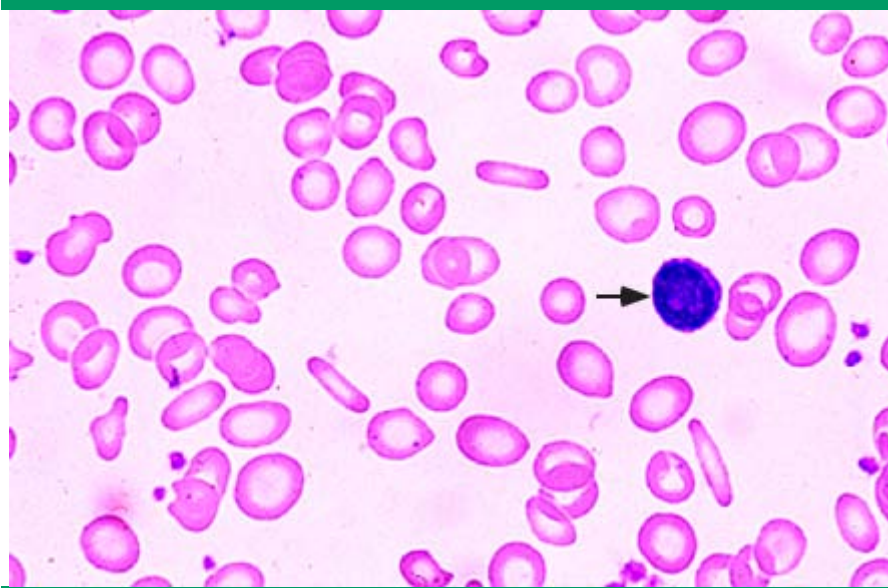
Normal values for red blood cell parameters in men and women

Red cell parameter	Adult men		Adult women
Hemoglobin, g/dL	15.7 ± 1.7		13.8 ± 1.5
Hematocrit, percent	46.0 ± 4.0		40.0 ± 4.0
RBC count, million/ μ L	5.2 ± 0.7		4.6 ± 0.5
Reticulocytes, percent	1.6 ± 0.5		1.4 ± 0.5
Mean corpuscular volume, fL		88.0 ± 8.0	
Mean cell hemoglobin, pg/RBC		30.4 ± 2.8	
Mean cell hemoglobin concentration, g/dL of RBC		34.4 ± 1.1	
Red cell volume distribution width, percent (RDW)		13.1 ± 1.4	

Values are mean \pm 2 standard deviations.

Adapted from Williams' Hematology, 6th ed, Beutler, E, Lichtman, MA, Coller, BS, et al (Eds), McGraw-Hill, New York, 2001.

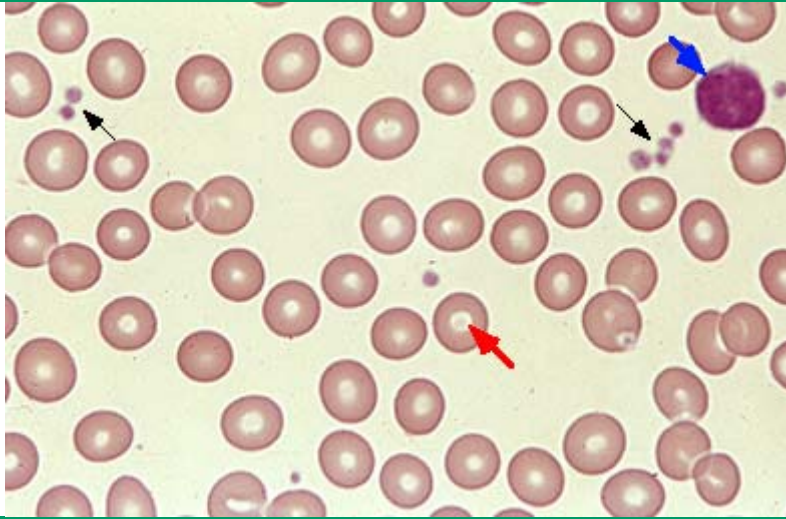
Microcytic hypochromic red cells



Peripheral smear from a patient with iron deficiency shows pale small red cells with just a scant rim of pink hemoglobin; occasional "pencil" shaped cells are also present. Normal red cells are similar in size to the nucleus of a small lymphocyte (arrow); thus, many microcytic cells are present in this smear. Thalassemia can produce similar findings.

Courtesy of Carola von Kapff, SH (ASCP).

Normal peripheral blood smear



High power view of a normal peripheral blood smear. Several platelets (black arrows) and a normal lymphocyte (blue arrow) can also be seen. The red cells are of relatively uniform size and shape. The diameter of the normal red cell should approximate that of the nucleus of the small lymphocyte; central pallor (red arrow) should equal one-third of its diameter.

Courtesy of Carola von Kapff, SH (ASCP).

Laboratory tests in iron deficiency of increasing severity

	Normal	Fe deficiency without anemia	Fe deficiency with mild anemia	Severe Fe deficiency with severe anemia
Marrow reticulo-endothelial iron	2+ to 3+	None	None	None
Serum iron, µg/dL	60 to 150	60 to 150	<60	<40
Iron binding capacity (transferrin), µg/dL	300 to 360	300 to 390	350 to 400	>410
Saturation (SI/TIBC), percent	20 to 50	30	<15	<10
Hemoglobin, g/dL	Normal	Normal	9 to 12	6 to 7
Red cell morphology	Normal	Normal	Normal or slight hypochromia	Hypochromia and microcytosis
Plasma or serum ferritin, ng/mL	40 to 200	<40	<20	<10
Erythrocyte protoporphyrin, ng/mL RBC	30 to 70	30 to 70	>100	100 to 200
Other tissue changes	None	None	None	Nail and epithelial changes

Note: Test results outlined in bold type are the ones most likely to define the various stages of iron deficiency. Thus, the presence or absence of iron stores (marrow reticuloendothelial iron) in a non-anemic patient serves to distinguish normal subjects from those with iron deficiency without anemia, respectively.

Causes for failure to respond to oral iron therapy

Coexisting disease interfering with marrow response
Infection
Inflammatory disorder (eg, rheumatoid arthritis)
Concomitant malignancy
Coexisting folic acid and/or vitamin B12 deficiency
Bone marrow suppression from another cause
Diagnosis is incorrect, possible correct diagnoses include
Thalassemia
Lead poisoning
Anemia of chronic disease (anemia of chronic inflammation)
Copper deficiency (zinc toxicity)
Myelodysplastic syndrome/refractory sideroblastic anemia
Patient is not taking the medication
Prescription has not been filled
Prescription has been filled but patient is no longer taking the medication
Medication is being taken but is not being absorbed
Rapid intestinal transport bypasses area of maximum absorption
Enteric coated product: coating is not dissolving
Patient has malabsorption for iron (eg, sprue, atrophic gastritis)
Medication taken in association with an agent interfering with absorption (eg, antacids, tetracycline, tea)
Continued blood loss or need in excess of iron dose ingested
Cause of blood loss treatable (eg, bleeding peptic ulcer)
Initiate appropriate treatment
Cause of blood loss not treatable (eg, Osler Weber Rendu disease) or need cannot be met by oral iron preparation (eg, renal failure responding to erythropoietin)
Switch patient to parenteral iron product

Assumes that original diagnosis was iron deficiency anemia with hypochromic microcytic red blood cells, low ferritin, and low transferrin saturation.

Dietary sources of iron

Food	Approximate measure	Iron, mg
High iron sources		
Cream of Wheat (quick or instant)*	1/2 cup	7.8
Kidney, beef•	2 oz (60 g)	5.3
Liver, beef•	2 oz (60 g)	5.8
Liver, calf•	2 oz (60 g)	9.0
Liver, chicken•	2 oz (60 g)	6.0
Liverwurst•	2 oz (60 g)	3.6
Prune juice	1/2 cup	5.1
Spinach	1/2 cup	3.2
Moderate iron sources		
All-Bran cereal	1/2 cup	2.9
Almonds, dried unblanched	1/2 cup	3.0
Dried beans and peas		
Baked beans, no pork	1/4 cup	1.5
Blackeye peas, cooked	1/4 cup	0.8
Chick peas, dry	1/4 cup	3.5
Great northern beans, cooked	1/4 cup	1.3
Green peas, cooked	1/4 cup	1.4
Lentils, dry	1/4 cup	3.4
Lima beans, cooked	1/4 cup	1.3
Navy beans, cooked	1/4 cup	1.3
Red beans, dry	1/4 cup	3.5
Soybeans, cooked	1/4 cup	1.4
White beans, dry	1/4 cup	3.9
Beef, cooked	2 oz (60 g)	2-3Δ
Ham, cooked	2 oz (60 g)	1.3
Lamb, cooked	2 oz (60 g)	1.9
Peaches, dried	1/4 cup	2.4
Peanuts, roasted without skins	3 1/2 oz (100 g)	3.2
Pork, cooked	2 oz (60 g)	2-3§
Prunes, dried	2 large	1.1

Scallops	2 oz (60 g)	1.6
Turkey, cooked	2 oz (60 g)	1.7
Approximate iron content of children's favorite foods		
Hamburger, small	1	3.0
Large	1	5.2
Big Mac	1	4.3
Quarter Pounder	1	5.1
Spaghetti with meatballs	1 cup	3.3
Frankfurter and beans	1 cup	4.8
Pork and beans	1 cup	5.9
Raisins◇	5/8 cup	3.5
Cereals, fortified	1 serving	4.5-17.8
Nuts◇	1 cup	5.0-7.0
Seeds, sunflower◇	3 1/2 oz (100 g)	7.1
Chile con carne	1 cup	3.6
Beef burrito or tostado	1 medium	3.4-4.6
Cheese pizza	2 slices	3.0
Cheese pizza with beef	2 slices	4.8
White bread	1 piece	0.7

* Or other fortified cereals which contain 10 mg of iron per ounce or 100 percent RDA per serving.

- As organ meats are generally high in cholesterol, these iron-rich foods should be eaten in moderation.

Δ Depending on cut, the greatest amounts of iron are generally found in the chuck, flank, and bottom round cuts of beef.

§ Depending on cut, the greatest amounts of iron are generally found in the loin, sirloin, tenderloin, and picnic shoulder cuts of pork.

◇ Raisins, nuts, and seeds are not generally recommended for children under age three because of risk of choking.

Data from Walker, WA, Watkins, JB (Eds), Nutrition in Pediatrics, 2nd ed, BC Decker, Inc, London 1997.