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Patient education: Anemia caused by low iron in adults (Beyond the Basics)

Author: Michael Auerbach, MD, FACP Section Editors: William C Mentzer, MD, Robert T Means, Jr, MD, MACP Deputy Editor: Jennifer S Tirnauer, MD

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IRON DEFICIENCY ANEMIA OVERVIEW

Anemia can be caused by a number of different conditions, including heavy menstrual periods, pregnancy, cancer, and bleeding in the digestive tract, to name a few. Iron deficiency anemia is a type of anemia that occurs when there is not enough iron to make the hemoglobin in red blood cells. The main causes of iron deficiency anemia in adults are bleeding and conditions that block iron absorption in the intestines.

Iron deficiency anemia can be mild or severe. The condition is common in the United States, especially in women who are still having menstrual periods or have been pregnant. It is less common in men. It is even more common in parts of the world where people cannot get sufficient iron from food and in regions where intestinal parasites are common.

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 (RBCs), as measured by one of the following blood tests:

- Hemoglobin (Hgb) is the iron-containing molecule in RBCs that carries oxygen. Iron is a critical component of hemoglobin; without iron, hemoglobin cannot be formed and fewer RBCs are produced. This is the most accurate of the tests as it is measured on specialized machinery in a laboratory or in the doctor's office.
- Hematocrit (Hct) is the percent of a sample of blood made up of RBCs. The rest of the blood is mostly made up of a fluid called plasma. This test used to be more popular, but the hemoglobin is considered more reliable.
- RBC count is the number of RBCs in a certain amount of whole blood, usually one microliter (one millionth of a liter).

Iron deficiency (too little iron) anemia occurs when there is insufficient iron in the body to make hemoglobin. When the quantity of hemoglobin is reduced, fewer RBCs are formed, and the RBCs that are formed are smaller. Symptoms of iron deficiency vary from person to person. Iron deficiency can even cause symptoms in the absence of anemia.

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 heartbeat)
- Brittle nails
- Sore tongue
- Restless legs syndrome
- Pica (an abnormal craving to eat non-food items, such as clay or dirt, paper products, or cornstarch)
- Pagophagia (an abnormal craving to eat ice)

CAUSES OF ANEMIA

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 in women who have heavy menstrual bleeding, or a person with a known bleeding ulcer. Pregnancy can use up as much as five- to six-fold more iron for the developing fetus and placenta (<u>figure 1</u>). Blood loss during childbirth can also contribute to iron deficiency.

In other cases, the source of the blood loss is not visible, as in someone who has chronic bleeding in their gastrointestinal (GI) tract (stomach, small intestine, colon). This may appear as diarrhea with black, tarry stools, or, if the blood loss is very slow, the stool may appear normal. Donating blood can also cause iron deficiency, especially if it is done on a regular basis.

Decreased iron absorption — Normally, the body absorbs iron from food through the GI tract. If the GI tract is not functioning correctly, as is the case in people with certain conditions such as celiac disease, autoimmune gastritis, *Helicobacter pylori* (*H. pylori*) infection, other forms of stomach inflammation, gastric bypass surgery (for weight loss), or other forms of weight loss surgery, an inadequate amount of iron may be absorbed, leading to iron deficiency anemia.

Other causes — In some parts of the world, there is not enough iron available from food, and iron deficiency may develop due to lack of iron intake. In some countries such as the United States some foods have added iron (breakfast cereal, bread, pasta). Iron is also available in some plant-based foods. (See <u>'Iron and diet'</u> below.)

ANEMIA DIAGNOSIS

Since iron deficiency occurs before anemia develops, a person may be diagnosed with iron deficiency alone, or with iron deficiency anemia. In some cases, testing is done to evaluate symptoms, and in others it is done for an unrelated reason.

The initial evaluation generally involves a medical history, to look for possible causes of iron deficiency; physical examination, to look for causes and typical findings of iron deficiency; and blood tests, to measure iron stores in the body and check for other possible conditions that could contribute to iron deficiency. This is especially important in early pregnancy, where the likelihood of having iron deficiency is as high as 40 percent.

Complete blood count — A complete blood count (CBC) is a group of tests that includes a red blood cell (RBC) count, hemoglobin (Hgb), and hematocrit (Hct). It also includes the mean corpuscular volume (MCV, referring to the size of the RBCs), mean corpuscular hemoglobin (MCH, referring to the amount of hemoglobin per RBC), and others. It also measures white blood cells and platelets, which are different types of blood cells.

In people with iron deficiency anemia, the RBC count, Hgb, and Hct are lower than normal. The MCV and MCH are usually normal early on but can become lower than normal, indicating that the RBCs are smaller (called microcytic) and carry less Hgb than normal RBCs.

As part of the CBC, the shape, color, and size of the RBCs are also evaluated (either by a machine or by a person using a microscope). This information can help to determine the type of anemia.

White blood cells are not affected by iron deficiency. Platelets may be increased in some cases, or they may be normal.

Other blood tests — In many cases, iron deficiency anemia is suspected based upon the results of the medical history and the CBC. Further testing is used to confirm the diagnosis. In some cases, the ferritin can be checked by itself. In others, an "iron studies panel" is used.

• Ferritin — Measures a protein that stores iron. This protein decreases when a person has iron deficiency. The ferritin measurement is most useful when it is low, as nothing other than iron deficiency causes a low ferritin.

Ferritin can increase in a variety of conditions unrelated to iron, which can confuse the interpretation of the results. These are generally conditions associated with inflammation, such as chronic rheumatologic disorders or infections. In people with chronic inflammation, the TSAT (see below) and sometimes other specialized testing can be used to see if there is a need for iron replacement.

- Serum iron Measures how much iron is circulating in the blood. The result can be affected by iron supplements and even recent meals. It is not a good measure of the iron stores in the body.
- 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. When iron stores are low, the TIBC or transferrin increases.
- Transferrin saturation (TSAT) Measures the percentage of iron-binding sites on transferrin that are occupied by iron. This number is calculated by dividing the serum iron

by the TIBC. A lower TSAT indicates iron deficiency. If this test is being used to make the diagnosis, it should be done on an overnight fast (after not eating for a night) because iron in foods can make the TSAT appear higher than it should be.

In a person with iron deficiency anemia, the serum iron, transferrin saturation, and ferritin are lower than normal and the TIBC may be higher than normal. The ferritin and the TSAT are the most useful tests.

Search for source of blood and iron loss — Once the diagnosis of iron deficiency anemia is made, it is important to identify the cause. The health care provider may ask questions about the following situations, which can increase the risk of developing iron deficiency anemia:

- History of heavy menstrual periods, pregnancies, and deliveries
- Gastrointestinal (GI) problems such as ulcers, *Helicobacter pylori (H. pylori)* infection, autoimmune gastritis, or celiac disease
- Surgery on the GI tract (such as gastric bypass for weight loss)
- Family or personal history of bleeding disorders
- Family or personal history of colon cancer
- Multiple blood donations
- Use of medications that can irritate the GI tract, such as nonsteroidal antiinflammatory drugs (NSAIDs), which include <u>ibuprofen</u> (sample brand names: Advil, Motrin) and <u>naproxen</u> (sample brand names: Aleve, Naprosyn)
- Symptoms of GI bleeding such as dark black, tarry stools, abdominal pain, or visible bleeding

If a cause of blood loss is not obvious, additional tests should be done. These include colonoscopy or upper endoscopy to look for areas of bleeding in the GI tract, and blood tests for certain conditions that interfere with iron absorption, such as autoimmune gastritis, celiac disease, and *H. pylori* infection. Looking for bleeding in the colon is especially important in people over the age of 50. (See <u>"Patient education: Colonoscopy (Beyond the Basics)"</u> and <u>"Patient education: Upper endoscopy (Beyond the Basics)"</u> and <u>"Patient education: Helicobacter pylori infection and treatment (Beyond the Basics)"</u>.)

ANEMIA TREATMENT

The first step in treating iron deficiency anemia is to determine the cause of the deficiency and correct it, so that iron does not continue to be lost, and any serious condition (for example, colon cancer) is treated as early as possible.

After that, the treatment for iron deficiency anemia is to give iron. Iron supplements may be taken by mouth or given as one or more intravenous doses (this is sometimes called "parenteral iron" or "IV iron"). Iron is needed to increase production of hemoglobin (Hgb) and also to rebuild the body's iron reserves. In rare cases, a blood transfusion is needed.

In general:

- Oral iron tablets are used in most people with iron deficiency anemia.
- Intravenous iron can be used for people whose GI tract cannot adequately absorb iron, during the second and third trimester of pregnancy, or, more commonly, in those who are unable to tolerate oral iron. (Some people experience side effects like constipation, nausea, or cramping, which can make the supplements hard to take). Intravenous iron is often given to people with chronic kidney disease. The developing fetus needs iron for normal brain development, and iron deficiency is associated with a number of problems for both mother and child.
- A blood transfusion may be given if a person is actively bleeding and/or the Hgb or hematocrit (Hct) levels are very low, but transfusions are not commonly needed.

All of these treatment approaches are discussed more in the following sections.

Oral iron — Oral iron tablets are a safe, inexpensive, and effective treatment for people with iron deficiency. Gastrointestinal (GI) side effects are common (see <u>'Side effects'</u> below). The following tips are recommended when taking oral iron:

- Iron is best absorbed if it is taken every other day (or, for example, on Monday, Wednesday, and Friday), for people who are able to keep track of this type of schedule.
- "Enteric coated" (EC) iron tablets have a special coating that does not dissolve quickly in the GI tract. These are **not** recommended because iron is best absorbed from the duodenum and jejunum (the first and middle parts of the small intestine), and EC iron releases iron further down in the intestinal tract, where it is not as easily absorbed. In some cases, an EC iron tablet can pass 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 usually should not be taken with food, certain antibiotics, tea, coffee, calcium supplements, or milk. Iron should be taken one hour before or two hours after these items. If you take antacids, your iron tablets should be taken at least two hours before or four hours after the antacids.

Types of oral iron — There are several types of oral iron, and with the exception of the enteric coated (EC) iron tablets mentioned above, they are all equally effective. The primary difference between the types is the amount of iron each product contains. For many products, the number of milligrams for the pill is different from the number of milligrams of actual iron molecules (called "elemental iron"):

- <u>Ferrous fumarate</u> 106 mg elemental iron/tablet
- <u>Ferrous sulfate</u> 65 mg elemental iron/tablet
- <u>Ferrous sulfate</u> liquid 44 mg elemental iron/teaspoon (5 mL)
- <u>Ferrous gluconate</u> 28 to 36 mg iron/tablet
- Polysaccharide iron complex various doses available

In the past, iron pills were typically prescribed for daily use, often at multiple doses per day. As noted above, more recent evidence suggests that taking oral iron every **other** day allows the body to absorb more iron in addition to reducing the risk of gastrointestinal side effects (see <u>'Side effects'</u> below). Your health care provider can help you figure out the dosing schedule that is most appropriate for you.

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

- Take a smaller dose
- Take iron with food (even though this will reduce the amount of iron your body absorbs, it's still better than not taking it at all)
- Use a formulation with a lower elemental iron content (eg, <u>ferrous gluconate</u> instead of <u>ferrous sulfate</u>)
- Take the liquid form of <u>ferrous sulfate</u> and adjust the dose until symptoms are tolerable
- Switch to intravenous iron

Taking iron tablets will turn the stool a dark, almost black color (actually dark green). This is normal, and does **not** mean that the iron tablets are causing intestinal bleeding.

Children are at particular risk of iron poisoning (overdose), making it very important to store iron tablets out of the reach of children. If you think a child ingested iron pills, call poison control (in the United States, 1-800-222-1222).

Duration of treatment — Treatment with oral iron is recommended for as long as it takes the hemoglobin (Hgb) and hematocrit (Hct), and usually the tests of iron stores, to return to

normal. Typically this takes about six months with oral iron and can be accomplished with a single infusion (15 to 60 minutes) with intravenous iron.

If oral iron does not increase hemoglobin — On occasion, a person's Hgb will not improve despite treatment with oral iron. There are several possible reasons for this. The next step depends upon why the person's Hgb did not increase, which needs to be evaluated by a clinician. However, several points are worth keeping in mind:

- It is important that iron be taken as directed. Not taking iron as prescribed is probably the most common reason it does not work.
- The type of iron preparation being taken is important. One should avoid any preparation that is labeled "slow release," or is enteric coated (EC), as these may prevent iron from being efficiently absorbed.
- Blood tests may be used to determine if the iron is not being absorbed properly due to another condition such as autoimmune gastritis, celiac disease, or *Helicobacter pylori* infection.
- In some people, there may be another cause of anemia in addition to iron deficiency. In others, the diagnosis of iron deficiency may be incorrect.
- If there is ongoing bleeding that depletes iron stores faster than they are being replaced, it may appear that the oral iron is not working.
- For some people, changing to intravenous iron may be a good option.

Intravenous iron — Iron may be given by intravenous injection (parenterally, IV) in certain situations, such as in people who cannot tolerate the side effects of oral iron or whose GI tract cannot absorb an adequate amount of iron from pills.

People who may be candidates for intravenous iron due to health conditions include those who:

- Have inflammatory bowel disease
- Have kidney disease
- Have had bariatric (weight loss) surgery
- Are pregnant, especially in the late second and third trimesters

Intravenous iron is infused into a vein. This is done in a health care provider's office or hospital, where the person can be monitored. The length of time required for the infusion and the

number of infusions needed depend on which intravenous iron product is used and the severity of iron deficiency.

Side effects — The intravenous iron used in the past (high molecular weight <u>iron dextran</u> [brand name: Dexferrum]) had a risk of severe allergic reactions. However, the intravenous iron products used today have an exceedingly low risk of allergic or anaphylactic reactions (less than one tenth of one percent). Infusion reactions are more common, and may include temporary flushing, back pain, and other symptoms that usually go away when the infusion is slowed or stopped. Some patients with a history of rheumatoid arthritis may have an arthritis flare, which can be reduced or prevented by a short course of steroids.

The best ways to minimize these reactions include avoiding the use of antihistamines as "premedication" or to treat minor symptoms, giving the infusion more slowly, or in some people (those with a history of multiple drug allergies) giving a steroid before the infusion.

If you have back pain or joint pain at home after the infusion, nonsteroidal antiinflammatory drugs (NSAIDs) may be helpful. NSAIDs include <u>ibuprofen</u> (sample brand names: Advil, Motrin) and <u>naproxen</u> (sample brand name: Aleve).

Blood transfusion — Blood transfusion may be used in people with anemia that is severe or causes significant symptoms such as chest pain or difficulty breathing.

Blood transfusion involves giving one or more units of packed red blood cells (pRBCs) into a vein. Each unit of pRBCs contains the RBCs from one unit of blood donated by a voluntary donor (with approximately 200 mg of iron) and will raise the Hgb by about 1 gram/deciliter (g/dL; 1 gram per 100 milliliters).

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. Typical symptoms of this include chest pain and/or shortness of breath, or in more extreme circumstances, passing out. A transfusion may also be recommended in select cases if the Hgb or hematocrit level is very low (eg, Hgb less than 7 g/dL or hematocrit less than 20 percent), although symptoms are also important.

Blood transfusion is described in detail in a separate topic. (See <u>"Patient education: Blood</u> <u>donation and transfusion (Beyond the Basics)"</u>.)

Side effects — There can be side effects of blood transfusion, with the most common being fever or itching. However, this only occurs in 0.1 to 1 percent of transfusions. More serious or

even life-threatening allergic reactions or other complications can occur, although this is even less common.

The risk of infection with the hepatitis C virus or the HIV virus is extremely low because of better screening of blood donors as well as improved laboratory testing. These infections occur only once in every two 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 <u>ferrous sulfate</u> tablet). Therefore, increasing dietary iron alone is not usually sufficient as a treatment for iron deficiency anemia.

Dietary sources of iron are found in meat, especially organ meats, grains, fruits, and vegetables (<u>table 1</u>). 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.

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. For example, people who have had weight loss surgery may continue to need iron supplements to maintain the body's iron stores.

Extra iron is commonly included in prenatal multivitamins for pregnant women.

However, iron supplements and multivitamins that contain iron should not be taken without consulting a healthcare provider, because too much iron in the body can also cause problems.

Further, the unnecessary use of iron supplements may interfere with the health care provider's ability to identify iron deficiency, which may be a sign of another serious illness such as colon cancer or other gastrointestinal disorders.

Most men and postmenopausal women do **not** need supplemental iron unless they have an underlying illness that reduces iron absorption or causes bleeding.

WHERE TO GET MORE INFORMATION

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

This article will be updated as needed on our web site (<u>www.uptodate.com/patients</u>). Related topics for patients, as well as selected articles written for health care professionals, are also available. Some of the most relevant are listed below.

Patient level information — UpToDate offers two types of patient education materials.

The Basics — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials.

Patient education: Complete blood count (CBC) (The Basics)Patient education: Anemia caused by low iron (The Basics)Patient education: Nutrition before and during pregnancy (The Basics)Patient education: Restless legs syndrome (The Basics)Patient education: Angiodysplasia of the GI tract (The Basics)Patient education: Medicines for chronic kidney disease (The Basics)

Beyond the Basics — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

Patient education: Screening for colorectal cancer (Beyond the Basics) Patient education: Blood donation and transfusion (Beyond the Basics)

Professional level information — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

<u>Diagnostic approach to anemia in adults</u> <u>Iron requirements and iron deficiency in adolescents</u> <u>Causes and diagnosis of iron deficiency and iron deficiency anemia in adults</u> <u>Treatment of iron deficiency anemia in adults</u> <u>Indications and hemoglobin thresholds for red blood cell transfusion in the adult</u>

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/dnpa/nutrition/nutrition_for_everyone/basics/iron.htm)

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GRAPHICS

Iron requirements during pregnancy



The graph shows approximate requirements needed to compensate for normal turnover (eg, from gastrointestinal sloughing), menstruation, expansion of the maternal RBC mass, and fetal and placental RBC needs. Weeks refer to weeks of gestation. Refer to UpToDate for details of iron supplementation and management of anemia in pregnancy.

RBC: red blood cell.

Graphic 116876 Version 1.0

Dietary sources of iron

Food	Approximate measure	Iron (mg)
ligh-iron sources		
Cereals, fortified	1 serving	4.5 to 17.8
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
Liver, chicken [¶]	2 oz (60 g)	6
Liverwurst¶	2 oz (60 g)	3.6
Nuts [∆]	1 cup	5 to 7
Prune juice	1/2 cup	5.1
Seeds, sunflower $^{\Delta}$	3 1/2 oz (100 g)	7.1
Noderate-iron sources		
Almonds, dried, unblanched	1/2 cup	3
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 to 3
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 to 3
Prunes, dried	2 large	1.1
Raisins [∆]	5/8 cup	3.5
Scallops	2 oz (60 g)	1.6
Spinach (cooked)	1/2 cup	3.2
Spinach (raw)	1 cup	0.9
Turkey, cooked	2 oz (60 g)	1.7
opproximate iron content of popular pre	pared foods	1

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Small	1	3
Large	1	5.2
Spaghetti with meatballs	1 cup	3.3
Frankfurter and beans	1 cup	4.8
Pork and beans	1 cup	5.9
Chile con carne	1 cup	3.6
Beef burrito or tostado	1 medium	3.4 to 4.6
Cheese pizza	2 slices	3
Cheese pizza with beef	2 slices	4.8
White bread	1 piece	0.7

* Or other fortified cereals that contain 10 mg of iron per ounce or 100% recommended dietary allowance per serving.

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

Δ Raisins, nuts, and seeds are not generally recommended for children under age 3, because of risk of choking.

 \diamond 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.

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

Graphic 73962 Version 8.0

Contributor Disclosures

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