

YOUR GUIDE TO ANEMIA

PREVENT | TREAT | CONTROL



National Heart, Lung,
and Blood Institute

**Blood Diseases
& Disorders
Education Program**



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YOUR GUIDE TO ANEMIA

Your Guide to Anemia is your first step to learning more about anemia—the most common blood disorder in the United States.


Whether you've been diagnosed with anemia or have a family member or friend who is living with it, or you simply want to learn more about this blood disorder, the National Heart, Lung, and Blood Institute's (NHLBI) **Your Guide to Anemia** gives reliable answers to your questions. The guide provides information on the causes of anemia; the signs and symptoms of anemia; how anemia can be prevented, diagnosed, and treated; and the different types of anemia.

It also offers tips on what to do after an anemia diagnosis. For example, it recommends adopting a heart-healthy lifestyle and talking with your family members about their own risk for developing anemia.

Because anemia can develop in people of all ages, races, and ethnicities, it is important that you speak to your doctor or healthcare professional if you think you are experiencing any of the signs or symptoms of the blood disorder.

For more information about anemia, please visit www.nhlbi.nih.gov/health-topics/anemia.





The solid part of **blood** **contains** three types of blood cells:

- **RED CELLS**
- **WHITE CELLS**
- **PLATELETS**



SIGNS AND SYMPTOMS OF ANEMIA

ANEMIA EXPLAINED

Anemia is a condition that develops when your blood has a lower-than-normal amount of red blood cells or hemoglobin. Hemoglobin, an iron-rich protein, helps red blood cells carry oxygen from the lungs to the rest of the body. If you have anemia, your body does not get enough oxygen-rich blood. This can cause you to feel tired or weak. You may also have shortness of breath, dizziness, headaches, or an irregular heartbeat.

There are many types and causes of anemia. While mild anemia is a common and treatable condition, anemia may also be a sign of a more serious condition. It may result from chronic (ongoing) bleeding in the stomach. Chronic inflammation from an infection, kidney disease, cancer, or autoimmune diseases also can cause the body to make fewer red blood cells.

Some people are at a higher risk for anemia, including women who are having their menstrual periods or are pregnant, people who donate blood frequently, those who do not get enough iron or certain vitamins, and people who take certain medicines or undergo particular treatments, such as chemotherapy for cancer.

Your doctor will consider your medical history, physical exam, and test results when diagnosing and treating anemia. A simple blood test is often used to confirm that you have low amounts of red blood cells or hemoglobin. For some types of mild to moderate anemia, your doctor may recommend solutions that help your body produce more red blood cells. These options include over-the-counter or prescription iron supplements, certain vitamins, or intravenous (IV) iron therapy. To prevent anemia in the future, your doctor may also suggest healthy lifestyle changes. If you have severe anemia, your doctor may recommend red blood cell transfusions.

WHAT YOUR BLOOD IS MADE OF

Blood is made of liquid and solids. The liquid part, called plasma, is mostly water. Plasma carries essential nutrients, hormones, and proteins throughout your body. Plasma also carries waste products from cells to the kidneys and digestive system to be removed from your body.

The solid part of blood contains three types of blood cells—red blood cells, white blood cells, and platelets. Here is a breakdown of each type:

- **Red blood cells** are shaped like discs and are slightly indented in the center. They contain hemoglobin, which is a protein that carries oxygen from your lungs to all parts of your body. Your body depends on oxygen to carry out its functions. Hemoglobin also carries carbon dioxide (a waste product) from the body to the lungs, which allow you to breathe it out. The hemoglobin in red blood cells gives blood its red color.
- **White blood cells** fight infection. They are part of your body's immune system. Your body makes five different types of white blood cells. When you get an infection or other type of illness, your body will make more of the specific type of white blood cells needed to fight that illness.
- **Platelets** are tiny oval-shaped blood cell fragments that help your blood clot. If you begin to bleed inside or on the surface of your body, platelets gather at the spot and stick together to seal small cuts or breaks on blood vessel walls. Then, proteins called clotting factors and red blood cells join the platelets to form a stable clot that stops the bleeding.

Blood cells are made in your bone marrow, which is the spongy tissue inside many of your bones. Blood cells live for various lengths of time. Red blood cells live about 120 days, and platelets live about six days. White blood cells have various lifespans. Some types live about one day, while others may live a long time. Your bone marrow is always making new blood cells to replace those that have died or have been destroyed or lost.

RECOGNIZING THE SIGNS AND SYMPTOMS OF ANEMIA

The signs and symptoms of anemia can be mild or severe. They depend on how severe the anemia is and how quickly it develops. Generally, signs and symptoms increase as anemia gets worse. Many of the signs and symptoms of anemia also occur in other diseases and conditions.

Mild anemia may have no signs or symptoms. If you do develop signs and symptoms, you may have tiredness, weakness, or pale or yellowish skin. These signs and symptoms also occur in more severe anemia and are far more noticeable or clear.

As anemia gets worse, you may also experience faintness or dizziness, increased thirst, sweating, weak and rapid pulse, or fast breathing. Severe anemia may cause lower leg cramps while exercising, shortness of breath, or brain damage. A lack of red blood cells may also cause heart-related symptoms because your heart must work harder to carry oxygen-rich blood throughout your body. These symptoms include arrhythmias or abnormal heart rhythms, a heart murmur (an extra or unusual sound heard during a heartbeat), an enlarged heart, or even heart failure.

WHAT IS THE DIFFERENCE BETWEEN SIGNS AND SYMPTOMS?

A **sign** is evidence of a disease or condition that someone else can see or measure (for example, yellowish skin, a low hemoglobin level, or abnormal heart rhythms).

A **symptom** is a feeling that a person experiences with a disease or condition (for example, tiredness or chest pain).





THE LEADING CAUSES OF ANEMIA

Anemia has three main causes: lack of red blood cell production, high rates of red blood cell destruction, and blood loss.

Conditions that may lead to anemia include:

- Heavy menstrual periods
- Pregnancy
- Ulcers
- Colon polyps or colon cancer
- Inherited disorders
- A diet that does not have enough iron, folic acid, or vitamin B12
- Blood disorders such as sickle cell disease and thalassemia
- Cancer
- Aplastic anemia, which is a condition that can be inherited or acquired
- Glucose-6-phosphate dehydrogenase (G6PD) deficiency, which is a metabolic disorder

Anemia can make you feel tired, cold, dizzy, and irritable. You may be short of breath or have a headache.

WHEN YOUR BODY DOES NOT MAKE ENOUGH RED BLOOD CELLS

To make enough healthy hemoglobin and red blood cells, your body needs iron, vitamin B12, folate (another B vitamin), small amounts of other vitamins and minerals, and protein. You get these nutrients from the foods you eat. Your body also needs a proper balance of hormones—especially erythropoietin, which is a hormone that boosts red blood cell production.

Certain chronic diseases—those that go on for a long time and often don't go away completely—can harm the body's ability to make enough red blood cells. These are diseases such as cancer, HIV/AIDS,

rheumatoid arthritis, chronic inflammatory diseases, and kidney disease.

Reasons Your Body May Not Make Enough Red Blood Cells

ACQUIRED CAUSES

- Folate or iron deficiency from a poor diet
- Demand for red blood cells exceeds the supply
- Some cancers (for example, leukemia, lymphoma, and multiple myeloma)
- Toxins (for example, pesticides)
- Radiation and chemotherapy treatments for cancer
- Some viral infections (for example, hepatitis and Epstein-Barr)
- Autoimmune disorders (for example, lupus)
- Pregnancy

INHERITED CAUSES

- Fanconi anemia
- Shwachman-Diamond syndrome
- Dyskeratosis congenita
- Diamond-Blackfan anemia
- Amegakaryocytic thrombocytopenia

WHEN YOUR BODY DESTROYS TOO MANY RED BLOOD CELLS

Sometimes your body destroys red blood cells before they reach the end of their natural lifespan of about 120 days. This process, called hemolysis, can be caused by an acquired or inherited condition. Red blood cells may also be destroyed in such large numbers that the bone marrow cannot make enough new red blood cells to keep up. Certain diseases or infections, such as lupus or hepatitis, are examples of acquired conditions that may cause your body to destroy too many red blood cells.

What Can Cause Your Body To Destroy Too Many Red Blood Cells

ACQUIRED CAUSES

- Immune hemolytic anemia (the immune system makes antibodies against red blood cells or medicines, leading to red blood cell destruction)
- Physical damage to red blood cells
- Paroxysmal nocturnal hemoglobinuria
- Infection (for example, malaria)

INHERITED CAUSES

- Sickle cell disease
- Thalassemias
- Hereditary spherocytosis
- Hereditary elliptocytosis
- G6PD deficiency
- Pyruvate kinase deficiency

WHEN YOUR BODY LOSES TOO MANY RED BLOOD CELLS

The third main way in which people develop anemia is through blood loss. When you lose blood, you can lose a large number of red blood cells, and that can cause anemia. The loss of those red blood cells also leads to low levels of iron in your body. Without enough iron, your body will make fewer red blood cells than it needs, and the red blood cells it does make will have less hemoglobin than normal. That, too, can lead to anemia.

These are some reasons why your body may lose too many red blood cells over a long period of time:

- **Heavy menstrual bleeding**
- **Heavy, frequent nosebleeds**
- **Bleeding in the digestive or urinary tract**
- **Ulcers**
- **Some cancers (for example, digestive tract, kidney, and bladder)**

These are some reasons your body may suddenly lose too many red blood cells:

- **Injuries**
- **Childbirth**
- **Burst blood vessel**
- **Heavy bleeding during surgery**





HOW ANEMIA IS DIAGNOSED

MEDICAL AND FAMILY HISTORIES

You can find out you have anemia in various ways. It may be detected when you are being tested for another condition. You also might find out that you have iron-deficiency anemia if you try to give blood and are turned down because you have a low hemoglobin level.

Or you may have signs or symptoms and go to your doctor, who discovers anemia through blood tests. Your doctor will likely take a few first steps to determine whether your signs and symptoms are the result of anemia or some other condition. The most important thing to remember is that, with an accurate diagnosis, many anemias are treatable.

Here is some of the information your doctor will need to help diagnose your condition:

- Signs and symptoms and how long you have had them
- Medical history, including how regular or heavy your menstrual periods are
- Pregnancy history

Your doctor may talk to you about the foods you eat, the medicines you take, and your family health history.

PHYSICAL EXAM

Here are some of the things your doctor may do during a physical exam:

- **Check your tongue, nails, or the inner lining** of your eyelids to see if they are pale.
- **Check your fingernails** to see whether they are pale or brittle, and how quickly they refill with blood.

- **Listen to your heart** for a rapid or irregular heartbeat and your lungs for rapid or uneven breathing.
- **Feel your abdomen** for an enlarged liver or spleen, check for bone pain, or conduct a pelvic or rectal exam to check for internal bleeding.
- **Conduct a neurological exam** to check how well your muscles, senses, and reflexes work, as well as your mental status, coordination, and ability to walk.

TESTING FOR ANEMIA

Based on your answers and the physical exam, your doctor will recommend tests to determine the type of anemia you may have and its severity. Often, the first test is a complete blood count (CBC), which is a broad-scale test that provides a count of all red blood cells, white blood cells, and platelets in a sample of your blood. It also includes other tests that provide useful information about your blood.

Your doctor can use this information to help determine whether you have anemia, what type you may have, and what underlying condition may be causing the anemia. Depending on the results of the CBC, your doctor may recommend further tests.

The table on the next page summarizes the CBC and other common tests and procedures that your doctor may recommend to diagnose anemia.

Complete Blood Count Tests

TEST	WHAT IT DOES	WHAT IT REVEALS
Red blood cell, white blood cell, and platelet count	Counts all red blood cells, white blood cells, and platelets in a sample of blood. Gives information about the size, shape, and physical characteristics of the blood cells.	A lower-than-normal number of red blood cells suggests anemia. Specific changes in number, size, or shape point to the cause of anemia.
White blood cells differential	Identifies the five types of white blood cells in a blood sample and the relative percentage of each in the sample.	A white blood cell's differential can help identify a condition that may be causing anemia.
Hemoglobin	Measures the amount of oxygen-carrying protein in the blood.	Low hemoglobin levels point to diseases that usually cause the body to make too few red blood cells.
Hematocrit	Measures how much space red blood cells take up in your blood.	A low hematocrit level points to anemia. An abnormal hematocrit level may also be a sign of a blood or bone marrow disorder.
Mean corpuscular volume	Measures the average size of the red blood cells.	Red blood cell size gives a clue to the type of anemia. Larger than normal red blood cells may suggest pernicious anemia caused by vitamin B12 or folate deficiency. Smaller than normal red blood cells suggest iron-deficiency anemia or thalassemia, which is a rare, inherited anemia.
Mean corpuscular hemoglobin	Calculates the average amount of oxygen-carrying hemoglobin inside red blood cells.	Larger than normal red blood cells have more oxygen-carrying hemoglobin. Smaller than normal red blood cells often have less hemoglobin.
Mean corpuscular hemoglobin concentration	Calculates the average concentration of hemoglobin inside red blood cells.	This test gives clues about the type of anemia or other possible conditions when abnormal values of hemoglobin are found.
Red cell distribution width	Calculates the difference in the size of red blood cells.	The body may be trying to make new red blood cells to correct the anemia, or the test may provide clues about the cause of the anemia.

Bone Marrow Test

TEST	WHAT IT DOES	WHAT IT REVEALS
Bone marrow aspiration and bone marrow biopsy	Gives information about the marrow's ability to make enough healthy blood cells. (The doctor collects and evaluates a sample of bone marrow.)	Abnormal results showing only a few cells in the bone marrow can point to aplastic anemia. Certain cancers may cause anemia, in particular leukemia, which is a cancer of the bone marrow itself. The bone marrow sample is a means to diagnose cancer affecting the bone marrow that may be the source of an anemia. Taking a bone marrow sample can help diagnose cancer that may be affecting the bone marrow and also causing an anemia.

Other Blood Tests

TEST	WHAT IT DOES	WHAT IT REVEALS
Blood smear	Shows the size, shape, and number of red blood cells, white blood cells, and platelets.	Possible causes for the anemia through the presence of abnormal or immature blood cells.
Reticulocyte count	Measures the number of young red blood cells in the blood. Shows whether the bone marrow is making enough red blood cells at the correct rate or at a higher rate in an appropriate response to the anemia.	The possibility of hemolytic anemia because of a markedly higher reticulocyte count, or the possibility of iron-deficiency anemia, pernicious anemia, aplastic anemia, or other anemias because of a lower reticulocyte count.
Serum iron	Measures the total amount of iron in the blood.	Iron-deficiency anemia due to abnormal amounts of transferrin (a protein that either transports iron to the bone marrow, where hemoglobin and red blood cells are made, or it transports iron to body tissues for storage).
Total iron-binding capacity	Measures the total amount of iron that can be bound by transferrin.	Iron-deficiency anemia due to abnormal amounts of transferrin (a protein that either transports iron to the bone marrow, where hemoglobin and red blood cells are made, or it transports iron to body tissues for storage).
Unsaturated iron-binding capacity	Determines the portion of transferrin that is not yet saturated with iron.	Iron-deficiency anemia due to abnormal amounts of transferrin (a protein that either transports iron to the bone marrow, where hemoglobin and red blood cells are made, or it transports iron to body tissues for storage).
Transferrin saturation	Shows the percentage of transferrin that is saturated with iron. It is calculated using the results of serum iron, total iron-binding capacity, and unsaturated iron-binding capacity tests.	Iron-deficiency anemia due to abnormal amounts of transferrin (a protein that either transports iron to the bone marrow, where hemoglobin and red blood cells are made, or it transports iron to body tissues for storage).
Serum ferritin	Reflects the amount of stored iron in your entire body.	Iron-deficiency anemia due to abnormal amounts of transferrin (a protein that transports iron to the bone marrow, where hemoglobin and red blood cells are made, or it transports iron to body tissues for storage).
Coombs test	Looks for antibodies directed against red blood cells.	A positive result points to the presence of antibodies (proteins made by the immune system). These results can point to hemolytic anemia.
G6PD test	Measures the amount of glucose-6-phosphate dehydrogenase (G6PD), an enzyme, in red blood cells.	Abnormal results can point to a G6PD deficiency, an inherited condition that can lead to hemolytic anemia.





HOW ANEMIA IS TREATED

THE GOALS OF TREATMENT

The good news is that anemia often is easily treated. The treatment your doctor chooses will depend on the type of anemia you have, its cause, and how severe it is.

These are the main goals of treatment:

- Increase your red blood cell count or hemoglobin level to improve the oxygen-carrying capacity of your blood
- Treat the underlying condition causing your anemia
- Prevent complications from the anemia, such as heart or nerve damage
- Relieve symptoms and improve your quality of life

People who have mild or moderate anemia with no symptoms, or people whose anemia is not getting worse, may not need treatment. Exceptions apply to those with nutritional anemias such as iron-deficiency anemia. In those cases, the low level of iron in the body may have other harmful effects besides anemia, and treatment is needed. For more information, see “People Who Are More Likely to Develop Iron-Deficiency Anemia” on page 15.

People who have severe anemia or anemia that is getting worse need treatment. Some rare anemias, such as severe aplastic anemia, can be fatal if it goes untreated. The risk of death may increase dramatically if a person has low levels of other blood cells besides red blood cells, such as white blood cells or platelets.

Anemia treatments are evolving, and the kind your doctor suggests for you is based on the type of anemia you have. For example, iron-deficiency anemia and pernicious anemia are

generally treated through dietary changes and supplements. Other types of anemia are treated with medicines, procedures, surgery, or lifestyle changes. Occasionally, a person may need blood transfusions, but this treatment is used only with severe anemia. The “Different Types of Anemia” section on page 13 provides more details on the treatments used for specific anemias.

YOUR ANEMIA HEALTHCARE TEAM

Primary care providers—family doctors, internists, pediatricians, and nurse practitioners—can treat many anemias. Your healthcare provider may also want to work with one or more specialists to help treat your anemia. These specialists may include:

- A **hematologist**, a doctor who specializes in treating blood disorders
- A **gastroenterologist**, a doctor who specializes in treating digestive system and liver diseases and conditions
- An **obstetrician/gynecologist**, a doctor who specializes in medical and surgical care for women and who focuses on pregnancy, childbirth, and disorders of the reproductive system
- A **cardiologist**, a doctor who specializes in treating heart and blood vessel diseases and conditions
- A **neurologist**, a doctor who specializes in treating nervous system disorders, including diseases of the brain, spinal cord, nerves, and muscles
- A **registered dietitian**, an accredited food and nutrition expert





DIFFERENT TYPES OF ANEMIA

IRON-DEFICIENCY ANEMIA

Iron-deficiency anemia is a common type of anemia that occurs when you do not have enough iron in your body. People with mild or moderate iron-deficiency anemia may not have any signs or symptoms. More severe iron-deficiency anemia may cause fatigue or tiredness, shortness of breath, or chest pain.

If your doctor diagnoses you with iron-deficiency anemia, your treatment will depend on the cause and severity of the condition. Your doctor may recommend healthy eating changes, iron supplements, intravenous (IV) iron therapy for mild to moderate iron-deficiency anemia, or red blood cell transfusions for severe iron-deficiency anemia. You may need to address the cause of your iron deficiency, such as underlying bleeding. If undiagnosed or untreated, iron-deficiency anemia can cause serious complications, including heart failure and developmental delays in children.



CAUSES

Iron-deficiency anemia usually develops over time because your body's intake of iron is too low. Low levels of iron can occur because of blood loss, a daily iron intake that is less than the recommended daily amount, and medical conditions that make it hard for your body to absorb iron from the gastrointestinal (GI) tract.

When you lose blood, you lose iron. Certain conditions or medicines can cause blood loss and lead to iron-deficiency anemia. Common causes of blood loss that lead to iron-deficiency anemia include:

- Bleeding in your GI tract (from an ulcer, colon cancer, or regular use of medicines such as aspirin or nonsteroidal anti-inflammatory drugs [NSAIDs], such as ibuprofen and naproxen)
- Certain rare genetic conditions such as hereditary hemorrhagic telangiectasia, which causes bleeding in the bowels
- Frequent blood donation
- Frequent blood tests, especially in infants and small children
- Heavy menstrual periods
- Injury or surgery
- Urinary tract bleeding

Iron-deficiency anemia can be caused by getting less than the recommended daily amounts of iron. The recommended daily amounts of iron will depend on your age, sex, and whether you are pregnant or breastfeeding.

Recommended daily amounts of iron, in milligrams (mg)

AGE	MALE	FEMALES	PREGNANCY	BREASTFEEDING
Birth to 6 months	0.27 mg	0.27 mg		
7 to 12 months	11 mg	11 mg		
1 to 3 years	7 mg	7 mg		
4 to 8 years	10 mg	10 mg		
9 to 13 years	8 mg	8 mg		
14 to 18 years	11 mg	15 mg	27 mg	10 mg
19 to 50 years	8 mg	18 mg	27 mg	9 mg
51 or older	8 mg	8 mg		

Recommended daily iron intake for children and adults. The table above lists the recommended amounts of iron, in milligrams (mg) at different ages and stages of life. Until the teen years, the recommended amount of iron is the same for boys and girls. From birth to 6 months, babies need 0.27 mg of iron. This number goes up to 11 mg for children ages 7 to 12 months, and down to 7 mg for children ages 1 to 3. From ages 4 to 8, children need 10 mg, and from ages 9 to 13, 8 mg. From ages 14 to 18, boys need 11 mg, while girls need 15 mg. From ages 19 to 50, men need 8 mg and women need 18 mg. After age 51, both men and women need 8 mg. Pregnant women need 27 mg. Breastfeeding girls under age 18 need 10 mg while breastfeeding women older than 18 need 9 mg.



Even if you consume the recommended daily amount of iron, your body may not be able to absorb the iron. Certain conditions or medicines can decrease your body's ability to absorb iron and lead to iron-deficiency anemia. These conditions include:

- **Intestinal and digestive conditions**, such as celiac disease; inflammatory bowel diseases, including ulcerative colitis and Crohn's disease; and *Helicobacter pylori* infection.
- **A history of gastrointestinal surgery**, such as weight-loss surgery—especially gastric bypass—or gastrectomy.
- **Certain rare genetic conditions**, such as a TMRPSS6 gene mutation that causes a person's body to make too much of a hormone called hepcidin. Hepcidin blocks intestine from taking up iron.

Other medical conditions that may lead to iron-deficiency anemia include:

- **End-stage kidney failure**, where there is blood loss during dialysis. People who have chronic kidney disease also often take other medicines—such as proton pump inhibitors, anticoagulants, or blood thinners—that may cause iron-deficiency anemia. Proton pump inhibitors interfere with iron absorption, and blood thinners increase the likelihood of bleeding in the GI tract.
- **Inflammation from heart failure or obesity.** These chronic conditions can lead to inflammation that may cause iron-deficiency anemia.

How does inflammation from chronic diseases cause iron-deficiency anemia?

When there is inflammation in your body, your liver makes more of a hormone called hepcidin. Hepcidin prevents iron from leaving cells where it is stored or from being absorbed in the duodenum, the first part of the small intestine just beyond the stomach.

- Even if you have enough iron in your body, inflammation may make it harder for your body to absorb or use iron.
- Without enough available iron in your blood, your body cannot make as many new red blood cells. The red blood cells it does make have less **hemoglobin** than normal. Hemoglobin is a protein inside red blood cells that carries oxygen from the lungs to tissues and organs in the body. Hemoglobin also carries carbon dioxide back to the lungs.

PEOPLE WHO ARE MORE LIKELY TO DEVELOP IRON-DEFICIENCY ANEMIA

You may have an increased risk for iron-deficiency anemia because of your age, sex, family history and genetics, or lifestyle habits, or because of unhealthy environments.

People who are at higher risk because they are a certain age include:

- **Infants between 6 and 12 months**, especially if they are fed only breast milk or are fed formula that is not fortified with iron. The iron that full-term infants have stored in their bodies is used up in the first 4 to 6 months of life. Babies born prematurely may be at an even higher risk, as most newborns' iron stores are developed during the third trimester of pregnancy.
- **Children between ages 1 and 2**, especially if they drink a lot of cow's milk, which is low in iron.
- **Teens**, who have an increased need for iron during growth spurts.
- **Older adults**, especially those over age 65.

People who are at higher risk due to their environment include:

- **Children** who have lead in their blood from their environment or the water they drink. Lead interferes with the body's ability to make hemoglobin.

People who are higher risk due to their family history and genetics include:

- **Those who have inherited Von Willebrand disease**, a bleeding disorder that affects the blood's ability to clot. This makes it harder to stop bleeding and can increase the risk of iron-deficiency anemia from trauma, surgery, or heavy menstrual periods.
- **Individuals with a gene for hemophilia**, including symptomatic female carriers who have heavy menstrual periods.

People who are at higher risk due to their lifestyle habits include:

- Those with **vegetarian or vegan eating patterns**. Not eating enough iron-rich foods, such as meat and fish, may result in you getting less than the recommended daily amount of iron.
- Individuals who **donate blood** often.
- **Athletes**, especially young females. Endurance athletes lose iron through their GI tracts. They also lose iron through the breakdown of red blood cells, called hemolysis. In this case, hemolysis is caused by strong muscle contractions and the impact of feet repeatedly striking the ground, such as with marathon runners.

Other people who are at higher risk include:

- **Girls and women** between ages 14 and 50. They tend to need more iron than boys and men of the same age.

Women who are at higher risk include:

- **Those who are experiencing menstruation**, especially if they have heavy periods.
- **Those who are pregnant, who recently gave birth, or who are breastfeeding.** These women may be consuming less than the recommended daily amount of iron. This is because their need for iron increases during these periods of growth and development, and it may be hard to get the recommended amount from food alone. Pregnant women need more iron to support their unborn babies' growth, so their bodies produce more blood. With more red blood cells on hand, their bodies can store iron to prepare for blood loss during delivery.

SIGNS AND SYMPTOMS OF IRON-DEFICIENCY ANEMIA

Common signs of iron-deficiency anemia include:

- Brittle or spoon-shaped nails
- Cracks at the sides of the mouth
- Pale skin
- Swelling or soreness of the tongue

Common symptoms of iron-deficiency anemia include:

- Chest pain
- Coldness in the hands and feet
- Difficulty concentrating
- Dizziness
- Fatigue, or feeling tired, which can make it hard to find the energy to do normal activities*
- Headache
- Irregular heartbeat, which is a sign of more serious iron-deficiency anemia
- Pica, which is an unusual craving for non-food items, such as ice, dirt, paint, or starch
- Restless legs syndrome
- Shortness of breath
- Weakness

*This is the most common symptom.

“Before my diagnosis I was always very, very tired. I thought my busy lifestyle—a full-time job and part-time school—was to blame. I didn’t think I had a medical condition. Some years later, I had surgery for a different health problem. At that time, doctors told me that my extreme tiredness was due to iron-deficiency anemia.

My doctor prescribed iron supplements and advised me to adopt an overall healthy lifestyle that includes good nutrition, physical activity, and better sleeping habits.”

Susan



HOW IRON-DEFICIENCY ANEMIA IS DIAGNOSED

Your doctor will use the basic tests described earlier (see “How Anemia Is Diagnosed” on page 7) to diagnose iron-deficiency anemia. If your anemia is mild, you may have no signs or symptoms at all. Your doctor may discover the anemia while testing you for something else.

If your doctor suspects iron-deficiency anemia, he or she will likely recommend a complete blood count. If this blood test confirms the diagnosis, your doctor may recommend other blood tests to find out what’s causing the anemia and how severe it is. These tests include a blood smear, a reticulocyte count, and blood iron tests (see “Testing for Anemia” on page 7 for more details).

Healthy and Low Iron Studies in Adults

Iron, $\mu\text{mol/L}$	Normal	10 to 30
	Iron-deficiency anemia	Less than 10
Ferritin, $\mu\text{g/L}$	Normal	Men 40 to 300 Women 20 to 200
	Iron-deficiency anemia	Less than 10

Different tests help your doctor diagnose iron-deficiency anemia.

In iron-deficiency anemia, blood levels of iron will be low, or less than 10 micromoles per liter (mmol/L) for both men and women. Normal levels are 10 to 30 mmol/L. Levels of ferritin will also be low, or less than 10 micrograms per liter (mg/L) for both men and women. Normal levels are 40 to 300 for men and 20 to 200 for women.

If iron-deficiency anemia is confirmed and your doctor thinks that it may be caused by internal bleeding, you may have one or more of the following procedures to guide treatment:

- **Fecal occult blood test** to check for blood in the stool. Blood in the stool would suggest bleeding in the GI tract and may require further testing.
- **Upper endoscopy** to look for bleeding in the esophagus, stomach, and the first part of the small intestine. A tube with a tiny camera is inserted through your mouth down to your stomach and upper small intestine to view the lining of your upper digestive tract.
- **Colonoscopy** to look for bleeding or other abnormalities, such as growths or cancer of the lining of the colon. For this test, you are sedated while a small camera is inserted into the colon to view it directly.



HOW IRON-DEFICIENCY ANEMIA IS TREATED

Treatment for iron-deficiency anemia will depend on its cause and severity. Treatments may include iron supplements, procedures, surgery, and dietary changes. Severe iron-deficiency anemia may require intravenous iron therapy or a blood transfusion.

Your doctor may recommend that you take iron supplements, also called iron pills or oral iron, by mouth once or several times a day to increase the amount of iron in your body. This is the most common treatment for iron deficiency. It generally takes three to six months to replenish your iron stores.

Iron supplements are sometimes recommended by your doctor during pregnancy. If your condition is caused by certain rare genetic conditions, such as a TMRPSS6 gene mutation, you may not respond to oral iron supplements.

Iron supplements are generally not recommended for people who do not have iron-deficiency anemia. This is because too much iron can damage your organs.

Do not stop taking your prescribed iron supplements without first talking to your doctor. Talk to your doctor if you are experiencing side effects such as a metallic taste, vomiting, diarrhea, constipation, or an upset stomach. Your doctor may be able to recommend options such as taking your supplements with food, lowering the dose, trying a different type of iron supplement, or receiving intravenous iron.

SAFETY NOTE

Keep Iron Supplements Out of Reach of Children

The high doses of iron in these supplements can quickly cause life-threatening poisoning if your child eats them.

This is particularly important for pregnant women taking prenatal vitamins. These vitamins are often brightly colored capsules that could attract young children, who may think that they are candy.

If iron supplements alone are not able to replenish the levels of iron in your body, your doctor may recommend a procedure such as:

- **Iron therapy, or intravenous (IV) iron.** This is sometimes used to deliver iron through a blood vessel to increase iron levels in the blood. One benefit of IV iron is that it often takes only one or a few sessions to replenish the amount of iron in your body. People with severe iron-deficiency anemia or who have chronic conditions such as kidney disease or celiac disease may be more likely to receive IV iron. You may experience vomiting, headache, or other side effects right after the IV iron, but these usually go away within a day or two.
- **Red blood cell transfusion(s).** These may be used for people with severe iron-deficiency anemia to quickly increase the amount of red blood cells and iron in the blood. Your doctor may recommend this if you have serious complications of iron-deficiency anemia, such as chest pain.
- **Surgery,** upper endoscopy or colonoscopy, to stop bleeding.

To help you meet your recommended daily intake of iron, your doctor may ask you to take these steps:

- Adopt healthy lifestyle changes, such as [heart-healthy eating patterns](#).
- Increase your daily intake of iron-rich foods to help treat your iron-deficiency anemia. See “Lead a Healthy Lifestyle” on page 31 to learn about foods that are high in iron. It is important to know that increasing your intake of iron may not be enough to replace the iron your body normally stores but has used up.
- Increase your intake of vitamin C to help your body absorb iron.
- Avoid drinking black tea, which reduces iron absorption.

If you have chronic kidney disease and iron-deficiency anemia, your doctor may recommend erythropoiesis stimulating agents (ESA). These medicines stimulate the bone marrow to make more red blood cells. ESAs are usually used with iron therapy or intravenous iron, or when iron therapy alone is not enough.

PERNICIOUS ANEMIA

Pernicious anemia is a condition that develops when the body does not have enough vitamin B12. The body needs vitamin B12 to make healthy red blood cells and to keep its nervous system working properly.

When your body does not have enough vitamin B12, the red blood cells don't divide normally and are too large. They may have trouble getting out of the bone marrow, a sponge-like tissue inside the bones where blood cells are made.

Without enough red blood cells to carry oxygen to your body, you may feel tired and weak. Severe or long-lasting pernicious anemia can damage the heart, brain, and other organs in the body.

CAUSES

Pernicious anemia is caused by a lack of a protein called intrinsic factor, or other issues, such as infections, surgery, medicines, or diet.

Lack of Intrinsic Factor

People who have pernicious anemia cannot absorb enough vitamin B12 from food. This is because they lack intrinsic factor, a protein made in the stomach. A lack of this protein leads to vitamin B12 deficiency.

In some people, an autoimmune response causes a lack of intrinsic factor.

An autoimmune response occurs if the body's immune system makes antibodies (proteins) that mistakenly attack and damage the body's tissues or cells.

In pernicious anemia, the body makes antibodies that attack and destroy the parietal cells. These cells line the stomach and make intrinsic factor. Why this autoimmune response occurs isn't known, but as a result of it, the stomach stops making intrinsic factor, and this leads to vitamin B12 deficiency.

As a result of this attack, the stomach stops making intrinsic factor. This leads to vitamin B12 deficiency.

A lack of intrinsic factor also can occur if you've had part or all of your stomach surgically removed. This type of surgery reduces the number of parietal cells available to make intrinsic factor.

PROBABLE OUTCOMES

Pernicious anemia was often fatal in the past, before vitamin B12 treatments were available. Now, the condition usually is easy to treat with vitamin B12 pills or shots.

With ongoing care and proper treatment, most people who have pernicious anemia can recover, feel well, and live normal lives. Without treatment, pernicious anemia can lead to serious problems with the heart, nerves, digestive tract, and other parts of the body. It can also cause neurological problems such as memory loss. Some of these problems may be permanent. People who have pernicious anemia may also be at higher risk for weakened bone strength and stomach cancer.

OTHER NAMES

Pernicious anemia is one of two major types of "macrocytic" or "megaloblastic" anemia. These terms refer to anemia in which the red blood cells are larger than normal. (The other major type of macrocytic anemia is caused by folic acid deficiency.)

In rare cases, children are born with an inherited disorder that prevents their bodies from making intrinsic factor. This disorder is called congenital pernicious anemia. Vitamin B12 deficiency also is called cobalamin deficiency and combined systems disease.

Malabsorption in the Small Intestine

Sometimes pernicious anemia occurs because the body's small intestine can't properly absorb vitamin B12. This may be the result of:

- Too many of the wrong kind of bacteria in the small intestine. This is a common cause of pernicious anemia in older adults. The bacteria use up the available vitamin B12 before the small intestine can absorb it.
- Diseases that interfere with vitamin B12 absorption. One example is celiac disease. This is a genetic disorder that makes your body unable to tolerate a protein called gluten. Another example is Crohn's disease, an inflammatory bowel disease. HIV also may interfere with vitamin B12 absorption.
- Certain medicines that alter bacterial growth or prevent the small intestine from properly absorbing vitamin B12. Examples include antibiotics and certain diabetes and seizure medicines.
- Surgical removal of part or all of the small intestine.
- A tapeworm infection. The tapeworm feeds off of the vitamin B12. Eating undercooked, infected fish may cause this type of infection.

Diet Lacking Vitamin B12

Some people get pernicious anemia because they don't have enough vitamin B12 in their diets. This cause of pernicious anemia is less common than other causes. Good food sources of vitamin B12 include:

- Breakfast cereals with added vitamin B12
- Meats such as beef, liver, poultry, and fish
- Eggs and dairy products such as milk, yogurt, and cheese
- Foods fortified with vitamin B12, such as soy-based beverages and vegetarian burgers

PEOPLE WHO ARE MORE LIKELY TO DEVELOP PERNICIOUS ANEMIA

Pernicious anemia is more common in people of Northern European and African descent than in other ethnic groups.

Older people also are at higher risk for the condition. As people grow older, they tend to make less stomach acid, which means less intrinsic factor is present as well. The lack of intrinsic factor prevents the small intestine from absorbing vitamin B12.

Breastfed infants of strict vegetarian mothers also are at risk for pernicious anemia. These infants can develop anemia within months of being born. This is because they haven't had enough time to store vitamin B12 in their bodies. Doctors treat these infants with vitamin B12 supplements.

Other groups, such as people who have alcohol use disorder, also may be at risk for pernicious anemia. These people may not get the proper nutrients in their diets.

Pernicious anemia also can occur in younger people and other populations. Some of the reasons you may be at higher risk for pernicious anemia include:

- Having a family history of the condition.
- Having had part or all of your stomach surgically removed. The stomach makes intrinsic factor, which is a protein that helps your body absorb vitamin B12.
- Having an autoimmune disorder that involves the endocrine glands, such as Addison's disease, type 1 diabetes, Graves' disease, or vitiligo. Research suggests that a link may exist between these autoimmune disorders and pernicious anemia, which is caused by an autoimmune response.

- Having had part or all of your small intestine surgically removed. The small intestine is where vitamin B12 is absorbed.
- Having certain intestinal diseases or other disorders that may prevent your body from properly absorbing vitamin B12 (for example, Crohn's disease, intestinal infections, and HIV).
- Taking medicines that prevent your body from properly absorbing vitamin B12 – for example, antibiotics and certain seizure medicines.
- Being a strict vegetarian who does not eat any animal or dairy products and does not take a vitamin B12 supplement, or having a poor diet overall.

“I went to the doctor for some routine blood tests and found out I had vitamin B12 deficiency, or pernicious anemia. I didn't have any symptoms and didn't know I had a B12 deficiency until the doctor told me. The doctor said that taking vitamin B12 shots would give me more pep. He started me out with vitamin B12 shots once a week for 6 weeks. Now I only need them once a month. I've always eaten pretty healthy. And while I've slowed down a bit since my diagnosis of pernicious anemia, I still walk 2 miles three or four times a week.”

Sherman



SIGNS AND SYMPTOMS

Some of the signs and symptoms of pernicious anemia also show up in all types of anemia. Other signs and symptoms are specific to a lack of vitamin B12.

Signs and Symptoms of Vitamin B12 Deficiency

Vitamin B12 deficiency can lead to nerve damage, which can cause tingling and numbness in your hands and feet, muscle weakness, and loss of reflexes. You may also feel unsteady, lose your balance, and have trouble walking. Vitamin B12 deficiency can cause weakened bones and may lead to hip fractures.

Severe vitamin B12 deficiency can cause neurological problems, such as confusion, dementia, depression, and memory loss.

Other symptoms of vitamin B12 deficiency involve the digestive tract. These symptoms include nausea (feeling sick to your stomach) and vomiting, heartburn, abdominal bloating and gas, constipation or diarrhea, loss of appetite, and weight loss. An enlarged liver is another symptom.

A smooth, thick, red tongue also is a sign of vitamin B12 deficiency and pernicious anemia.

Infants who have vitamin B12 deficiency may have poor reflexes or unusual movements, such as face tremors. They may have trouble feeding due to tongue and throat problems. They may also be irritable. If vitamin B12 deficiency isn't treated, these infants may have permanent growth problems.

HOW PERNICIOUS ANEMIA IS DIAGNOSED

Pernicious anemia is diagnosed based on your medical and family histories, a physical exam, and the results from tests. Your doctor may ask about your signs and symptoms, your diet, and any medicines you may take. He or she may also ask whether you have or have had the following:

- Any stomach or intestinal surgeries.
- Any digestive disorders, such as celiac disease or Crohn's disease.
- A family history of anemia or pernicious anemia.
- A family history of autoimmune disorders—such as Addison's disease, type 1 diabetes, Graves' disease, or vitiligo. Research suggests that a link may exist between these autoimmune disorders and the kind of pernicious anemia that is caused by an autoimmune response.

This information will give your doctor important clues about whether you have pernicious anemia and its possible cause.

During the physical exam, your doctor may check for pale or yellowish skin and an enlarged liver. He or she may listen to your heart for rapid or irregular heartbeats or a heart murmur.

Your doctor may also check for signs of nerve damage. He or she may want to see how well your muscles, eyes, senses, and reflexes work. Your doctor may ask questions or do tests to check your mental status, coordination, and ability to walk.

Your doctor may recommend tests to help diagnose pernicious anemia and find out what is causing it. Often, the first test used to diagnose anemia is a complete blood count. This test measures many parts of your blood and looks at the number and appearance of your blood cells. With pernicious anemia, the red blood cells are larger than normal. (For more information about the complete blood count, see "Testing for Anemia" on page 7.)

If your complete blood count shows that you have anemia, your doctor may recommend other tests, including:

- A reticulocyte count. This test measures the number of young red blood cells in your blood. The results tell your doctor whether your bone marrow is making enough healthy red blood cells. People who have pernicious anemia have low reticulocyte counts.
- Tests for the blood levels of vitamins. These tests measure the levels of vitamin B12, folate, and vitamin C in your blood.
- Tests for homocysteine and methylmalonic acid levels. People who have pernicious anemia have higher-than-normal levels of these substances in their blood.
- An antibody test. This test measures whether your body is making antibodies to attack the stomach cells that make intrinsic factor. The results of this test will reveal the cause of your pernicious anemia.
- Bone marrow tests. These tests indicate whether your bone marrow is healthy and making enough healthy red blood cells. People who have pernicious anemia have larger than normal bone marrow cells.

HOW PERNICIOUS ANEMIA IS TREATED

Doctors treat pernicious anemia by replacing the missing vitamin B12 in the body. People who have pernicious anemia may need lifelong treatment.

The goals of treating pernicious anemia include:

- Preventing or treating the anemia and its signs and symptoms
- Preventing or managing complications, such as heart and nerve damage
- Treating the cause of the pernicious anemia (if a cause can be found)

Specific Types of Treatment

Pernicious anemia usually is easy to treat with vitamin B12 shots or pills.

If you have severe pernicious anemia, your doctor may recommend shots first. Shots usually are given in a muscle every day or every week until the level of vitamin B12 in your blood increases. After your vitamin B12 blood level returns to normal, you may get a shot only once a month.

For less severe pernicious anemia, your doctor may recommend large doses of vitamin B12 pills. A vitamin B12 nose gel and spray also are available. These products may be useful for people who have trouble swallowing pills, such as older people who have had strokes.

Your signs and symptoms may begin to improve within a few days after you start treatment. Your doctor may advise you to limit your physical activity until your condition improves.

If your pernicious anemia is caused by something other than a lack of intrinsic factor, you may get treatment for the cause—if a cause can be found. For example, your doctor may prescribe medicines to treat a condition that prevents your body from absorbing vitamin B12.

If medicines are the cause of your pernicious anemia, your doctor may change the type or dose of medicine you take. Infants of strict vegetarian mothers may be given vitamin B12 supplements from birth.

APLASTIC ANEMIA

Aplastic anemia is a rare but serious blood disorder that occurs when your bone marrow cannot make enough new blood cells for your body to work normally.

CAUSES

Aplastic anemia occurs because of damage to stem cells inside bone marrow, which is the sponge-like tissue within your bones. Many diseases and conditions can damage the stem cells in bone marrow. As a result, the bone marrow makes fewer red blood cells, white blood cells, and platelets.

The most common cause of bone marrow damage is from your immune system attacking and destroying the stem cells in your bone marrow, which is a kind of autoimmune disorder. The genes you inherit from your parents, some medicines, and certain toxins in the environment may also cause aplastic anemia.

PEOPLE WHO ARE MORE LIKELY TO DEVELOP APLASTIC ANEMIA

People of all ages can develop aplastic anemia. Those at increased risk may include:

- People undergoing high-dose radiation or chemotherapy for cancer
- People exposed to certain environmental toxins, such as pesticides, arsenic, and benzene
- People taking certain medicines, such as those used to treat rheumatoid arthritis and some types of antibiotics
- People with certain infectious diseases, autoimmune disorders, or inherited conditions that can damage the bone marrow

SIGNS AND SYMPTOMS

Lower-than-normal numbers of red blood cells, white blood cells, and platelets cause the signs and symptoms of aplastic anemia. While signs and symptoms can be mild, moderate, or severe, severe aplastic anemia can be life-threatening.

A lower-than-normal number of red blood cells can cause fatigue; weakness; shortness of breath; pale skin, gums, and nail beds; dizziness; headaches; cold hands and feet; and chest pain. A lower-than-normal number of white blood cells can cause fever, frequent or severe infections, and lingering flu-like symptoms. A lower-than-normal number of platelets can cause easy bleeding or bruising, petechiae (pinpoint red spots on the skin), nosebleeds, bleeding gums, blood in the stool, and heavy menstrual periods.

Other signs and symptoms of aplastic anemia can include nausea and skin rashes.

People who have another blood disorder called paroxysmal nocturnal hemoglobinuria (PNH) and aplastic anemia may have other signs and symptoms, including blood in the urine, swelling or pain in the abdomen, swelling in the legs, headaches, and jaundice (a medical condition marked by a yellowing of the skin or the whites of the eyes).

HOW APLASTIC ANEMIA IS DIAGNOSED

To diagnose aplastic anemia, your doctor will order tests to determine whether you have low numbers of cells in your bone marrow and blood.

Your doctor will use your medical and family histories, a physical exam, and other tests to determine possible causes of aplastic anemia.

- **Medical and family histories.** Your doctor will ask about your symptoms and how long you have had them. He or she also will want to know whether you've had any viral infections, been exposed to toxins, or had cancer treatments. Another important diagnostic clue is whether you or anyone in your family has had anemia.
- **Physical exam.** During the physical exam, your doctor will look at your skin and check for signs of bleeding or infection. He or she may also listen to your heart and lungs for any abnormal sounds and feel your abdomen and legs to determine whether they feel normal. The physical exam findings will help your doctor determine the severity of your condition and what may be causing it.
- **Other tests.** In addition to the bone marrow test, your doctor may recommend a chest x-ray, a computed tomography (CT) scan, ultrasound imaging, liver tests, tests for viral infections, tests for vitamin B12 and folate levels in your blood, and/or a specialized test for PNH. These tests can help your doctor determine the severity of your anemia, what is causing it, and whether you have PNH. The signs and symptoms of aplastic anemia are similar to those of other conditions and other types of anemia.

These tests can help your doctor rule out certain conditions as the cause of your anemia.

“I found out I had aplastic anemia in an odd way. The day after a scuba diving trip, I was covered with bruises that I could not explain. I went to the doctor and was immediately hospitalized and given a blood transfusion. The doctors told me I almost didn't have enough blood in my body. They diagnosed me with aplastic anemia, a blood disorder where your body has trouble making new blood cells. Looking back, there were little signs that I ignored—previous bruising and tiredness—and I now know that I should have seen a doctor much earlier than I did.”

Shirah



HOW APLASTIC ANEMIA IS TREATED

Treatments may include medicines to suppress your immune system, blood transfusions, or a blood and bone marrow transplant. A blood and bone marrow transplant may cure the disorder in some people. Removing a known cause of aplastic anemia, such as exposure to a toxin, may also cure the condition. Because people who have aplastic anemia are more likely to develop blood disorders, your doctor will monitor your condition and screen you for blood disorders regularly. If you take medicine to suppress your immune system, you also will need to take steps to prevent infection and the flu, including taking medicine and getting vaccines such as an annual flu shot.

Medicines

Your doctor may recommend medications to treat the cause of your anemia or help prevent or treat complications. For example, your doctor may prescribe medicines to suppress your immune system or stimulate your bone marrow to make red blood cells. One example of a medicine that can stimulate your bone marrow is erythropoietin therapy. Your doctor may also prescribe medicines to prevent or treat an infection that may occur because your white blood cell count is low.

Blood Transfusions

This is a common procedure in which you receive blood through an IV line inserted in one of your blood vessels. The blood you receive is carefully matched to your own blood type. Transfusions can help increase your blood cell counts up to a normal level. They help relieve symptoms but are not a permanent treatment.

Blood and Marrow Stem Cell Transplants

These procedures are implemented to replace damaged stem cells in your bone marrow with healthy cells. For this procedure, high doses of chemotherapy and possibly radiation are used to destroy your faulty stem cells. Then, donor stem cells are put into a blood vessel through an intravenous tube placed in your chest. These cells are carefully matched to your own cell type. Once the stem cells are in your body, they travel to your bone marrow and begin making new red blood cells, white blood cells, and platelets.

Blood and marrow stem cell transplants generally are the best treatment option for people who have severe aplastic anemia and are eligible for this

treatment. This type of transplant works best in children and young adults who are in good health and have donors with closely matching cell types.

Other Treatments and Lifestyle Changes

Aplastic anemia also is treated in other ways. For example, removing a known cause of aplastic anemia may cure the condition. Examples of known causes include high-dose radiation or chemotherapy treatment, exposure to environmental toxins, and certain medicines.

Lifestyle changes also can help protect you from problems linked to aplastic anemia. For example, because your red blood cell count is low, you may feel tired or short of breath. Conserve your energy and do not overdo physical activity. Because your platelet count is low, you're at risk of bleeding. Avoid activities in which you might cut or injure yourself. Because your white blood cell count is low, your body is less able to fight infections. Protect yourself by washing your hands often and avoiding crowds and people who are sick. See your doctor if you develop a fever, which is a sign that you may have an infection. Talk to your doctor about other lifestyle changes that can protect you from problems linked to aplastic anemia.

HEMOLYTIC ANEMIA

This blood disorder occurs when your red blood cells are destroyed faster than they can be replaced.

CAUSES

This form of anemia develops when your bone marrow cannot make enough new red blood cells to replace the ones that have been destroyed too soon. There are many types of hemolytic anemia and many causes. Hemolytic anemia can be acquired or inherited. Sometimes, the cause is not known.

Doctors diagnose hemolytic anemia based on the underlying cause of your anemia. Certain conditions can cause hemolysis to happen too fast or too often. Conditions that may lead to hemolytic anemia include inherited blood disorders such as sickle cell disease or thalassemia, autoimmune disorders, bone marrow failure, or infections. Some medicines or side effects from blood transfusions may cause hemolytic anemia.

Types of Hemolytic Anemia

TYPE	CHARACTERISTIC
Immune hemolytic anemia	<p>The immune system destroys red blood cells. These are the three types of immune hemolytic anemia:</p> <ul style="list-style-type: none">• Autoimmune hemolytic anemia (AIHA). AIHA is the main cause of hemolytic anemia. The immune system makes antibodies (proteins) that attack the red blood cells. AIHA can develop very suddenly. Certain diseases or infections can raise the risk for AIHA (for example, lupus, chronic lymphocytic leukemia, non-Hodgkin's lymphoma, other blood cancers, Epstein-Barr virus, cytomegalovirus, mycoplasma pneumonia, hepatitis, and HIV). Some AIHA antibodies become active only in warm temperatures, others only in cold temperatures.• Alloimmune hemolytic anemia. With this hemolytic anemia, a person's immune system makes antibodies against blood that is a different type from his or her own blood. This may occur in a blood transfusion from a donor who has a different blood type. It also can occur during pregnancy if the fetus has a different blood type than the mother (this condition is called Rh incompatibility).• Drug-induced hemolytic anemia. Some medicines (for example, penicillin, acetaminophen, antimalaria medicines, and levodopa) may cause an immune reaction that destroys red blood cells.
Mechanical hemolytic anemia	<ul style="list-style-type: none">• Hemolytic anemia develops because red blood cells are physically damaged. This damage may result from a heart-lung bypass machine (used during open-heart surgery), an artificial heart valve that is not working well, an increase in body temperature due to exposure to extreme heat or extensive burns, or preeclampsia (very high blood pressure during pregnancy).
Paroxysmal nocturnal hemoglobinuria	<ul style="list-style-type: none">• Abnormal stem cells in the bone marrow make blood cells with a faulty outer membrane. This causes the body to destroy its red blood cells and make too few white blood cells and platelets.
Other causes of acquired hemolytic anemia	<ul style="list-style-type: none">• Some infections and toxic substances can damage or destroy red blood cells, leading to hemolytic anemia. Examples include malaria, blackwater fever, tick-borne diseases, snake venom, and toxic chemicals.

Autoimmune hemolytic anemia is the main cause of hemolytic anemia.



Types of Inherited Hemolytic Anemia

TYPE	CHARACTERISTIC
Sickle cell disease	<ul style="list-style-type: none">• The body makes abnormal hemoglobin that causes red blood cells to have a sickle, or C, shape. These sickle cells are sticky and do not travel easily through blood vessels.• Sickle cells live only about 10–20 days, and the bone marrow cannot make new red blood cells fast enough to replace the dying ones.• In the United States, sickle cell anemia mainly affects people of African and Hispanic descent.• All states require sickle cell disease screening for newborn babies.
Thalassemias	<ul style="list-style-type: none">• The body does not make enough of certain types of hemoglobin, which prevents it from making enough healthy red blood cells.• Thalassemias often affect people of Southeast Asian, Indian, Chinese, Filipino, Mediterranean, or African descent.
Hereditary spherocytosis	<ul style="list-style-type: none">• A defect in the red blood cells' outer membranes causes them to have a spherical, or ball-like, shape.• The ball-shaped red blood cells have a shorter-than-normal lifespan.• Hereditary spherocytosis is the most common cause of hemolytic anemia among people of Northern European descent.
Hereditary elliptocytosis (ovalocytosis)	<ul style="list-style-type: none">• A defect in the red blood cells' outer membranes makes them oval-shaped and less flexible than normal. They have a shorter than normal lifespan.
G6PD (Glucose-6-phosphate dehydrogenase deficiency)	<ul style="list-style-type: none">• The red blood cells are missing an enzyme called G6PD. (Enzymes are proteins that drive chemical reactions in the body.) The missing enzyme makes the red blood cells fragile and more likely to break down.• If the red blood cells come in contact with certain substances in the bloodstream, they rupture and die.• Many factors, including certain medicines, foods (like fava beans), and infections, can trigger the breakdown of the red blood cells• G6PD deficiency mostly affects men of African or Mediterranean descent.• Most states require G6PD deficiency screening for newborn babies.
Pyruvate kinase deficiency	<ul style="list-style-type: none">• The red blood cells are missing an enzyme called pyruvate kinase. This causes them to break down easily.• Pyruvate kinase deficiency is more common among the Amish.

PEOPLE WHO ARE MORE LIKELY TO DEVELOP HEMOLYTIC ANEMIA

Hemolytic anemia affects people of all ages and races and both sexes. The different types of hemolytic anemia affect various populations.

Some types of acquired hemolytic anemia also affect certain populations. For example, alloimmune hemolytic anemia can occur in pregnant women and their fetuses. Mechanical hemolytic anemia may occur in people who have artificial heart valves or who use a heart-lung bypass machine during open-heart surgery.

SIGNS AND SYMPTOMS

These signs and symptoms vary widely and depend on the type and severity of the hemolytic anemia. Some signs and symptoms are common to all types of anemia, such as:

- Fatigue and weakness
- Pale skin, gums, and nail beds
- Dizziness
- Shortness of breath
- Headaches
- Cold hands and feet
- Chest pain

Other signs and symptoms that are specific to hemolytic anemia include:

- Jaundice (a medical condition marked by a yellow color of the skin or the whites of the eyes). This sign often is very severe in hemolytic anemia.
- Pain in the upper abdomen or back
- An enlarged spleen (see “The Spleen: Your Body’s Natural Filter” immediately below for more information)
- Chills

THE SPLEEN: YOUR BODY’S NATURAL FILTER

The spleen is a small organ that lies behind the stomach on the left side of the abdomen. This organ filters blood and helps fight infections. One of the spleen’s jobs is to remove red blood cells when they come to the end of their lifespans. If large numbers of red blood cells are destroyed during a short period, they will become trapped in the spleen. Over time, this can cause the spleen to become larger than normal.

HOW HEMOLYTIC ANEMIA IS DIAGNOSED

Like other types of anemia, hemolytic anemia is diagnosed based on your personal and family medical histories, a physical exam, and the results of tests.

First, your doctor may ask about your symptoms and how long you have had them. He or she also will review your medical history, as well as your family’s, and may ask questions such as these:

- Do any of your relatives have inherited anemia, such as sickle cell anemia, thalassemia, or G6PD deficiency?
- Have any of your family members had jaundice?
- Have you recently had any illnesses or other medical conditions?
- Do you take medicines? Which ones?
- Have you been exposed to any chemicals or toxic substances?
- Do you have an artificial heart valve?

Your answers to these questions will help determine whether you have hemolytic anemia and provide clues about the cause and severity of the condition.

During the physical exam, your doctor will check for signs of anemia, such as pale skin and fingernails, fast breathing, and rapid heartbeats. He or she may also feel your abdomen to determine whether you have an enlarged spleen.

Many tests are used to confirm a diagnosis of hemolytic anemia and determine the specific type of this anemia. Often, the first test used to diagnose anemia is a complete blood count. This test measures many parts of your blood and looks at the number and appearance of your blood cells. (For more information about the test, see “Testing for Anemia” on page 7.) If the complete blood count confirms that you have anemia, your doctor may recommend additional blood and other tests.

BLOOD TESTS

- **Reticulocyte count.** This test measures the number of young red blood cells in your blood. The results tell your doctor whether your bone marrow is making enough healthy red blood cells.
- **Blood smear.** This test shows the shape of your red blood cells. An abnormal shape is a sign of inherited hemolytic anemia; the exact shape indicates the type of inherited hemolytic anemia. For example, sphere-shaped red blood cells indicate hereditary spherocytosis.
- **Coombs' test.** This test determines whether your immune system is making antibodies to destroy your red blood cells.
- **Haptoglobin and bilirubin tests.** When red blood cells break down, they release hemoglobin into your bloodstream. Hemoglobin combines with a chemical called haptoglobin. A low level of haptoglobin in the blood indicates hemolytic anemia. Hemoglobin also breaks down into a compound called bilirubin. High levels of bilirubin may suggest hemolytic anemia.
- **Hemoglobin electrophoresis.** This test shows the different types of hemoglobin in your blood; it also can help identify the type of anemia you may have.
- **Test for paroxysmal nocturnal hemoglobinuria.** This test indicates whether red blood cells lack a particular protein.
- **Osmotic fragility.** This test shows whether your red blood cells are more fragile than normal. It also can point to the type of anemia you may have.
- **Test for G6PD deficiency.** A lack of G6PD enzymes in your red blood cells indicates that you have G6PD deficiency.

OTHER TESTS

If the results of the blood tests do not clearly show that you have hemolytic anemia, your doctor may recommend bone marrow tests. These tests show whether your bone marrow is making enough healthy blood cells.

HOW HEMOLYTIC ANEMIA IS TREATED

Treatment for hemolytic anemia depends on the type of hemolytic anemia you have and its severity. Your doctor will consider your age, medical history, and overall health when planning your treatment. You may not need treatment if your anemia is mild and is not getting worse. Severe hemolytic anemia generally needs ongoing treatment and can be fatal if not treated properly.

Treatment depends on the type and cause of the hemolytic anemia.

- During emergencies, a blood transfusion may be necessary.
- Medicines that suppress the immune system may be used when the anemia is caused by an immune system response.
- When blood cells are being destroyed at a fast pace, the body may need extra folic acid and iron supplements to replace what is being lost.
- In rare cases, surgery is needed to remove the spleen. This is because the spleen acts as a filter that removes abnormal cells from the blood.

If your hemolytic anemia is caused by medicines or another health condition, your doctor may change your treatment to control or stop the hemolytic anemia.

“I have an inherited genetic type of hemolytic anemia—G6PD deficiency. My Italian heritage was an important clue to figuring out my illness, because it is an inherited illness that is common in Sicily, where my family came from. Since being diagnosed, my whole life has changed. I follow a healthy diet, avoiding triggers like fava beans and certain medications. Staying healthy and avoiding the foods and other triggers can almost totally prevent the symptoms.”

Linda



Treatments for Acquired Hemolytic Anemia

TYPE	POSSIBLE TREATMENTS
Immune hemolytic anemia	<ul style="list-style-type: none"> • Corticosteroids and other medicines to suppress the immune system • Removal of the spleen • Plasmapheresis (a procedure to remove antibodies from the blood) • Avoidance of cold temperatures (for example, wear gloves, a hat, and a scarf; dress warmly in air conditioning; keep your car warm when driving in cold weather) • Intravenous gamma globulin, a medicine that may increase the lifespan of red blood cells and possibly reduce the number of antibodies produced
Mechanical hemolytic anemia	<ul style="list-style-type: none"> • Folic acid supplements • Blood transfusions
Paroxysmal nocturnal hemoglobinuria	<ul style="list-style-type: none"> • Iron and folic acid supplements • Eculizumab, an antibody that blocks the destruction of red blood cells in this form of anemia

Treatments for Inherited Hemolytic Anemia

TYPE	POSSIBLE TREATMENTS
Hemoglobin disorders (sickle cell disease and thalassemias)	<p>For sickle cell disease: Folic acid supplements (made from the synthetic form of folate), antibiotics to prevent infection, medicine to reduce the number of faulty red blood cells in the blood, and a medicine called hydroxyurea, which may help the body make more healthy hemoglobin and reduce the amount of faulty hemoglobin that leads to sickle cells</p> <p>For thalassemias: Blood transfusions to replace destroyed red blood cells, and blood and marrow stem cell transplants</p> <ul style="list-style-type: none"> • Folic acid supplements
Disorders of the red blood cell outer membrane (hereditary spherocytosis and hereditary elliptocytosis)	<ul style="list-style-type: none"> • Blood transfusions • Removal of the spleen (rarely) <p>For G6PD deficiency: Avoidance of substances that trigger the condition, such as fava beans, naphthalene (a substance in mothballs), and certain medicines</p>
Enzyme deficiencies	<p>For pyruvate kinase deficiency: Folic acid supplements and blood transfusions.</p>





HOW TO PREVENT ANEMIA OR KEEP YOUR ANEMIA UNDER CONTROL

Many types of anemia can be mild, short term, or even prevented. Other types may last a lifetime but are easily treated. Still other anemias are severe, life-threatening conditions that need prompt and intense treatment.

You can take action to prevent, treat, and control anemia. These actions can give you greater energy, improve your quality of life, and help you live a long time.

LEAD A HEALTHY LIFESTYLE

Make healthy food choices. Eating healthy means following a healthy eating pattern that includes a variety of nutritious foods and drinks. It also means getting the number of calories that's right for you (not eating too much or too little).

To eat healthy, try to follow these tips:

- Choose nutrient-dense foods and beverages. Eat vegetables, fruits, whole grains, fat-free or low-fat dairy products, and a variety of foods with protein, such as seafood, lean meats and poultry, eggs, beans, peas, nuts, seeds, and soy products.
- Limit certain nutrients and ingredients, such as salt, added sugars, saturated fats, and refined grains.
- Stay at a healthy weight by balancing the calories you eat and drink with the calories you burn.
- Clean, handle, cook, and chill food properly to prevent foodborne illnesses.

Help your family make healthy choices together.

Infants, young children, and teens grow rapidly. A healthy diet supports growth and development and can help prevent anemia. Keep healthy foods at home, and help your children learn how to make healthy choices when they are away from home. Also, help your older relatives enjoy a healthy, nutrient-rich diet. Anemia is common in older adults because of chronic (ongoing) diseases, lack of iron, and poor diet.

Making healthy lifestyle choices, such as adopting a nutritious, iron-rich diet, can help prevent common types of anemia. That way, you can have more energy and feel your best.

Avoid substances that can cause or trigger anemia.

For example, exposure to chemicals or toxins in the environment can cause some types of anemia. Other types of anemia are triggered by certain foods or cold temperatures. If you have one of these types of anemia, avoid these triggers if you can. If you have hemolytic anemia, reduce your chances of getting an infection by washing your hands often, avoiding people who have colds, and staying away from crowds.

WORK WITH YOUR DOCTOR OR ANEMIA HEALTHCARE TEAM

Visit your doctor if you develop signs or symptoms of anemia. If you are diagnosed with anemia, follow your doctor's advice about diet, supplements, medicines, and other treatment methods.

Visit your doctor regularly for checkups and ongoing care, and tell him or her about any new or changing symptoms.

Older children and teens who have severe anemia may have an increased risk of injury or infection. Talk with your doctor about ways to keep them as healthy as possible and discuss whether they need to avoid certain activities.

Girls and women who have heavy menstrual periods may need regular screenings and follow-up care with their doctors to prevent or control iron-deficiency anemia.

TALKING TO YOUR FAMILY AND FRIENDS

Some types of anemia—such as pernicious anemia, Fanconi anemia, or thalassemia—can be inherited. If you have been diagnosed with one of these types of anemia, talk to your family members. Suggest they visit their doctors for a checkup to see whether they might have anemia.

If you have children or teens who have anemia, talk to them about how they can take an active role in their own care by learning about their condition and making decisions with their doctor. This can help young people feel more in control and have a more positive outlook regarding their health.

A FINAL THOUGHT

You can do a lot to keep yourself and your family healthy. The tips above can help you prevent or cope with anemia and improve your overall health and well-being. Make healthy choices today for a brighter tomorrow.

“My main lifestyle change has been to commit to regular physical activity. My physical therapist gave me an exercise plan that I try to stick to every day. The key to living with a chronic illness is to not let it limit you. I can't always do something I used to do, but I still look for new ways to enjoy life. I'm grateful for the emotional support I get from my husband and family in helping me manage my condition.”

Shirah





MAKING PROGRESS AGAINST ANEMIA

THE LATEST RESEARCH

For many years, the National Heart, Lung, and Blood Institute (NHLBI) has supported research aimed at finding the causes of blood disorders and ways to prevent and treat them. Researchers have learned a lot about anemia and other blood disorders through these studies. That knowledge has led to improvements in prevention and care.

Common types of anemias are generally straightforward and easily treated. As a result, the NHLBI's clinical research on anemias is focused on specific types, including sickle cell disease and thalassemia. Research on these and other blood disorders continues to be an important priority for the NHLBI.

The success of these efforts depends on the willingness of volunteers to participate in clinical research. If you would like to help researchers gather information about your disorder and possible treatments, talk to your doctor.

CLINICAL TRIALS

To fully understand a disorder and how best to diagnose and treat it, researchers need to do clinical research with people who have the disorder. Clinical research is often conducted in clinical settings, such as hospitals or doctors' offices. Clinical trials test new ways to prevent, detect, or treat various disorders. For example, treatments—such as medicines, medical devices, surgery, or other procedures—need to be tested in people who have the disorder. A trial helps determine whether a treatment is safe and effective in humans before it is made available for public use. In a clinical trial, participants are randomly assigned to a group

that receives the new treatment being tested. Other groups may receive a different treatment or a placebo (an inactive substance resembling a drug being tested). Comparing the results from the groups gives researchers confidence that changes in the test group are due to the new treatment and not to other factors.

Other types of clinical trials are done to discover the factors, including environmental, behavioral, or genetic factors, that cause or worsen various disorders. Researchers may follow a group of people over time to learn which factors contribute to becoming sick. For example, these types of studies gave us the important information that smoking is a risk factor for both heart disease and lung cancer.

Clinical trials may be relatively brief, or they may last for years and require many visits to the study sites. These sites usually are university hospitals or research centers; however, they can include private doctors' offices and community hospitals.

If you participate in a clinical trial, the process will be explained to you in detail. You will be given a chance to ask questions, and you will be asked to provide written permission. You may not directly benefit from the results of the clinical trial in which you participate; however, the information gathered will help others and will add to scientific knowledge. Taking part in clinical trials has other benefits, as well. You will learn more about your disorder, you will have the support of a team of healthcare providers, and your health will likely be monitored closely. However, participation also can have risks, which you should discuss with your doctor. No matter what you decide, your regular medical care will not be affected.

If you are thinking about participating in a clinical trial, you may have questions about the purpose of the study, the types of tests and treatment involved, how participation will affect your daily life, and whether any costs are involved. Your doctor may be able to answer some of your questions and help you find clinical trials in which you can participate. You also can visit the following websites to find clinical trials related to your disorder and to learn about being in a study:

- ClinicalTrials.gov
- [NHLBI clinical trials page](#)

COPING AND SUPPORT

Support in managing your anemia is vital. Here's why. Going at anything alone can sometimes cause more harm than good. In short, you are more able and better enabled when you have a stable support system.

This support does not have to be limited to family or friends. Support groups and community organizations are available and will make dealing with your condition easier. Within these organizations you will find empathy, acceptance, and wisdom so you don't go at it alone.

FOR CAREGIVERS

It would be short-sighted to look at this condition from the viewpoint of just the patient. Caregivers are affected by anemia as well. Very often they take on the physical, emotional, and logistical needs of a loved one.

If you are a caregiver, here are two valuable tips:

- Make sure *you* have support so you can better support your loved one.
- Ask for help. Waiting until you're overwhelmed will only result in added stress. Look to others in your circle to pitch in so you can have time for self-care.

IN TIMES OF CRISIS

Due to your blood condition, your needs have changed. That means you should be prepared for an emergency that might affect your health. Here are a few simple but valuable things to have on hand in case traditional support may not be available:

- **Prescriptions:** Two weeks of prescription medicine
- **Medical supplies:** Two weeks of food, water, and general medications
- **Documents:** Your electronic medical records, along with your insurance card and emergency contact card





DEFINITIONS

Arrhythmia (a-rhyth-mi-a): A problem with the rate or rhythm of the heartbeat. During an arrhythmia, the heart can beat too fast, too slowly, or with an irregular rhythm.

Blood donation (bluhd do-na-shen): A safe and simple procedure that involves a donor giving one of the following blood products: whole blood, red blood cells, plasma, or platelets.

Blood transfusion (bluhd trans-fyoo-zuhhn): A common, safe medical procedure in which healthy blood is given to you through an intravenous (IV) line that has been inserted in one of your blood vessels.

Blood type (bluhd tipe): The classification of human blood based on certain markers found on red blood cells. The four main blood types are A, B, O, and AB.

Bone marrow tests (bohn mar-oh tests): Tests that check whether your bone marrow is healthy and making normal amounts of blood cells.

Chronic (KRAH-nik): Describes a condition, disease, sign, or symptom that lasts persistently, recurs frequently, or worsens progressively over a long time.

Erythropoiesis stimulating agent (ESA) (eh-RITH-roh-poy-EE-sis-STIM-yoo-LAY-ting AY-jent): A substance that stimulates the bone marrow to make more red blood cells. ESAs are used to treat anemia caused by chronic kidney failure, some anticancer drugs, and certain treatments for HIV. They may also be used to lower the number of blood transfusions needed during and after certain major surgeries.

Gastrointestinal tract (GAS-troh-in-TES-tih-nul trakt): The stomach and intestines. The gastrointestinal tract is part of the digestive system, which also includes the salivary glands, mouth, esophagus, liver, pancreas, gallbladder, and rectum.

Genetic (jeh-NEH-tik): Having to do with genes. Most genes are sequences of DNA that contain information for making specific proteins or molecules of RNA that perform important functions in a cell. The information in genes is passed from parents to children.

Heart failure (hAHRt fAY-lyuhr): A condition that develops when your heart doesn't pump enough blood for your body's needs. This can happen if your heart can't fill up with enough blood. It can also happen when your heart is too weak to pump properly.

Heart murmur (mUHR-muhr): An unusual sound heard between heartbeats.

Hemoglobin (HEE-moh-GLOH-bin): A protein in red blood cells that carries oxygen throughout the body.

Hemolysis (hee-MAH-lih-sis): The breakdown of red blood cells. Red blood cells normally live for up to 120 days. After that, they naturally break down and are most often removed from the blood by the spleen.

Hormone (HOR-moan): A substance made in glands throughout the body. Hormones are released into the blood to travel throughout the body to control other body functions.

Inflammation (IN-fluh-MAY-shun): The body's response to infection or injury. It can affect many areas of the body and is a cause of many major diseases, including cancer, ischemic heart disease, and autoimmune diseases.

Inherited (in-HAYR-ih-ted): The passing of genetic information from a parent to a child through genes.

Mutation (myoo-TAY-shun): Any change in a nucleic acid sequence, such as DNA or RNA.

Obesity (oh-bee-si-tee): A serious medical condition that can cause complications such as metabolic syndrome, high blood pressure, atherosclerosis, heart disease, diabetes, high cholesterol, cancers and sleep disorders.

Pica (PI-ka): A pattern of unusual cravings for nonfood items or food with no nutritional value, such as ice, dirt, paint, or starch.

Red blood cell (red bluhd sel): A type of blood cell that carries oxygen to all parts of the body; also known as an erythrocyte.





FOR MORE INFORMATION

For more information on anemia, visit the NHLBI website at www.nhlbi.nih.gov/health-topics/anemia or contact the NHLBI Center for Health Information:

P.O. Box 30105
Bethesda, MD 20824-0105
1-877-NHLBI4U (1-877-645-2448)
TRS: 7-1-1
Email: nhlbiinfo@nhlbi.nih.gov



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