Aplastic Anemia

Aplastic anemia also known as **Bone marrow failure**, **Aregenerative anemia**, **Erythroblastophthisis**, **Hypoplastic anemia**, **Refractory anemia** or **Toxic paralytic anemia** is a rare and serious blood disorder in which bone marrow stops making enough new blood cells. Patients with aplastic anemia have a deficiency of red blood cells, white blood cells and platelets.

Bone marrow is the spongy material inside bones that makes new blood cells called stem cells. Stem cells normally develop into three main types of blood cells: red blood cells, white blood cells, and platelets. Each type of blood cell has its own functions in the body.
It is normal for blood cells to die. The lifespan of red blood cells is about 120 days. White blood cells live less than a day. Platelets live about six days. As a result, bone marrow must constantly make new blood cells.
The term anemia is most often used to describe a condition in which a person's number of red blood cells is too low or their red blood cells do not carry enough hemoglobin. However, in aplastic anemia, normal production of all blood cells, red cells, white cells, and platelets slows or stops. This is because the stem cells have been damaged. The cause of this damage is often unknown.

Types

- Acquired aplastic anemia means a person develops the condition during his or her lifetime. Acquired aplastic anemia is the **most common type**, and it is sometimes a temporary condition. It can be triggered by exposure to toxins, chemotherapy drugs, ionizing radiation, or viral infections. The specific cause of acquired aplastic anemia is often not known.
- Hereditary aplastic anemia means a person is born with the condition. Hereditary aplastic anemia is rare and usually occurs in association with other abnormalities. Fanconi anemia is one kind of hereditary aplastic anemia.

Signs and Symptoms

Most of the signs and symptoms of aplastic anemia are caused by low numbers of each of the three main types of blood cells: red blood cells, white blood cells, and platelets. Other signs and symptoms, though, are not linked to a shortage of any particular blood cell type.

Low red blood cell count

The most common symptom of a low red blood cell count is **fatigue**. This is caused by lack of enough hemoglobin, an iron-rich protein contained in red blood cells that carries oxygen to the body. A lack of enough oxygen in the blood can cause people to feel short of breath and dizzy, especially when standing up. Since the heart must work harder to circulate the reduced amount of oxygen, symptoms also can include a rapid or irregular heartbeat or an extra or unusual sound heard during the heartbeat (heart murmur). The hemoglobin in red blood cells gives blood its red color. Lack of hemoglobin due to a low red blood cell count can lead to pale skin, gums, and nail beds.

Low white blood cell count

White blood cells help fight infections. Symptoms of a low white blood cell count are **fever, frequent infections** which can be severe, and flu-like illnesses that linger.

Low platelet count

Too few platelets may cause **easy bleeding and bruising**. The bleeding may be hard to stop. Common types of bleeding related to low platelets include nosebleeds, bleeding gums, pinpoint red bleeding spots on the skin, and blood in the stool. Women also may have heavy menstrual bleeding.

Other Symptoms

Aplastic anemia can cause other signs and symptoms as well, such as headache, tender sinuses, and white patches in the mouth (thrush). Other signs and symptoms are nausea and rash. A person with aplastic anemia also may have an enlarged spleen or liver.

Causes

Aplastic anemia is caused by **damage to stem cells in the bone marrow**. Stem cells normally develop into three types of blood cells: red blood cells, white blood cells, and platelets. When stem cells are damaged, they do not grow into healthy blood cells.

Causes of Acquired Aplastic Anemia

Many cases of acquired aplastic anemia are **idiopathic**, meaning that the cause is unknown. **Secondary** causes of acquired aplastic anemia often involve outside agents and diseases. Outside agents include toxins such as pesticides, arsenic, and benzene; radiation and chemotherapy used to treat cancer; and medicines such as chloramphenicol, an antibiotic now rarely used in the United States. Infectious diseases also can cause aplastic anemia. Some of these diseases are hepatitis, Epstein-Barr virus, cytomegalovirus, parvovirus B19, and HIV/AIDS. Autoimmune diseases, such as lupus and rheumatoid arthritis also can cause this condition. It is thought that there are two major factors in the development of aplastic anemia: [1]

- Disruption of the creation of new cells in the bone marrow, and
- Destruction of the diseased cell-producing marrow by the body's immune system as it tries to overcome the disease.

Causes of Hereditary Aplastic Anemia

Some inherited genetic disorders can lead to aplastic anemia. These include Fanconi anemia, Shwachman-Diamond syndrome, and dyskeratosis congenita.

Diagnosis

Aplastic anemia is diagnosed using a medical and family history, a physical exam, and tests to discover the type and cause of anemia. A doctor can use these methods to find out how severe the anemia is and to decide the appropriate treatment.

Specialists involved

A person with suspected aplastic anemia may be referred to a hematologist (an expert in treating blood conditions).

Medical and family history

A medical history will involve detailed questions about any symptoms. A history of anemia, an illness or condition that could cause anemia, or any exposure to drugs, chemicals, or radiation will also be sought. A family history of anemia is also important. Finally, any medications should be listed, as they may be a cause of aplastic anemia.

Physical exam

The doctor will do a physical exam to see how severe the anemia is and to check for its possible causes. This exam may include:

- Checking for pale or yellowish skin
- Listening to the heart for rapid or irregular heartbeats
- Listening to the lungs for rapid or uneven breathing
- Feeling the abdomen to check the size of the liver and spleen and checking for swelling in the legs
- Checking for signs of bleeding

Diagnostic tests and procedures

Several tests of the blood and bone marrow may be used to diagnose aplastic anemia. The reasons for testing are to:

- Confirm a diagnosis of aplastic anemia and look for its cause
- Rule out blood cancers that can cause bone marrow failure
- Determine the severity of the aplastic anemia
- Check for the presence of paroxysmal nocturnal hemoglobinuria

Complete blood count

Usually, the first test used to diagnose anemia is a complete blood count (CBC). The CBC tells a number of things about a person's blood, including:

- The hemoglobin level. Hemoglobin is the iron-rich protein in red blood cells that carries oxygen through the body. The normal range of hemoglobin levels for the general population is 11-15 g/dL. A low hemoglobin level means a person has anemia.
- The hematocrit level. The hematocrit level measures how much of the blood is made up of red blood cells. The normal range for hematocrit levels for the general population is 32% to 43%. A low hematocrit level is another sign of anemia.

The normal range of these levels may be lower in certain racial and ethnic populations. The doctor can explain individual test results. The CBC also checks:

- The number of red blood cells. Too few red blood cells means a person has anemia. A low number of red blood cells is usually seen with either a low hemoglobin or a low hematocrit level, or both.
- The number of white blood cells. White blood cells are involved in fighting infection.
- The number of platelets in the blood. Platelets are small cell fragments that are involved in blood clotting.

- Red blood cell size. The mean cell volume measures the average size (volume) of red blood cells.

Reticulocyte count

This test measures the number of **new red blood cells** in the blood. It helps doctors find out whether bone marrow is producing red blood cells at the proper rate. A lower than average level can mean that the bone marrow is not making enough red blood cells. The reticulocyte level is low in people with aplastic anemia.

Bone marrow tests

This test looks at the bone marrow to see if it is healthy and if it is making enough blood cells. A small amount of bone marrow may be removed and examined. Removing a small bit of liquid bone marrow is called a bone marrow aspiration. Removing bone marrow tissue is called a bone marrow biopsy.
A bone marrow aspiration may be done to find what is causing the low production of blood cells. Since blood cells are formed inside the bones, doctors use a needle to remove a small amount of liquid bone marrow. The sample is then examined under a microscope to check for abnormal cells. A bone marrow biopsy is usually done at the same time, especially if an aspiration was not productive. A small number of bone marrow cells with a small piece of bone is removed using a needle. This test checks the number and type of cells in the bone marrow. In aplastic anemia, the bone marrow has a lower than normal number of cells.

Other Tests

Additional tests may be used to help diagnose aplastic anemia, including:

- X ray, CT scan, or an ultrasound of the abdomen to look for an enlarged spleen or lymph nodes, which could indicate blood cancer. These tests also may be used to examine the kidneys, arms, and hands, which are sometimes abnormal in young people with Fanconi anemia.
- Chest x-ray to provide a picture of the heart and lungs and rule out infection
- Liver tests and viral studies to check for hepatitis and viruses
- Tests that check vitamin B12 and folate levels to rule out vitamin deficiency
- Blood tests for paroxysmal nocturnal hemoglobinuria and to check the immune system for antibodies

Treatment

Aplastic anemia may be classified as mild, moderate, severe or very severe. Treatment varies accordingly.

- People with mild or moderate aplastic anemia have low blood counts that the doctor will check often. If the blood counts do not get worse, treatment may not be needed.
- People with severe aplastic anemia have very low blood counts. The condition can become life-threatening if it is not treated.
- People with very severe aplastic anemia have extremely low blood counts. This condition is life-threatening. It needs emergency hospital treatment.

Although aplastic anemia is not cancer, the treatments for it are similar to those used for some types of cancer. Treatments for aplastic anemia include:

- Blood transfusion
- Bone marrow transplant
- Several medicines used to suppress the immune system, stimulate the bone marrow, and prevent and treat infections

In rare cases, no treatment is needed. In general, treatments for aplastic anemia can limit and prevent complications, relieve symptoms, and improve quality of life. For some, a cure may be possible. Bone marrow transplants can be a cure for those people who are eligible for a transplant. Removing a known cause of aplastic anemia (such as exposure to a toxic chemical) also can cure the disorder. Other treatments can restore blood cell counts to levels high enough so that a person can live a normal life.
People with mild or moderate aplastic anemia may not need treatment as long as the condition does not get worse. People with severe aplastic anemia need immediate medical treatment to prevent complications from the very low levels of blood cells in their bodies. People with very severe aplastic anemia need emergency medical care and hospitalization or the anemia can be fatal in a short time.

Blood transfusions

Blood transfusions are used to keep blood counts high enough in people with aplastic anemia. Healthy blood is taken from matched donors and then given to the person with aplastic anemia through an injection in a vein. Blood transfusions help relieve symptoms, but are not an effective long-term treatment.
Red blood cell transfusions help relieve lack of energy, tiredness, and shortness of breath. However, if red blood cells are given often, the immune system in the body can learn to recognize these new cells, develop antibodies against them, and destroy the newly transfused cells. Also, if red blood cells are given often, the body can build up too much iron. Excess iron from transfusions can damage the heart, liver, and other organs. If this happens, treatment may be needed to remove excess iron from the body.
White blood cells are not routinely transfused because they live in the bloodstream for less than a day. However, they may be used for severe infections that are not being helped by antibiotics.

Platelet transfusions reduce the risk of fatal bleeding. Several transfusions a month are often needed because platelets live only a few days. However, in time, the immune system will learn to recognize and destroy newly transfused platelets by making antibodies, just as it does with red blood cells.

Bone marrow transplantation

A bone marrow transplant replaces damaged stem cells in bone marrow with healthy stem cells from a donor's bone marrow. It is the best treatment choice for eligible people because it usually cures aplastic anemia.
A bone marrow transplant works best in children and young adults with severe aplastic anemia who are in good health and who have **matched donors**. Older people are less able to tolerate the treatments needed to prepare the body for the transplant. They also are more likely to have complications after the transplant. There are age limits for who can receive a bone marrow transplant, but they vary among hospitals.

Finding a donor

For best results, the donor's bone marrow must be a close match with the bone marrow of the person with aplastic anemia. A matched donor is found by means of a blood test that looks at proteins on the surface of body cells. These proteins are called human leukocyte antigens (HLA). The donor and the person with aplastic anemia are both tested. The HLA antigens on their cells are compared. Bone marrow transplants work best if the donated marrow is an exact match and comes from a family member, such as a brother or sister. A person receiving bone marrow that is an exact match usually has fewer complications. Only about 20% to 35% percent of people with severe aplastic anemia have an HLA-matched family member to donate bone marrow. If no matching family member is found, the search for bone marrow widens. Millions of volunteer donors are registered with the National Marrow Donor Program. Doctors will look for:

- Donors who are HLA matches but are not family members
- Family members who are not exact HLA matches
- Unrelated donors who are not exact HLA matches
- Umbilical cord blood that is an HLA match

A person who is going to have a bone marrow transplant should not receive blood transfusions from close family members before the transplant. When a person receives blood transfusions, their bodies can develop antibodies against the donated blood. If a person develops antibodies against the blood of a close family member, the person would not be able to receive a bone marrow transplant from that family member.

Receiving the transplant

Bone marrow transplants are done in special units in hospitals to try to protect the person with aplastic anemia from any infections. Before the transplant, the person receives high doses of chemotherapy, radiation therapy, or both. These treatments destroy the abnormal bone marrow that is not producing blood cells.
A sample of bone marrow is taken from the donor and is given to the recipient through a vein. The donated bone marrow stem cells travel to the recipient's bone marrow and start to make healthy blood cells. If the transplant is successful, the new stem cells multiply and begin making new, healthy blood cells within 3 to 4 weeks.

Possible Complications

After a bone marrow transplant, the recipient is in the hospital for weeks or months. During this time, he or she is isolated and closely watched for infections and other complications. Complications are most likely to occur in the first 100 days after a transplant. Complications include rejection of the graft and what is called graft-versus-host disease (GVHD).
Graft rejection. Sometimes, the recipient's immune system destroys the new bone marrow cells. This occurs in five to 10 percent of recipients, and it is more likely to happen in people who have had several bone marrow transplants.
GVHD. GVHD happens when the new immune system cells, created by the donated bone marrow, attack the recipient's body. Signs and symptoms are skin inflammation, diarrhea, and liver disease. GVHD can occur soon after transplant, or it can develop slowly and can last for months or years. GVHD most often happens in older people and those who receive unmatched transplants.
To help prevent GVHD, donor marrow is sometimes treated or people may be given medicines that suppress the immune system after the transplant. Those who develop mild but acute GVHD are treated with medicines such as steroids.

Medicines to stimulate bone marrow

Man made versions of substances that occur naturally in the body are used to stimulate the bone marrow to produce more blood cells. Bone marrow that can produce more blood cells can help a person with aplastic anemia avoid blood transfusions. An increased number of white cells can help protect a person from infection. Examples of bone marrow stimulation medicines used to treat aplastic anemia are: Erythropoietin - a hormone produced by the kidney that causes the production of red blood cells. Colony-stimulating factors are proteins that bind to stem cells and cause them to proliferate (increase in numbers) and to become specific types of cells (for example, red blood cells, white blood cells, or platelets).

Medicines to suppress the immune system

Since research suggests that aplastic anemia may occur because the body's immune system attacks its own cells by mistake,[2] certain medicines may be used to suppress the body's immune system. They allow the bone marrow to start making blood cells again, and they help avoid the need for blood transfusions. Medicines that suppress the immune system do not cure aplastic anemia, but they can relieve its symptoms and reduce its complications. These medicines are often used for people who are not good candidates for a bone marrow transplant or who are waiting for a bone marrow transplant. There are three medicines often given together that will suppress the body's immune system:

- Antithymocyte globulin (ATG)
- Cyclosporine
- Methylprednisolone (a corticosteroid)

If this treatment is successful, it may take a few months to notice the effects of these medicines. Most often, as blood counts rise, symptoms lessen. Blood counts in people who respond well to these drugs don't usually reach normal levels, but they are often high enough to allow people to take part in their normal activities. People with aplastic anemia may need to take the medicines indefinitely to keep their blood counts high enough to resume normal daily life.
Medicines that suppress the immune system can have side effects. They also may increase the risk of developing leukemia or myelodysplasia (MDS). Leukemia is a type of cancer in which the number of white blood cells increases. MDS is a condition in which the bone marrow produces too many defective blood cells.

Antibiotics

Antibiotics and antivirals are given to people with aplastic anemia to prevent and treat infections.

Living With Aplastic Anemia

Many people with aplastic anemia can be treated successfully and some can be cured. Most people are able to resume their normal activities after treatment. If being treated for aplastic anemia, it may take a long time to get a good response from the treatment. It may necessary to repeat treatments, or try several treatments before finding one that works.
Treatment for aplastic anemia can result in side effects or complications. A doctor can talk about how to cope with symptoms of aplastic anemia, side effects of treatment, and complications from treatment.
Lifelong follow-up is needed to make sure the disorder doesn't return, as well as to check for possible complications.

Recommended physical activity

It may be necessary to avoid activities that cause chest pain or shortness of breath, as well as those that could result in injuries and bleeding, such as contact sports.

Protection from infection

The doctor also might discuss ways to reduce the chance of getting an infection. These ways include staying away from people who are ill, avoiding crowds, and avoiding certain kinds of foods that could be a source of bacteria (for example, uncooked food). It is important to wash hands thoroughly several times throughout the day and to care of the teeth and gums to reduce the risk of infection in the mouth or throat. It is also important to recognize the symptoms of an infection.

Chances of Developing Aplastic Anemia

Aplastic anemia is rare. In the United States, about 500 to 1,000 people develop this type of anemia each year. It is two to three times more common in **Asian** countries.
People of all ages can develop aplastic anemia. Men and women are equally likely to have it. It is most common in adolescents and young adults as well as the elderly.
Aplastic anemia is more likely to develop in people who:

- Have been exposed to toxins, certain drugs, or radiation
- Are infected with viruses, such as hepatitis and HIV
- Have an inherited disorder, such as Fanconi anemia, or an autoimmune disease

Related Problems

Paroxysmal nocturnal hemoglobinuria

About one-third of people with aplastic anemia have a condition called paroxysmal nocturnal hemoglobinuria (PNH). This is a disorder of the red blood cells. Some people have PNH first and then develop aplastic anemia, while others have aplastic anemia first and then develop PNH later. Most people with PNH don't have any signs or symptoms. If they do occur, they may include:

- A low number of red blood cells, which can lead to shortness of breath
- Swelling or pain in the abdomen or swelling in the legs caused by blood clots

- Blood in the urine
- Headache
- Jaundice (yellowish color of the eyes or skin)

History

Aplastic anemia was discovered in 1888 by "the father of immunology and pioneer of chemotherapy", Paul Ehrlich. (1854–1915) [3] Dr. Ehrlich described the condition after performing an autopsy on a young pregnant woman who died of bone marrow failure. He was awarded the Nobel Prize in 1908.

References

1. Nissen C. The pathophysiology of aplastic anemia. Semin Hematol. 1991;28(4):313-8.
2. Ascensao J, Pahwa R, Kagan W, Hansen J, Moore M, Good R. Aplastic anaemia: Evidence for an immunological mechanism. Lancet. 1976;1(7961):669-71.
3. Jay V. Paul Ehrlich. Arch Path Lab Med. 2001; 125(6): 725.

External links

-