Aplastic Anemia

What is aplastic anemia?

Aplastic anemia is a disorder in which the bone marrow fails to make enough blood cells. The bone marrow is the soft, inner part of bones where the 3 types of blood cells are made:

- **Red blood cells**, which carry oxygen to the tissues from the lungs
- **White blood cells**, which fight infection
- **Platelets**, which seal damaged blood vessels to prevent bleeding

These cells are made by blood-forming *stem cells* in the bone marrow. In aplastic anemia, the stem cells are damaged and there are very few of them. As a result, too few blood cells are produced. In most cases of aplastic anemia, all 3 types of blood cells are low (which is called *pancytopenia*). Rarely, just one of the cell lines, such as red cells, white cells, or platelets, is abnormal.

Aplastic anemia is not a type of cancer but may be associated with certain cancers (especially those affecting the bone marrow, such as leukemia) or cancer treatments. A small number of patients with aplastic anemia may develop leukemia.

Aplastic anemia can be inherited or acquired. Acquired aplastic anemia is much more common than the inherited type.

Inherited aplastic anemia

Aplastic anemia is considered inherited when it is caused by gene mutations (abnormal copies of genes) that have been passed on from the parents to their child. Inherited aplastic anemia is more common in children and young adults.

Fanconi anemia

The most common cause of inherited aplastic anemia is called *Fanconi anemia* (FA). There are many different genes that can cause Fanconi anemia. They are named FANC plus another letter (or a letter and a number), such as *FANCA*, *FANCB*, *FANCC*, etc. In

order to get FA, a child must inherit 2 abnormal copies of one of these genes -- one from each parent. Someone with only one abnormal copy will not develop the disease and is called a *carrier*.

The genetic material (DNA) in our cells is packaged into chromosomes. In FA, the chromosomes are easily damaged by things in the environment like toxins or radiation. This can lead to aplastic anemia, leukemia, and other cancers. Cancers of the mouth and throat, esophagus, and the vulva (female genital area) are seen at a higher rate and at a younger age in those with FA (as compared with people who don't have FA).

In many cases, FA is suspected when a child is born because he or she is missing a thumb or a bone in the arm called the radius. A child with FA anemia also may not grow well (called *growth retardation*) or have a small head (called *microcephaly*). Dark spots on the skin (called *café au lait spots*) can be another sign of FA. In some cases though, the child will look completely normal. People with FA may have low blood counts from an early age. The low blood counts may be treated with medications called *androgens* at first, but only a stem cell transplant can actually cure aplastic anemia in someone with FA.

Some people with FA do not develop low blood counts (or aplastic anemia), but may first be diagnosed with FA when they get cancer.

In order to diagnose FA anemia, a *chromosome breakage test* will be ordered. For this test, a small sample of blood is taken from the patient. Then some of the cells in the blood (the lymphocytes) are exposed to a certain chemical to see if it causes the chromosomes in the cells to break and rearrange. Chromosomes in normal cells aren't damaged easily, but the chromosomes in FA cells will be damaged.

Dyskeratosis congenita

Another inherited cause of aplastic anemia is called *dyskeratosis congenita* (DC). Defects in some of the genes that help protect the chromosomes cause this disease. The chromosomes in our cells are fitted with caps at each end called *telomeres*. These caps help protect the ends of the chromosomes from being damaged. Telomerase is the protein that maintains the telomeres. Two different genes, called *TERC* and *TERT*, are needed to make telomerase. An abnormal copy of either one of these genes can cause DC. Another gene, *DKC1*, makes a protein called dyskerin that is needed for telomerase to work. Abnormalities in this gene also cause DC. Signs of this disorder include abnormal skin pigmentation, abnormal nails, and white patches in the mouth (called leukoplakia). People with this problem have a high risk of developing aplastic anemia and certain cancers, such as cancer of the mouth and throat and cancer of the anus. Some people are only diagnosed with DC when they come in with aplastic anemia and are found to have abnormal telomerase genes. These people may not have any of the other signs or symptoms of DC.

Other causes of inherited aplastic anemia

Another cause of inherited aplastic anemia is called the *Diamond-Blackfan* syndrome. In this disease, red blood cells are low, but the number of other blood cells is normal.

Patients with Diamond-Blackfan syndrome also have an increased risk of certain cancers, including myelodysplastic syndrome, leukemia, colon cancer, and bone cancer.

A fourth disorder is the *Shwachman-Diamond* syndrome, which is caused by abnormal copies of a gene called *SDS*. Here, the major problem is poor production of white blood cells, although the other cell lines can also be abnormal. In both of these, patients will often have other problems such as short stature and other bone abnormalities.

Acquired aplastic anemia

Acquired aplastic anemia usually occurs in adults, but children may also be affected. Most have no gene abnormalities. Scientists have found that some of the people who they thought had a form of acquired aplastic anemia actually have an abnormality in one of the genes responsible for inherited aplastic anemia. The aplastic anemia in these people is not really acquired -- it is inherited. Some cases of aplastic anemia seem to be triggered by a drug, exposure to a toxic chemical, or infection with some types of viruses. In most cases of aplastic anemia, however, the cause is never found.

Paroxysmal nocturnal hemoglobinuria

Paroxysmal nocturnal hemoglobinuria (PNH) is a disease in which some of the stem cells in the bone marrow become damaged and make abnormal red blood cells. The red blood cells in PNH are missing certain proteins that normally help protect the cells. Without these proteins, the red blood cells are killed by the immune system (this is called *hemolysis*). PNH is caused when the gene called *PIG-A* is damaged (mutated) in some of the stem cells in the bone marrow. People with PNH have anemia (low red blood cells) along with fatigue, stomach pain, and blood clots. Sometimes the hemoglobin from the destroyed red blood cells will cause the urine to become very dark (like the color of tea). PNH seems to be linked to aplastic anemia. Some patients have small numbers of PNH cells when they are diagnosed with aplastic anemia. Also, some survivors of aplastic anemia will go on to develop PNH. PNH can be treated with stem cell transplant or with a drug called eculizumab that blocks the hemolysis.

What are the key statistics about aplastic anemia?

Aplastic anemia is a rare disease, occurring in only 1 to 2 people per year for every million people in the United States. That means somewhere between 300 and 600 new cases will develop each year. It affects people of all ages and all races. It is more common in developing countries, perhaps because there is more exposure to toxic chemicals

What are the risk factors for aplastic anemia?

A risk factor is anything that changes your chance of getting a disease. For example, certain cancers have different risk factors. Exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for many cancers. But risk factors don't tell us everything. Having a risk factor, or even several, does not mean that you will get the disease. And not having a risk factor doesn't mean that you won't get the disease.

We know that certain aplastic anemias are inherited. Having Fanconi anemia or dyskeratosis congenita increases the risk of developing aplastic anemia.

Exposure to certain drugs and chemicals may increase the risk of acquired aplastic anemia. It's important to realize that these medications are safe for most of the people who take them. In some cases, however, people develop aplastic anemia after receiving one of these drugs. Likewise, some viruses are linked to acquired aplastic anemia, but aplastic anemia develops only in a very small percentage of people with these infections.

Medicines

Some of the medicines linked to aplastic anemia include:

- Nonsteroidal anti-inflammatory drugs (NSAIDs) -- medicines used to treat pain and inflammation. Examples include indomethacin (Indocin®), piroxicam (Feldene®), and diclofenac (Voltaren®)
- Amphetamines, including MDMA (Ectasy)
- Antibiotics, including sulfonamides ("sulfa drugs") and forms of penicillin
- Anti-thyroid drugs, such as propylthiouracil and methimazole (Tapazole®)
- Carbonic anhydrase inhibitors, including acetazolamide and methazolamide (these are used to treat glaucoma)
- Diabetes medications, including tolbutamide, carbutamide, and chlorpropamide
- Diuretics (water pills), such as furosemide (Lasix®) and thiazides
- Drugs used against malaria, including quinacrine and chloroquine
- Phenothiazines (Thorazine®, Compazine®) -- medicines used for nausea and certain psychiatric problems
- Allopurinol (Zyloprim®) -- used for treating gout
- Ticlopidine -- used to prevent strokes and heart attacks

- Anti-seizure drugs like carbemazepine (Tegretol®), phenytoin (Dilantin®), and valproic acid
- Chloramphenicol, an antibiotic (no longer available in the United States)
- Mesalazine which is used to treat ulcerative colitis and Crohns disease

This is only a partial list of the drugs most often associated with aplastic anemia. Other drugs may also cause this disease. The best way to avoid aplastic anemia from drugs is to take medicines only if they are necessary.

Chemicals

Exposure to chemicals such as solvents and pesticides at home or in the workplace is also a risk factor. These include:

- Benzene, which is found in gasoline, automobile exhaust fumes, cigarette smoke, emissions from coke ovens and other industrial processes, and waste water from certain industries, is the most common offender.
- Industrial pesticides, like organophosphates and carbamates

Other risk factors

Other conditions have been linked to aplastic anemia, such as:

- Hepatitis
- Viruses such as Epstein-Barr virus, cytomegalovirus (CMV), parvovirus B19, and HIV.
- Pregnancy
- Auto-immune diseases like lupus (systemic lupus erythematosus) and rheumatoid arthritis
- Severe radiation poisoning (as seen after an atomic bomb explosion)

Do we know what causes aplastic anemia?

Most cases of acquired aplastic anemia have no known cause. In rare cases, the cause is exposure to certain chemicals such as benzene. Although many chemotherapy drugs and radiation treatment can damage the bone marrow, they don’t usually cause aplastic anemia. When a cause can be found, it is most often a drug or a viral infection. Environmental pollutants are another possible cause.

Doctors have tried to figure out how medicines, chemicals, and viruses can cause this disease. The most commonly accepted explanation is that these agents trigger an

abnormal immune reaction in the body of some people. In this reaction, a type of immune cell called the T-cell (or T-lymphocyte) starts making too much of certain substances called cytokines. These cytokines are toxic to bone marrow cells and can cause them to die. Knowing that the anemia is caused by an abnormal immune reaction explains why the modern treatment of this disease with drugs that suppress the immune system has been very successful (see the section “How is aplastic anemia treated?”).

How is aplastic anemia diagnosed?

Signs and symptoms of aplastic anemia

If you have aplastic anemia, you may have some of the following problems:

- Feeling very tired (fatigued) and short of breath, which is caused by *anemia* (too few red blood cells). People with anemia also tend to be pale.
- Problems with infections that keep coming back or are severe (even life-threatening). This is caused by not having enough infection-fighting white blood cells (called *neutropenia/leukopenia*)
- Abnormal bruising or bleeding because of a shortage of platelets (*thrombocytopenia*)

Some people may not have any symptoms, but results of a routine blood test may suggest a diagnosis of aplastic anemia. There are other conditions in which blood formation may be abnormal. Your doctor will consider all of these when determining your diagnosis.

Tests to diagnose aplastic anemia

Two main tests are used to diagnose aplastic anemia.

- **Complete blood count** (commonly called a CBC). In aplastic anemia this test will show that the red cell count, white cell count, and platelet count are low.
- **Bone marrow biopsy**. This test looks at the bone marrow, which contains the blood-forming cells.

Complete blood count

The complete blood count (CBC) is a test that measures the different cells in the blood, such as the red blood cells, the white blood cells, and the platelets. This test is done on a sample of blood, usually taken from a vein in your arm.

If this test shows that your blood counts are low, other tests may be done to look for the cause. Often the levels of vitamins (like vitamin B12 and folate) and iron will be checked to be sure that low levels aren’t causing the low blood counts. Poor kidney function can sometimes cause anemia, so blood chemistry tests are often checked as well.

If these tests do not find an underlying cause of the low blood counts, you will need to have a bone marrow biopsy.

You can learn more about blood tests that are commonly used in our document *Understanding Your Lab Test Results*.

Bone marrow biopsy

A bone marrow biopsy has 2 parts: the aspiration and the biopsy. This procedure is usually done while you are lying on your stomach. A part of the pelvic bone (located about 2 inches to the side of the spine) and the skin above it are numbed with local anesthetic. A tiny cut (about 1/8 inch) may be made in the skin to make it easier to insert the needle. Then, for the aspiration, a large needle is placed through the incision into the bone. A syringe is used to remove a small amount of liquid bone marrow (about 1 teaspoon). Even with the numbing medicine, this often causes a brief, sharp pain.

For the biopsy, the needle is repositioned and used to remove a small cylinder-shaped piece of bone and marrow (about 1/16 inch in diameter and 1/3 inch long). Both samples usually are taken during the same procedure from the same place in the back of the pelvic (hip) bone. In spite of local anesthesia, this procedure may still be uncomfortable.

A pathologist, a doctor specializing in diagnosing disease by lab tests, examines the bone marrow under a microscope. A hematologist (internist who specializes in blood diseases) or a hematopathologist (a pathologist who specializes in blood diseases) might also look at the bone marrow sample. Normally, the bone marrow contains many cells that produce the different types of blood cells. Finding an “empty” bone marrow -- that is, one that lacks normal blood-producing cells -- confirms the diagnosis of aplastic anemia. Leukemia or other kinds of cancers can also cause low blood counts, but in that case the bone marrow would be filled with leukemia cells or other cancer cells.

How is aplastic anemia treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society’s Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don’t hesitate to ask him or her questions about your treatment options.

Treatment for aplastic anemia can be divided into 2 groups: primary and supportive. Primary treatment, such as stem cell transplant or immunosuppressive therapy, is aimed at treating or curing the disease.

Supportive treatment is aimed at helping the symptoms of aplastic anemia without actually treating the underlying cause. Treating anemia with transfusions is a type of supportive treatment.

Stem cell transplant

Allogeneic stem cell transplant is considered the best treatment for younger people with aplastic anemia. In this type of transplant, you receive stem cells (from the bone marrow or blood) from another person (donor). This type of transplant works best in children and young adults. As people get older, it's harder for them to tolerate this procedure. For people older than 30 or 40, many doctors prefer using immune therapy as the first treatment. In order for transplant to be an option, you need to have a donor who is matched to you. Someone who is closely related to you, like a brother or sister, is generally the best choice. In aplastic anemia, this stem cell transplant is successful up to 80% to 90% of the time if cells from a matched related donor are used.

Matching is determined by a type of test called HLA typing, which is done in the laboratory. If there is no match from a brother or sister, sometimes an unrelated donor will match. A transplant from a matched-unrelated donor is riskier than using a sibling match. Another option is to use stem cells from the umbilical cord of a newborn baby. A nationwide registry of potential stem cell donors and stored umbilical cord blood has been developed (www.marrow.org). Many doctors recommend using a non-related donor only if immune treatments described below don't work.

For a stem cell transplant, you will first receive chemotherapy (chemo). The chemo drugs used most often include cyclophosphamide (Cytoxan®) and fludarabine (Fludara®). A drug to suppress your immune system, like anti-thymocyte globulin (ATG) or alemtuzumab (Campath®), is also given. A newer drug, daclizumab (Zenapax®), may also be used. This immune treatment is important to keep your immune system from killing the new bone marrow (like it killed your original bone marrow). Immune treatment is also important to prevent the new bone marrow from attacking your body (this is called *graft-versus-host disease* and is discussed later in this section). You may also get a low dose of radiation therapy to your whole body. People with inherited forms of aplastic anemia are very sensitive to chemotherapy and radiation, and so often receive lower doses.

Soon after the radiation and/or chemotherapy, you will receive a transfusion with blood-forming stem cells from a donor. The stem cells can be obtained from the donor by removing bone marrow in the operating room while he or she is under general anesthesia. Sometimes a procedure called *apheresis* is used to remove stem cells from the bloodstream. Apheresis uses a machine that is hooked up to a large vein (through a catheter) and removes stem cells from the blood (returning the other cells). No matter which way they are collected, the stem cells are infused through your vein into the blood and then travel to the bone marrow, where they will grow.

Stem cell transplantation is a major procedure with many risks and side effects. Some people may die during this procedure. The most serious side effects often occur during the first few weeks after the transplant. But with advances in this treatment, death from these early side effects is less common. The chance of severe side effects increases with the age of the patient.

In the first few weeks after the transplant there are usually side effects from the chemotherapy or radiation therapy. You may develop nausea, vomiting, diarrhea, and mouth sores from the treatment. Very low blood counts requiring red blood cell and platelet transfusions are common. Low white blood cell counts can lead to serious infections that require treatment with intravenous (IV) antibiotics. All of these problems generally go away in 3 to 4 weeks when the transplanted blood-forming stem cells start to produce normal blood cells.

If ATG is used, there is also a risk of serious allergic reactions during the infusion. These reactions can range from skin rashes to low blood pressure and problems breathing. Generally, these side effects can be controlled with medicines. This is discussed in more detail in the next section.

A very serious side effect of a stem cell transplant is *graft-versus-host disease* (GVHD). This occurs when the transplanted donor cells attack your own cells through an immune reaction. GVHD is more common with unrelated or mismatched donors. The risk of GVHD is also higher in older patients. GVHD can occur very early after the transplant. This is called *acute GVHD*. When GVHD develops later on or lasts a long time it is called chronic GVHD. Early signs of GVHD include skin rashes with severe itching and bowel disturbances such as diarrhea. There may be abnormal lab tests showing liver damage. GVHD is treated with medications (like prednisone, methotrexate, or tacrolimus) to try to suppress the immune system. In some cases, GVHD goes away and the medications can be stopped. In other cases, GVHD is only partly controlled, and medications are needed for a long time. GVHD can sometimes be very disabling and occasionally even cause death.

For more information, please see our document *Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants.*

Immunosuppressive therapy

For people with acquired aplastic anemia who are not able to have a transplant (because of age or because they do not have a matched donor), doctors will often give *immunosuppressive treatment.* Most cases of acquired aplastic anemia are caused by the immune system attacking the bone marrow. This treatment helps stop the immune system from killing the bone marrow cells. It is not usually helpful for cases of inherited aplastic anemia because they are not caused by the immune system.

The major drugs used are *antithymocyte globulin* (ATG) and cyclosporine. ATG contains antibodies against human T-lymphocytes. This medicine is given in the hospital through an intravenous (IV) line. ATG decreases (suppresses) your immune system function by lowering the number of T-cells in the body. The antibodies in ATG come from an animal (like a horse or a rabbit), so there is a risk of a serious allergic reaction when the ATG is given. Sometimes patients getting ATG also receive a corticosteroid medicine (like prednisone) to reduce the chance that a serious reaction will occur. Often the drug called *cyclosporine* is given as well. This drug suppresses the immune system in a different way than ATG.

Combining ATG and cyclosporine improves the blood counts in about 70% of patients with the most severe disease. The aplastic anemia may not actually be cured in most of these patients. Still, even when the blood counts do not become completely normal, they often improve enough for the patient to feel well and live a normal life. Often, after a period of remission, the aplastic anemia will come back. Usually, it will respond again to immune treatment, which can be safely repeated.

Some doctors also give a drug called G-CSF (filgrastim, Neupogen®) along with ATG and cyclosporine. This drug is a growth factor for white blood cells; it tells the bone marrow to make more of these cells. In one study, this drug helped lower the chance of a serious infection and lower the number of days that patients had to be in the hospital for their aplastic anemia treatment. However, it didn't increase the chance that immunosuppressive therapy would be successful.

Another drug, alemtuzumab (Campath®), also can treat aplastic anemia by lowering T-cells. It is a monoclonal antibody (a man-made version of an antibody) that targets the CD52 antigen, which is found on the surface of many T-lymphocytes. This drug can help if aplastic anemia hasn't gotten better with ATG and cyclosporine. It is also helpful to treat aplastic anemia that has come back again after treatment with these 2 drugs. It can sometimes be used instead of ATG as a part of the first treatment, but doctors aren't sure that it works as well as ATG.. Alemtuzumab is not FDA approved to treat aplastic anemia, but it is approved to treat other diseases, such as chronic lymphocytic leukemia.

Another option for immunosuppressive therapy is to use the chemo drug cyclophosphamide in high doses. Cyclophosphamide is a chemo drug that can suppress the immune system and damage T-lymphocytes. Using it to treat aplastic anemia is controversial. Although this treatment can be effective, many experts believe that it is more dangerous than ATG. Most doctors in the United States prefer to delay using cyclophosphamide until ATG and cyclosporine are no longer working.

Immunosuppressive therapy can have serious side effects. Holding back the immune system impairs the body's ability to fight infection. People on immunosuppression can get life-threatening infections with bacteria, viruses, and fungi.

The drugs used in this therapy also have serious side effects. For example, ATG can cause serious allergic reactions with symptoms including skin rashes, low blood pressure, and problems breathing. Generally, these side effects can be controlled with medicines. Also, about 15% of patients develop leukemia or myelodysplasia several years after getting ATG. Myelodysplasia is a disorder of the bone marrow that can turn into leukemia (see our document *Myelodysplastic Syndromes*.)

Side effects of cyclosporine include high blood pressure as well as kidney and liver damage. To help prevent these problems, the doctor will check the level of cyclosporine in the blood regularly. Blood tests will also be done to check kidney and liver function.

Corticosteroids (like prednisone) can cause increases in blood sugar (like diabetes), high blood pressure, weight gain, changes in mood, and weak bones.

Supportive treatment for aplastic anemia

Transfusion

While your blood counts are low, you may need transfusions of red blood cells or platelets. Although blood transfusions are generally safe, their long-term use creates problems. The main problem is that the red cells contain iron. The transfused cells only live a few weeks and iron from these cells builds up in the body. Eventually this will result in a high level of body iron, which may be toxic. Although the buildup of iron can be treated with drugs, these aren't always successful and some organs, mainly the liver and heart, can become damaged. Also, getting transfusions before a stem cell transplant increases the chance that the transplant won't work. This is why doctors avoid giving transfusions when a transplant is planned.

See our document *Blood Transfusion and Donation* to learn more about this topic.

Antibiotics

Because of your low white blood cell count, you might develop an infection and need antibiotics. Infection is the major cause of death from aplastic anemia. Treatment with antibiotics should be started as soon as infection is suspected. Transfusing white blood cells is not generally practical. They survive only a very short time, and it's not possible to get enough white blood cells from normal donors to raise a person's white blood cell count.

Growth factors

Drugs can be given to increase the white blood cell count. These are called filgrastim (also called G-CSF or Neupogen®), pegfilgrastim (Neulasta®), and sargramostim (also called GM-CSF or Leukine®). These work only slightly for most patients with aplastic anemia.

Androgens

Some patients with early or mild aplastic anemia can be treated with androgens (instead of stem cell transplantation or ATG). Androgens are also often the first treatment given to patients with inherited forms of aplastic anemia (like Fanconi anemia and dyskeratosis congenita). Androgens are male sex hormones that also stimulate blood production. They are the reason that men have higher red blood cell counts than do women. Although they can be effective in improving blood counts, they do not cure aplastic anemia. Also, using androgens for a long time has been linked to liver tumors and liver cancer. Androgens are male hormones, so women taking this medicine can develop masculine characteristics such as facial hair, balding, deepening voice, *etc*.

Treatment to lower iron levels

Blood transfusions can cause excess iron to build up in the body. This extra iron can deposit in the liver and heart, causing the organs to function poorly. This buildup of iron is only seen in people who receive many transfusions over a period of years. Drugs called *chelating agents* (substances that bind with metal so that the body can get rid of it) can be used in patients who may develop iron overload from transfusions. The most commonly used drug is desferoxamine. This drug helps treat and prevent iron overload. This is given intravenously or as an injection under the skin. It is inconvenient because the injection must be given slowly (over several hours) 5 to 7 times per week. In some patients, treatment continues for years. Deferasirox (Exjade®) is a newer drug that is taken by mouth once a day to treat iron overload. Although it has been used more for patients with certain congenital anemias (like thalassemia), it can also help patients with aplastic anemia and iron overload.

Clinical trials for aplastic anemia

You may have had to make a lot of decisions since you've been told you have aplastic anemia. One of the most important decisions you will make is choosing which treatment is best for you. You may have heard about clinical trials being done for aplastic anemia. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our Web site at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials.

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the art treatment. They are the only way for doctors to learn better methods to treat aplastic anemia. Still, they are not right for everyone.

You can get a lot more information on clinical trials in our document called *Clinical Trials: What You Need to Know*. You can read it on our Web site or call our toll-free number (1-800-227-2345) and have it sent to you.

Complementary and alternative therapies for aplastic anemia

When you have a disease you are likely to hear about ways to treat it or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and Web sites may offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not be helpful, and a few have even been found harmful.

Alternative treatments: Alternative treatments may be offered as disease cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may make it less likely that treatment will help.

Finding out more

It is easy to see why people with serious diseases think about alternative methods. You want to do all you can to fight the disease, and the idea of a treatment with no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating diseases like aplastic anemia.

As you consider your options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers and serious diseases? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at. You

can also check them out on the *Complementary and Alternative Medicine* page of our Web site.

The choice is yours

Decisions about how to treat or manage your disease are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

General considerations in treating aplastic anemia

Many years ago, aplastic anemia was considered a fatal disease unless the patient recovered without treatment (spontaneously). Now that we understand this is often an immune disease, treatments have been devised that have a high success rate.

Children with inherited causes of aplastic anemia are treated with supportive therapy (such as androgens) and stem cell transplant. Immunosuppressants don't help these patients.

Those with acquired aplastic anemia are treated with supportive care until their disease becomes severe (with very low blood counts). This is followed by immunosuppressant therapy (also called immunosuppressive therapy) or stem cell transplant. Stem cell transplant is preferred when the patient has a matched, related donor, and is young and otherwise healthy. Immune treatments may be the first option for older patients and those without a matched donor.

A small number of people with aplastic anemia will develop leukemia or other cancers after several years. But it isn't clear if this is caused by the treatment or is just part of the disease itself. For example, many people with Fanconi anemia who don't get aplastic anemia will still go on to develop leukemia.

Aplastic anemia is rare, and treating it is very specialized, so it may best be done at a major medical center where they have experience with this disease. This is particularly true for stem cell transplants.

Sometimes the first treatment isn't successful and will need to be repeated. Often the second treatment will be effective, even if the first wasn't. Also, the treatment may be only partially effective, and the blood counts may not return to normal. In this situation, many people can still lead a normal life and not need treatment. Their blood counts, although not normal, will be high enough for a normal life.

Sometimes, none of the treatments is successful. In this case a person with aplastic anemia might want to consider taking part in a clinical trial, that is, a study of a new therapy that hasn't yet been proven successful.

What should you ask your doctor about aplastic anemia?

It's important to have frank, open discussions with your medical team. They want to answer all of your questions, no matter how minor they might seem. For instance, consider asking these questions:

- Do you know what caused my aplastic anemia?
- What treatment choices do I have?
- Which treatment do you recommend, and why?
- What are the side effects to the treatments that you recommend?
- What can I do to help reduce the side effects I may have from the treatment?
- What are the chances that my aplastic anemia will come back once I am in remission?
- Do you suggest that I get a second opinion about my diagnosis or treatment, and who do you recommend?
- What is the outlook for my survival?

Along with these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so that you can plan your work or activity schedule. Or you may want to ask about clinical trials for which you may qualify. You can find more information about communicating with your health care team in our document *Talking With Your Doctor*.

What happens after treatment for aplastic anemia?

For some people with aplastic anemia, treatment may control the disease. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, yet it is hard not to worry about aplastic anemia coming back (when a disease returns, it is called *recurrence* or *relapse*). This is a very common concern.

It may take a while before your confidence in your own recovery begins to feel real and your fears are somewhat relieved. Even with no recurrences, people who have had aplastic anemia learn to live with uncertainty. Our document *Living With Uncertainty: The Fear of Cancer Recurrence*, gives more detailed information on this and has information that applies to people with diseases besides cancer.

For some people with aplastic anemia, treatment improves blood counts, but the disease doesn't go away completely. These people may have frequent follow-up visits with their doctor and may need transfusions and other treatments. Learning to live with a disease that does not go away can be difficult and very stressful. It has its own type of

uncertainty. Our document *When Cancer Doesn't Go Away*, talks more about this (and contains information that applies to people with diseases besides cancer).

Follow-up care

When treatment ends, your doctors will still want to watch you closely. It's very important to go to all of your follow-up appointments. During these visits, your doctors will ask questions about any problems you may have and do exams and lab tests. The doctors will continue to watch your blood counts for signs of the disease coming back, as well as for short-term and long-term side effects of treatment. Almost any treatment can have side effects. Some may last for a few weeks to months, but others can last the rest of your life. This is the time for you to talk to your care team about any changes or problems you notice and any questions or concerns you have.

Your blood doctor will see you for many years after your treatment. Ask what kind of follow-up schedule you can expect.

If aplastic anemia returns, it is often in the first year after treatment. Another concern is that some people with aplastic anemia go on to develop other blood problems, such as paroxysmal nocturnal hemoglobinuria (PNH), myelodysplastic syndrome, or acute leukemia. These conditions can be found early with the blood tests done as a part of your follow-up.

It's important to keep medical insurance. Tests and doctor visits cost a lot, and even though no one wants to think of their disease coming back, this could happen.

Seeing a new doctor

At some point after your diagnosis and treatment, you may find yourself seeing a new doctor who does not know anything about your medical history. It is important that you be able to give your new doctor the details of your diagnosis and treatment Make sure you have the following information handy:

- A copy of your pathology report(s) from any biopsies (including bone marrow biopsies) or surgeries
- If you had surgery, a copy of your operative report(s)
- If you were in the hospital, a copy of the discharge summary that the doctor prepares when patients are sent home
- If you had radiation therapy, a copy of the treatment summary
- A summary of your drug treatment, including a list of the drugs given, the doses, and when you took them

The doctor may want copies of this information for his records, but always keep copies for yourself.

Lifestyle changes after having aplastic anemia

You can't change the fact that you have had a serious illness. What you can change is how you live the rest of your life – making choices to help you stay healthy and feel as well as you can. This can be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even start during cancer treatment.

Making healthier choices

For many people, having a serious illness like aplastic anemia helps them focus on their health in ways they may not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on the alcohol, or give up tobacco. Even things like keeping your stress level under control may help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society at 1-800-227-2345.

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after treatment for aplastic anemia. Treatment may change your sense of taste. Nausea can be a problem. You may not feel like eating and lose weight when you don't want to. Or you may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment caused weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do is put healthy eating habits into place. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of diseases, as well as having many other health benefits.

Our document *Nutrition for the Person With Cancer During Treatment: A Guide for Patients and Families* has information that may help you during and after treatment. See the section "Additional resources for aplastic anemia" for a list of some other documents that may be helpful.

Rest, fatigue, and exercise

Extreme tiredness, called fatigue, is very common in people treated for aplastic anemia. This is not a normal tiredness, but a “bone-weary” exhaustion that doesn’t get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to exercise and do other things they want to do. But exercise can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it is normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis twice a week. If you haven’t exercised in a few years, you will have to start slowly – maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, try to find an exercise buddy so you’re not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn’t there.

If you are very tired, you will need to balance activity with rest. It is OK to rest when you need to. Sometimes it’s really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. For more information on dealing with fatigue, please see *Fatigue in People With Cancer* and *Anemia in People With Cancer*. (Much of the information in these documents also applies to people with anemia and fatigue that isn’t from cancer). For a list of some other documents about side effects, please see the “Additional resources for aplastic anemia” section.

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- Along with a good diet, it will help you get to and stay at a healthy weight.
- It makes your muscles stronger.
- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.
- It can make you feel happier.
- It helps you feel better about yourself.

And long term, we know that getting regular physical activity plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

How does having aplastic anemia affect your emotional health?

When treatment ends, you may find yourself overcome with many different emotions. This happens to a lot of people. You may have been going through so much during treatment that you could only focus on getting through each day. Now it may feel like a lot of other issues are catching up with you.

You may find yourself thinking about death and dying. Or maybe you're more aware of the effect this disease has on your family, friends, and career. You may take a new look at your relationship with those around you. Unexpected issues may also cause concern. For instance, as you feel better and have fewer doctor visits, you will see your health care team less often and have more time on your hands. These changes can make some people anxious.

Almost everyone who has been through a serious illness like aplastic anemia can benefit from getting some type of support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, support groups, church or spiritual groups, online support communities, or one-on-one counselors. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

This journey can feel very lonely. It is not necessary or good for you to try to deal with everything on your own. And your friends and family may feel shut out if you do not include them. Let them in, and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you. You can also read our document *Distress in People with Cancer* or see the "Emotional Side Effects" section of our Web site for more information.

If treatment for aplastic anemia stops working

If aplastic anemia keeps coming back after one kind of treatment, it is possible that another treatment plan might still help. But when a person has tried many different treatments, the chances of another treatment helping becomes slight. If this happens, it's important to weigh the possible limited benefits of a new treatment against the possible downsides. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with this disease -- when you have been through every medical treatment the doctors offer you and nothing's working anymore. Your doctor may offer you new options, but at some point you need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment as long as you can, you still need to think about the odds of treatment having any benefit. In many cases, your doctor can estimate how likely the aplastic anemia will respond to treatment you are considering. For instance, the doctors may say that a certain treatment may have about a 1% chance of working. Some people are still tempted to try this. But it is important to think about and understand your reasons for choosing this plan.

No matter what you decide to do, you need to feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative treatment*.

Palliative care helps relieve symptoms, but is not expected to cure the disease. It can be given along with treatment, or can even be a type of treatment. The difference is its purpose - the main purpose of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using drugs to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat aplastic anemia. For instance, transfusions are a type of palliative treatment for aplastic anemia. They can help relieve the fatigue and shortness of breath that goes along with anemia, but they don't treat the underlying cause. This is not the same as treatment to try to cure your disease. You can learn more about physical and emotional changes, as well as plans and preparations for yourself and your family, in our document *Nearing the End of Life.*

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your disease may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as immunosuppressants and sometimes even transfusions, it doesn't mean you can't have treatment for the problems caused by your disease or other health conditions. In hospice the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. You can learn more in our document *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that are filled with happiness and meaning. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do. Though the cancer may be beyond your control, there are still choices you can make.

What's new in aplastic anemia research and treatment?

New understanding about the causes of some forms of inherited aplastic anemia, especially Fanconi Anemia, Diamond-Blackfan Syndrome, and Schwachman-Diamond Syndrome, may provide entirely new approaches to treatment of aplastic anemia in the future.

Other major advances in treating aplastic anemia may come from further research on the immune system. As doctors learn more about how the immune system works, they can develop new methods of suppressing it. Researchers are working to improve the drugs used for immunosuppression and stem cell transplantation. The goal is to find treatments that have fewer side effects and better results than the current treatments.

One drug under study is called daclizumab (Zenapax®). This is a monoclonal antibody (a laboratory-made antibody that attaches to specific substances) that blocks the action of interleukin-2 (IL-2). IL-2 is a normal part of the immune system that stimulates the immune response. Blocking IL-2 suppresses the immune system in a different way from anti-thymocyte globulin (ATG). Allergic reactions to this drug are rare. It is currently being used as a part of stem cell transplants, and is under study as a treatment for aplastic anemia.

Another drug being looked at is called mycophenolate mofetil. It is already used as an immunosuppressant in people who have received organ transplants and is being studied as a treatment for acquired aplastic anemia.

A new drug called eltrombopag (Promacta®) has become available to treat some people with low platelet counts caused by the immune system. In one study of patients with acquired aplastic anemia that was no longer responding to immunosuppression, it helped improve blood counts in some patients. This drug didn't just affect platelet counts. In some patients, it improved white counts and/or red blood cell counts. More studies of this drug in aplastic anemia are going on now.

Alefacept is a new drug that can turn off T cells. It has been helpful in treating psoriasis and graft-versus-host disease and is now being studied in the treatment of severe acquired aplastic anemia.

Researchers are also studying the possibility of using gene therapy to treat some inherited forms of aplastic anemia. Another approach is to give a drug called amifostine (Ethyol®) to help protect the bone marrow in children with Fanconi anemia.

Doctors are also trying to make stem cell transplants safer and more available. One approach is to use stem cells that come from the umbilical cord blood of newborns. This is a very rich source of stem cells. Efforts are being made nationwide to develop storage facilities for cord blood. The advantage of cord blood stem cells is that they may lead to less graft-versus-host disease. The disadvantage is that there may be too few cells to successfully "take." In one case, doctors have overcome this by transplanting cord blood stem cells from 2 separate donors. This has proven successful and may have an even lower risk of graft versus host disease. This method is currently under study.

Additional resources for aplastic anemia

More information from your American Cancer Society

Here is more information you might find helpful. Although many of them are aimed at people with cancer, the information often also applies to people with other diseases. You also can order free copies of our documents from our toll-free number, 1-800-227-2345, or read them on our Web site, www.cancer.org.

Dealing with diagnosis and treatment

Health Professionals Associated With Cancer Care

Talking With Your Doctor (also in Spanish)

After Diagnosis: A Guide for Patients and Families (also in Spanish)

Nutrition for the Person With Cancer During Treatment: A Guide for Patients and Families (also in Spanish)

Coping With Cancer in Everyday Life (also in Spanish)

Family and caregiver concerns

Talking With Friends and Relatives About Your Cancer (also in Spanish)

Helping Children When A Family Member Has Cancer: Dealing With Diagnosis (also in Spanish)

What It Takes to Be a Caregiver

Insurance and financial issues

In Treatment: Financial Guidance for Cancer Survivors and Their Families (also in Spanish)

Health Insurance and Financial Assistance for the Cancer Patient (also in Spanish

More on treatment

Understanding Chemotherapy: A Guide for Patients and Families (also in Spanish)

Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants) (also in Spanish)

Blood Product Donation and Transfusion

Clinical Trials: What You Need to Know

Treatment side effects

Caring for the Patient With Cancer at Home: A Guide for Patients and Families (also in Spanish)

Distress in People With Cancer

Anxiety, Fear, and Depression

Nausea and Vomiting

Anemia in People With Cancer

Fatigue in People With Cancer

More on other cancers linked to aplastic anemia

Leukemia: Acute Lymphocytic (also in Spanish)

Leukemia: Acute Myeloid (Myelogenous) (also in Spanish)

Childhood Leukemia (also in Spanish)

Myelodysplastic Syndromes (also in Spanish)

Your American Cancer Society also has books that you might find helpful. Call us at 1-800-227-2345 or visit our bookstore online at cancer.org/bookstore to find out about costs or to place an order.

National organizations and Web sites*

Along with the American Cancer Society, other sources of information and support include:

Aplastic Anemia & MDS International Foundation, Inc
Toll-free number: 1-800-747-2820
Web site: www.aamds.org

> Provides information and support for patients and families suffering from aplastic anemia; has a medical board that can answer medical questions; maintains a list of clinical trials on treatment for aplastic anemia; makes referrals to local chapters and other organizations offering support and financial assistance; has the Global Support Network volunteers — patients and family members who talk with other families about their treatment experiences and emotional aspects of coping with aplastic anemia; and provides a quarterly newsletter and monthly e-bulletins

Be the Match — National Marrow Donor Program
Toll-free number: 1-800-627-7692
Web site: www.bethematch.org

For information on aplastic anemia and details about the stem cell transplant process; maintains the largest registry of volunteer bone marrow donors and cord blood units in the world; offers free support services to patients and their doctors throughout the transplant process, from diagnosis through survivorship; and matches patients with the best donor or cord blood available

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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