

# Acquired Aplastic Anemia

## Basic Explanations

This publication provides general information about aplastic anemia for patients and their families. Although the Aplastic Anemia & MDS International Foundation strives to provide the most accurate and up-to-date information, it does not warrant or guarantee this information. Patients should always seek medical advice from a qualified physician and discuss these materials, individual questions, and concerns with their physician.



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*Fighting Bone Marrow Diseases through Patient Support & Research  
20 Years of Commitment & Service 1983-2003*

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*The secret of getting ahead is getting started. The secret of getting started is breaking your complex, overwhelming tasks into small manageable tasks, and then starting on the first one.*

—Mark Twain

## Dear Friend,

Like most people, you probably never heard of aplastic anemia until you or a loved one was diagnosed with it. Now you face the challenge of understanding and coping with the physical and emotional aspects of this very complex disease.

You don't have to face this alone. **The Aplastic Anemia & MDS International Foundation is here to help you.** We will answer your questions, give you the latest information on treatments and research, help pay for your travel expenses, and put you in touch with other patients who will share their experiences with you. We also offer many other publications and newsletters that provide information on managing the disease, medical updates, research findings, clinical trials, and Foundation events.

All of our services are free of charge. We are a nonprofit 501(c)(3) organization as recognized by the Internal Revenue Service.

The purpose of this brochure is to provide basic information about aplastic anemia and the human blood system. While this information is not intended as a substitute for the advice of a physician, it is vitally important that you learn as much as you can about the disease, research findings, and all of the treatment options available to you.

I also recommend that you review past issues of our newsletters, which are available from our website. If you do not have access to the Internet, ask your local librarian or a friend or family member for assistance. AA&MDSIF newsletters contain many articles on medical research, wellness, and success stories from other patients.

Since 1983, the AA&MDSIF has been leading the fight against bone marrow failure diseases with the help of a distinguished medical board, a dedicated board of directors, and hundreds of devoted volunteers around the world. Our mission is to serve as a resource for patient assistance, advocacy, and support; to provide educational materials and medical information; and to support research to find treatments and cures for aplastic anemia, myelodysplastic syndromes, and related bone marrow diseases such as PNH.

Contact us today for someone to talk to, have your questions answered, discuss our free services, or to help us to help others. We look forward to hearing from you.

Good luck and best wishes,

Marilyn Baker  
Executive Director

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# Preface

Chapter 1 explains how aplastic anemia occurs, how it is treated, and what to expect if you or a loved one develops this disease. In Chapter 2, you will find a more detailed explanation of how the body's blood system works, both under normal circumstances and in the presence of aplastic anemia. This second chapter provides an expanded look at the physical processes discussed in the first chapter, and can give you a fuller understanding of how the body produces blood cells and fights infection. Chapter 3 provides information on transfusions, which play a critical role in the treatment of aplastic anemia. Finally, a Glossary is provided at the end of Chapter 3, giving brief definitions of terms related to aplastic anemia and the blood system. You will notice that key terms in each chapter are underlined to make them easy to find in the Glossary.

## Chapter 1: Aplastic Anemia Explained

Aplastic anemia is a non contagious disease that occurs when the bone marrow stops making enough blood cells as the body needs.

Aplastic anemia (AA) was identified in 1888 when a distinguished German pathologist, Dr. Paul Ehrlich, studied the case of a pregnant woman who died of bone marrow failure. The term "aplastic anemia" was first used in 1904. Aplastic anemia is relatively unusual and most **hematologists** (doctors who specialize in blood disorders) have seen only a few cases.

The human body makes three types of blood cells: red cells, which contain **hemoglobin** and deliver oxygen to all parts of the body; white cells, which help fight infections; and **platelets**, which help blood clot when we bleed. When aplastic anemia strikes, the body stops making these blood cells.

Blood production takes place in the **bone marrow**, a red spongy substance in the center of the bones. The marrow produces **stem cells**, which grow and **differentiate** into red cells, white cells, and platelets. Stem cells are also able to replace themselves, as needed, by creating exact duplicates. Normal bone marrow is like a factory churning out as many blood cells as the body needs. For example, if you get an infection, the bone marrow steps up production of white cells; if you start bleeding, then it makes more platelets. For a more detailed explanation of the blood system, please refer to Chapter 2.

In patients with aplastic anemia, there are not enough stem cells in the bone marrow to produce a sufficient quantity of blood cells. The generally accepted thinking about aplastic anemia is that the patient's immune system is reacting against the bone marrow, interfering with its ability to make blood cells. Thus, aplastic anemia is an autoimmune disease with similar **pathophysiology** (i.e., changes in the body) to diseases like diabetes, ulcerative colitis, and multiple sclerosis. Stem cells are no longer being replaced and the remaining stem cells are working less effectively, so the levels of red cells, white cells and platelets begin to drop. If blood levels drop too low, a person can experience fatigue (low red cells), bleeding under the skin, in the mouth and from the nose, or heavy periods (low platelets), and/or an increase in the number and severity of infections (low white cells).

### SYMPTOMS

The symptoms of aplastic anemia can include *increased bleeding, bruising, **petechiae** (pinpoint red spots on the skin), susceptibility to infections, shortness of breath, fatigue, decreased alertness, shortened attention span, unusually pale skin color, dizziness, and lingering illness.* However, you should note that experiencing one or more of these symptoms does not necessarily indicate that you have the disease, since all of these symptoms can occur with other conditions. It is essential to consult a medical physician for a professional diagnosis.

Many aplastic anemia patients are also affected by a separate disorder called paroxysmal nocturnal hemoglobinuria (PNH). In PNH, there is a decrease in red blood cells (**anemia**) and the presence of blood in the urine. PNH is also characterized by a tendency to form blood clots that may cause leg swelling, shortness of breath, headache, abdominal pain or swelling, or yellow discoloration of the eyes or skin. There is evidence that PNH exists in most aplastic anemia cases without showing symptoms so patients should know to ask for PNH testing.

### DIAGNOSIS

Diagnosis begins with your doctor reviewing your symptoms and history, including possible exposure to toxins and other risk factors (*see Causes and Risk Factors* below). Your doctor will ask you for a blood sample (usually taken from an arm vein) in order to obtain a Complete Blood Count (CBC). This test gives a profile of the components of your blood and allows the doctor to compare your counts with accepted

standards (*see* Chapter 2 for a chart of normal blood counts). Below normal counts of one or more blood components may indicate aplastic anemia.

To further aid in the diagnosis of aplastic anemia, your doctor will also need to examine a sample of your bone marrow under a microscope. The sample is taken during a procedure called **bone marrow aspiration** (BMA) in which a small amount of bone marrow is extracted through a needle inserted into the back of the hip. Bone marrow aspiration provides important information on the presence or absence of abnormal cells. Because aspiration disturbs the marrow structure, the degree of bone marrow **cellularity** (the quantity and quality of the bone marrow cells) cannot be accurately determined.

Your doctor can get a more precise picture of marrow blood production through a **bone marrow biopsy** (BMB), in which an intact piece of marrow is removed and studied. This provides the most reliable and specific information regarding bone marrow cellularity. BMAs and BMBs are usually done at the same time so that the patient does not have to undergo multiple procedures. Other tests (e.g., chromosomes, liver function, PNH) may also be needed to rule out alternative causes of bone marrow failure. If your doctor is not a specialist in blood disorders, a **hematologist** should examine the samples to confirm the diagnosis.

## APLASTIC ANEMIA AND MDS— SIMILARITIES & DIFFERENCES

There are many similarities between aplastic anemia and MDS. Patients with these diseases suffer from **anemia**. Although some anemias are caused by a nutritional deficiency and can be corrected by a change in the diet and/or the addition of specific supplements, in patients with aplastic anemia and MDS, these medications will not correct the anemia because these patients do not have healthy bone marrow capable of producing an adequate number of blood cells.

Doctors sometimes have difficulty telling aplastic anemia and MDS apart. Aplastic anemia (AA) involves an injury to the stem cells in the bone marrow that results in decreased production of all three types of blood cells. Bone marrow damage may be caused by exposure to toxins, chemicals, viruses, or drugs. In most cases, the cause is not known. MDS also involves injury to the stem cells in the bone marrow, but in this case the result is an overproduction of defective cells. Aplastic anemia and MDS patients often share many of the same symptoms, including anemia and reduced numbers of platelets and white

blood cells. For instance, the hypoplastic form of MDS, in which there is a decrease in cell growth, can look very similar to severe aplastic anemia. A hematologist can usually determine which one is present by careful examination of the marrow cells.

In aplastic anemia the bone marrow produces normal blood cells, but does not make enough of them (**hypoplastic** bone marrow); in MDS the bone marrow may be stuffed with cells (**hyperplastic** bone marrow), or may be hypoplastic. In either case, MDS marrow has abnormal stem cells that produce insufficient or ineffective blood cells. The abnormalities in MDS marrow cells can sometimes be seen as alterations in the chromosomes of these cells, and sometimes in the physical characteristics of the blood cells they produce. The end result is similar to aplastic anemia—not enough of the right sort of cells for each job.

There is also a difference in the populations typically affected by these diseases: aplastic anemia is more prevalent among young people, while the incidence of MDS increases with age. For reasons that are not completely understood at this time, some aplastic anemia patients progress to MDS. Patients should be monitored regularly for possible changes in diagnosis.

## TYPES OF APLASTIC ANEMIA

Doctors classify aplastic anemia into 3 categories: Moderate, Severe and Very Severe. Although basic symptoms, treatment and medication are similar for patients in each group, the time frame for administering certain treatments may vary according to severity. A patient's blood counts may vary from month to month, week to week, or even day to day, but the general trend of all counts will be downward. The prognosis for recovery also depends on severity of the disease. Most doctors use these criteria defined in 1975 by leading hematologist Dr. Bruce Camitta and his team:

◆ **Moderate aplastic anemia (MAA)** is the classification for those who have significantly reduced blood counts but not as reduced as occurs in severe aplastic anemia. In many cases, doctors will not prescribe treatment for moderate aplastic anemia patients but will simply monitor blood counts. Moderate aplastic anemia may remain unchanged for many years. Sometimes it is detected during a routine physical exam, or is discovered only if it escalates to severe aplastic anemia and more symptoms occur.

◆ **Severe aplastic anemia (SAA)** is defined by a bone marrow cellularity (a measurement of blood cell production) of less than 25% and at least two of the

following: a **neutrophil** count less than half a billion per liter ( $<500/\text{mm}^3$ ), a platelet count less than 20 billion per liter ( $<20,000/\text{mm}^3$ ), a **reticulocyte** count less than 20 billion per liter ( $<20,000/\text{mm}^3$ ).

◆ **Very severe aplastic anemia (VSAA)** is defined by a **neutrophil** count of less than 0.2 billion per liter ( $<200/\text{mm}^3$ .)

## CAUSES AND RISK FACTORS

Aplastic anemia can strike anyone of any age, race, or gender. In western countries the incidence of aplastic anemia is about two cases per million people per year (or approximately 500 new cases in the U.S. per year). But these estimates are not precise because aplastic anemia is not a reportable disease—that is, the Centers for Disease Control and Prevention (CDC) does not require that cases be reported to them as is done with many other diseases. Aplastic anemia is two to three times more common in Asian countries.

In about 50% of cases, aplastic anemia is considered to be **idiopathic**, meaning that the cause of the disease is unknown. **Acquired** aplastic anemia refers to those cases where environmental factors and physical conditions seem to be associated with development of the disease. High doses of radiation and **cytotoxic** chemotherapy can produce aplastic anemia. Aplastic anemia can also follow exposure to some environmental toxins (such as benzene), some medications and certain viruses. Acquired aplastic anemia is not contagious nor is it hereditary. **Hereditary** aplastic anemia is relatively rare, but does occur with diseases such as Fanconi's anemia, Dyskeratosis Congenita, and Shwachman-Diamond syndrome.

## PROGNOSIS

Aplastic anemia is a serious illness that requires immediate medical attention. Many years ago there were no treatments for aplastic anemia and it was considered a fatal illness. Now, with the standard treatments described below—bone marrow transplant and immunosuppressive drug therapy—70% to 90% of patients can be treated successfully. Treatments are being refined all the time as research continues and our understanding of the disease grows. It is important to remember, though, that statistics are only indicators—all patients react to their illness and treatment differently. The likely course of the disease will vary greatly depending on the specific circumstances of a particular patient.

## TREATMENTS

### Bone Marrow Transplants

The most successful treatment option for aplastic anemia is a bone marrow transplant. Bone marrow transplants are most successful (restoration of blood counts equivalent to normal marrow function) in otherwise-healthy children and teenagers or very young adults with matched marrow donors. To increase the likelihood of a successful transplant and to minimize potential complications, the patient needs a donor whose marrow matches his or her own as closely as possible. The patient and prospective donors are given a special blood test to identify proteins on the surface of their cells called human leukocyte-associated (HLA) **antigens**. This HLA type is then used to identify a matching donor.

Many patients can receive transplants from their brothers or sisters or other close relatives. But 70% of patients do not find matching donors within their families, and must search for an **unrelated donor**. If a patient doesn't have a matched sibling or other relative, a search can be made of various bone marrow registries to find a matched unrelated donor (MUD). About 80% of transplants conducted with marrow from matched related donors are successful, while transplants with matched unrelated donors are only about half as effective. It is a good idea to explore donor possibilities as soon as aplastic anemia is diagnosed since it can take time to locate an unrelated donor if no related donor is found. Transplants involving partially matched (called "mismatched") donors may also be possible depending on the type of mismatch.

To prepare for a bone marrow transplant, the patient's diseased marrow must be destroyed (usually with some combination of chemotherapy and radiation) to make room for the healthy marrow that will be transplanted. The transplant process itself is fairly straightforward: about 15ml (one tablespoon) of donor marrow is given by intravenous transfusion for every kilogram (2.2 pounds) of body weight. Cells in the transfused marrow then migrate to the bones and, in 2 to 4 weeks, begin making new, healthy blood cells. Blood counts are monitored continuously for signs of this **engraftment** and the patient may receive various medications to keep infections away while the new immune system is growing. In 5% to 10% of patients, the new bone marrow does not grow and the transplant must be repeated.

The outcome of a bone marrow transplant and recovery times can be affected by a number of factors. Success rates (restoration of blood counts equivalent to normal marrow function) range from 50% for matched unrelated donor transplants to 70% to 90%

for matched sibling transplants. Unrelated donor transplants have an increased risk of graft rejection and of graft-versus-host disease (GVHD), a complication in which the new marrow reacts against the patient. The severity of GVHD can range from mild to life threatening and its incidence is higher among older patients and in mismatched transplants. GVHD can be prevented or treated with medication, or by removing **T-lymphocytes**, a type of white blood cell, from the donor bone marrow (*see* Chapter 2 for more information on lymphocytes).

The chances of success can also be reduced if there is a prolonged interval between diagnosis and transplant, or if the patient has received numerous blood transfusions or experienced serious infections that leave the body weakened.

### **Immunosuppressive Drug Therapy**

**Immunosuppressive** drug therapy is considered the standard initial treatment for older patients and for all patients without a matched related donor. The treatment is generally well tolerated and usually requires only brief hospitalization. Response rates, which are defined by the patient becoming transfusion-independent and risk-free from infection, are 70% to 80%. Some patients may experience normal blood counts while other patients attain near normal counts. However, responses tend to be less complete and less permanent than in patients treated with bone marrow transplants. The need to repeat immunosuppressive drug therapy is common. Also, after treatment the risks of developing leukemia or MDS later in life are higher, with the combined risk of such complications between in the range between 15% and 20% according to some studies. The generally accepted thinking about aplastic anemia is that the patient's immune system is reacting against the bone marrow, interfering with its ability to make blood cells. Immunosuppressive drugs are believed to counter this problem by reducing the immune response, allowing the bone marrow to once again make blood cells.

The two immunosuppressive drugs most frequently used to treat aplastic anemia are antithymocyte globulin (ATG) and cyclosporine. The most effective immunosuppressive treatment for aplastic anemia today combines ATG, cyclosporine and steroids.

**Antithymocyte globulin (ATG)** is a purified animal (horse or rabbit) serum that reacts against specific cells of the human immune system. The cells it targets are called **T-lymphocytes**—the cells that are responsible for destroying or suppressing the stem cells in patients with aplastic anemia. ATG is typically

given intravenously over four days for approximately four hours a day. The schedule may vary depending on the type of ATG used, the needs of the patient, and the particular methods of the doctor or hospital. No schedule has been shown to be better than another.

When used alone, ATG helps to restore blood production about 50% of the time. When used in conjunction with cyclosporine, the chances of the treatment working increase to 70% or more. If it is successful, ATG will usually eliminate the need for transfusions within two to three months but it can take nine months or more to achieve a full response. As blood counts rise, patients will feel better. However, even after a substantial response to ATG, blood counts may still be below normal. Some patients who respond to ATG may need to have treatment again because of falling blood counts. Others who do not respond to ATG the first time may respond if the treatment is repeated.

ATG has side effects that patients should discuss with their doctors. Each patient reacts to the drug differently. Less serious side effects include fever, chills, and hives that can occur during the administration of the serum. These effects disappear when the treatment is finished, but can cause substantial discomfort if they occur. A rare but severe side effect is anaphylaxis, a life-threatening allergic reaction in which blood pressure drops and breathing becomes difficult. Because of the risk of anaphylaxis, patients will usually be given a skin test to determine if they are likely to develop allergies to ATG. Allergic patients can still receive ATG therapy, but will need to undergo a desensitization procedure in which small, gradually increasing doses of ATG are given to reduce the body's reaction. Another side effect of ATG is serum sickness, an immune response to the presence of the foreign proteins in ATG and characterized by fever, rash, joint pain, and muscle aches. If it occurs, serum sickness usually begins about one to two weeks after the first dose of ATG is given. Steroids, which reduce antibody production by the immune system, are given to reduce the incidence and severity of serum sickness.

**Cyclosporine** is another immunosuppressive drug that targets T-lymphocytes. Studies have shown that cyclosporine used alone is not as effective as ATG. However, the combination of cyclosporine and ATG has been found to be more effective than either drug alone. Cyclosporine comes in liquid and pill forms. Initial doses are based on body weight. Subsequent doses are adjusted based on the amount of the drug in the blood; too much will cause side effects and too little won't be effective.

Cyclosporine has side effects that patients should discuss with their doctor. Two of the most serious side effects are high blood pressure and kidney damage. Both of these problems, however, are usually easy to manage and reversible. Blood pressure lowering medication and supplemental magnesium are often prescribed for patients taking cyclosporine. It may be necessary to continue taking cyclosporine for months or even years so it is important to pay attention to the possible side effects. Patients should be monitored regularly while taking this drug. For patients that have a stable, positive response to the drug (i.e., blood counts improve and side effects are limited), the doctor will gradually decrease the dosage.

**Other drugs.** The usefulness of other immunosuppressive drugs, including cyclophosphamide, is currently being researched. Because most research shows cyclophosphamide to be significantly less effective than ATG with cyclosporine, the use of cyclophosphamide should be considered experimental. While some investigators have reported good results without long-term complications, other investigators have found the treatment immediately toxic with long-term problems.

### **Growth Factors**

Growth factors are normal body products that encourage production of blood cells. Although most people with aplastic anemia already have unusually high levels of growth factors in their blood, very high medicinal doses may occasionally help the bone marrow to work better.

There are a number of different types of growth factors that are used both individually and in combination. Erythropoietin and similar growth factors (trade name Epogen, Procrit, Aranesp) have been successfully used to stimulate red cell growth in some patients. Recently researchers have been able to improve the effectiveness of erythropoietin by combining it with another growth factor called granulocyte colony-stimulating factor (G-CSF, Filgrastim, Neupogen) or granulocyte-macrophage colony-stimulating factor (GM-CSF, Sargramostim, Leukine). These combined treatments have been successful in generating red cell production in as many as 40% of patients. Given by itself G-CSF has been successful in stimulating white cell production in some patients.

Many other growth factors are in the process of being developed and tested. Not all patients respond to growth factors. Those who do respond usually need to receive them on an ongoing basis.

It is important to remember that growth factors may help damaged bone marrow to work better but they do not cure aplastic anemia. Growth factors help support the patient by increasing blood counts until other treatments have a chance to reverse the processes causing the marrow damage.

### **ALTERNATIVE TYPES OF TRANSPLANTS**

There are several types of transplants that use sources other than bone marrow to replace the patient's diseased marrow.

**Peripheral Blood Stem Cell Transplants.** In peripheral blood stem cell transplants (PBSCT), healthy stem cells are harvested from the bloodstream (i.e., peripheral blood) of the donor rather than from the bone marrow and are transfused into the patient. These stem cells appear to be as effective as bone marrow stem cells in patients with leukemias; however, in patients with aplastic anemia, peripheral blood stem cell transplants seem to be slightly less effective in restoring normal blood function.

**Mini-Transplants.** Mini-transplants, also called non-myeloablative transplants use a less toxic pre-treatment regimen than is used for the standard bone marrow transplant. Some of the patient's stem cells coexist with the donor stem cells for a time after transplant, thereby decreasing the chances of developing severe graft-versus-host disease. This procedure is used more frequently in older patients, and its usefulness in younger patients, who have not responded to standard treatments, is being researched. Mini-transplants are still considered experimental.

**Cord Blood Transplants.** Doctors are now using stem cells harvested from umbilical cord blood to transplant patients with aplastic anemia. Cord blood, which is collected immediately after the birth of a baby, is usually transported to a facility where it is frozen at very low temperatures for future use. Patients who receive cord blood transplants may have a lower risk of severe graft-versus-host disease (GVHD) than those transplanted with bone marrow. However, because the number of stem cells available in cord blood is small, only patients weighing less than 40kg (80 pounds) typically qualify for cord blood transplants. Research is currently underway to explore the use of cord blood for heavier patients.

**Autologous Transplants.** Recently, a small number of **autologous** transplants, in which the patient serves as his/her own donor, have been performed on patients who did not have matching donors, but did have some healthy stem cells of their own. In this type of transplant stem cells are removed

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from the patient and then re-implanted after diseased bone marrow has been destroyed with radiation and/or chemotherapy. This approach should also be considered experimental.

## OTHER TREATMENTS

Most people can be effectively treated by one of the above treatments. However, if none of these treatments are available or effective for a particular patient, several other options are available. These include other immunosuppressive drugs, marrow stimulants (**cytokines**) such as stem cell factor, and hormones (androgens). Many of these approaches are considered experimental and are available only at university-affiliated medical centers conducting clinical trials of these treatments.

“Herbal” or “Alternative” or “Vitamin” treatments are not effective treatment for aplastic anemia and can worsen a patient’s health and hinder treatment. Patients should consult with their hematologist before taking any supplements. Proper nutrition is important to optimize blood production. Folic acid and vitamins should only be taken upon advice from your hematologist and they can worsen a patient’s condition.

## CLINICAL TRIALS

In medical research, a clinical trial is a study conducted to evaluate a promising new treatment or to continue to learn about a currently successful treatment. Each study is designed to answer scientific questions and to find new and better ways to help patients. In a typical clinical trial, the current best (standard) treatment is compared to the new treatment or compared to the standard treatment plus the new treatment. For patients who have not responded to standard treatments, new treatments may be tested without any comparison group. Clinical trials are important because the research data they provide is the route to safer and more effective treatments.

Clinical trials offer some of the best medical care available. Trials not only provide the latest and best medical expertise, but patients receive close attention and monitoring. In addition, trials offer consistency in treatment protocols and quality controls that might vary in other settings. Usually, clinical trials are free-of-charge for the patient, with some facilities even financing travel expenses. Most insurance companies cover treatment received in a clinical trial.

You should consider participating in a clinical trial only after your doctor has explained the trial’s specific purposes, risks, and benefits.

Clinical trials are typically organized into three phases:

**Phase I:** Involves a treatment that is in an early stage of development, using a drug or treatment on humans for the first time. A small dose is given and the goal is to gain knowledge about the new therapy, including its safety, correct dosage, and side effects.

**Phase II:** The identified correct dose is given to patients to see how effective the therapy is in combating disease.

**Phase III:** The new treatment is tested against the standard treatment. Phase III trials can offer patients the most benefits from a new treatment.

There are also Phase IV studies that take place after a drug has been approved and is available to the public. These studies are designed to collect additional information about a treatment.

In the United States, clinical trials are usually carried out at hospitals associated with medical schools or at the National Institutes of Health (NIH). Independent committees, called Institutional Review Boards, are established at each medical center to evaluate proposed clinical trials to make certain that any risks to patients are offset by potential benefits. These boards also are responsible for making sure that clinical trials adhere to high ethical standards and that patient rights are protected.

Another safeguard for patients is Food and Drug Administration’s requirement that anyone participating in a clinical trial must give informed consent. Patients must be told exactly how the study will be conducted, the possible risks and benefits that exist with the therapy, and how the therapy compares with existing treatments. Patients also have the option to leave a clinical trial at any time and for any reason without compromising future medical care.

To learn more about clinical trials, visit our website at [www.aamds.org](http://www.aamds.org). A listing of many NIH-associated studies is available at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) or by calling (888) 346-3656. Centerwatch at [www.centerwatch.gov](http://www.centerwatch.gov) and [rarediseases.info.nih.gov](http://rarediseases.info.nih.gov) also are excellent resources.

## BLOOD TRANSFUSIONS

If red blood cell or platelet levels are low, patients may need to receive transfusions. Important advice about transfusions: do not ask close family members to donate red blood cells or platelets until after a bone marrow transplant has been done or ruled out. This is because if a family member turns out to be the best bone marrow donor, a prior donation from that family member could reduce the chances for a successful transplant.

Blood products used for transfusion are usually treated in some way (such as being irradiated or filtered) to remove **leukocytes**. These measures reduce the risk of certain complications from transfusion—irradiation minimizes the risk of graft-versus-host disease, while leukocyte filters decrease the risk of sensitization to proteins present in the transfused blood product and also reduce the risk of transmitting **cytomegalovirus**. Irradiation and filtering are important in cases where the patient is severely immunosuppressed.

Blood transfusions are an important aspect of treatment for immediate problems associated with bone marrow failure. A patient will almost certainly receive transfusions when aplastic anemia is initially diagnosed, even before a full course of treatment has been selected. Transfusions are also used as a supportive measure when there has not been full response to treatment.

Transfusions are not effective as a long-term treatment strategy for the following reasons:

- ◆ **Red blood cells** can be given indefinitely but are not a substitute for treatment of aplastic anemia. Frequent red cell transfusions can cause iron overload, a buildup of iron can damage key organs such as the heart and liver (*see* Chapter 2 for more detailed information). Left untreated, iron overload can lead to severe organ damage that can be fatal. However, iron can be removed by treatment with metal chelators like Desferal.

- ◆ **Platelets** last only a few days, so transfusions could be required several times a month. The immune system can eventually learn to recognize and destroy transfused platelets.

- ◆ **White blood cells** last only a few hours and cannot be administered routinely or to prevent infections. White cell transfusions may be used in cases of severe infections that have not responded to antibiotics.

## WELLNESS

Apart from specific treatments and medications, there are actions you can take or avoid to maintain an optimum level of wellness. Here are some of the main do's and don'ts:

- ◆ Avoid contact with toxic substances that can be ingested, inhaled, or absorbed through the skin.

- ◆ Do not take any type of medication, supplements, vitamins or herbs without first consulting with your doctor.

- ◆ If you have *low red cell counts*, avoid excessive exercise, high altitudes, or any activity that causes chest pain, severe shortness of breath, or a fast heart rate. However, some form of regular exercise is important to your physical health.

- ◆ If you have *low white cell counts*, take steps to avoid contagious illness by staying away from sick people and from crowds. Wash your hands regularly throughout the day.

- ◆ If you have *low platelets*, avoid activities that could result in injuries. If you develop severe headache or severe or persistent pain anywhere, which could indicate a bleeding problem, you should notify your doctor.

- ◆ Practice good dental hygiene to reduce the risk of bacterial infection in the mouth or throat. Damage to the lining of the mouth or throat from hot food or dental work are common causes of infection.

- ◆ Keep minor infections from becoming more serious. Be alert to early symptoms of infection. Fever or increased fatigue can be warning signs and should be reported to your doctor promptly.

- ◆ Report any symptoms to your doctor so that immediate treatment can be administered and medication adjusted as necessary.

When a patient's neutrophil counts are very low, a doctor may recommend a "neutropenic" diet to reduce risk of exposure to bacterial contamination. These patients should not eat at buffet restaurants or salad bars and should wash and peel all fresh fruit and vegetables. Foods containing living fungi such as aged cheeses and unpasteurized dairy or fermentation products should be avoided.

## EMOTIONAL ISSUES

When you are diagnosed with aplastic anemia, you may feel shock, anger, and fear, and even relief at learning what is wrong. You will need to make time for medical appointments and treatments. And everyday life must go on for you and your family. Although all of this may seem overwhelming at first, many other patients in the same situation have come through it to lead full lives. People often describe becoming stronger as individuals, as well as spiritually, and feeling closer bonds in their families after their diagnosis. The AA&MDSIF publishes two booklets that can help you with the emotional impact of learning you have aplastic anemia: *Families Coping with AA & MDS* and *Managing Treatment Decisions*. You can also contact us to be put in touch with other patients who have volunteered to share their treatment experiences.

Many patients find comfort and support by consulting with a Chronic Illness Counselor who specializes in helping patients and their families, to cope with the stress and emotional issues that accompany this diagnosis. Some patients may find that anti-depressant medication is helpful. Others may find that joining a support group or studying books on the subject is helpful. It is recommended that families seek assistance when learning how to cope with the demanding emotional aspects of bone marrow failure diseases.

You can also call on our executive director, Marilyn Baker, who has been talking to aplastic anemia patients and family members for 13 years. Marilyn will be glad to discuss disease management, emotional issues, and family relations involving bone marrow disease with you. Call her toll-free (800) 747-2820.

## TAKING ACTION

Here are some important first steps that will help you to feel more in control of your illness and its treatment:

- ◆ **Find a hematologist who is an experienced expert in treating your disease.** Make sure that the hematologist takes the time to clearly answer your questions, explain all of your treatment options, and include you in the decision-making process. The best place to begin looking for a doctor is usually a teaching hospital affiliated with a university medical school. These institutions are typically more familiar with the treatment of rare diseases and will be able to offer you information on a variety of standard and experimental treatments. Make sure you consult the “Managing Treatment Decisions” brochure, which includes information on choosing a doctor. You should consider consulting two or three or more other doctors for additional opinions.

- ◆ **Learn all you can about the disease and possible treatment options.** In addition to this brochure, the AA&MDSIF has many other educational materials available. Our website ([www.aamds.org](http://www.aamds.org)) provides links to several helpful websites. Talk with other patients about their treatment experiences—AA&MDSIF can put you in touch with people who have experienced what you are going through.

- ◆ **Ask questions of your doctor and other health professionals.** Ask about all possible treatment options and about clinical trials. Discuss information that you may have found on the Internet or learned

from friends. Do not be afraid to keep asking questions until you fully understand the answers. Request printed reference materials whenever possible. Refer to the “Managing Treatment Decisions” brochure for a list of questions for the doctor.

- ◆ **Start keeping track of all of your medical information in a notebook or on a computer.** Write down questions that you want to ask your doctor and keep track of the answers for later reference.

## Chapter 2: The Blood System

Blood is a “circulating tissue” of the body. It is composed of many specialized cells suspended in **plasma**. Two of its main functions are to transport oxygen and nutritive materials (food) to the tissues of the body and to transfer waste products to disposal sites. Blood also transports the body’s defense cells to areas damaged through injury or infection.

There are three major types of blood cells: Red Blood Cells (RBCs) or **erythrocytes**; White Blood Cells (WBCs) or **leukocytes**; and Platelets.

The bone marrow in a healthy adult produces about 2.5 billion red blood cells (RBCs), 1 billion white blood cells (WBCs), and 2 billion platelets for every kilogram (2.2 lbs) of body weight every day.

### PRODUCTION OF BLOOD CELLS

The process of blood cell production is called **hematopoiesis**. Before birth, the fetus produces blood cells in both the liver and the spleen. After birth, blood cells are produced in the **bone marrow**, a spongy tissue filling the center of the bones. The bone marrow produces **stem cells**, which are the precursor or “parent” cells for red blood cells, white blood cells, and platelets. Stem cells respond to chemical signals (**cytokines**) that are produced by the body to increase a specific population of blood cells as needed. Stem cells proliferate by dividing to make duplicates of themselves and to generate immature **blast cells**. Blast cells then **differentiate**, (mature and specialize) to make the three types of blood cells.

### COMPLETE BLOOD COUNT (CBC)

The Complete Blood Count (CBC) is a group of laboratory tests performed on a small amount of blood, usually taken from an arm vein. Together, these tests provide detailed information about the quantity and quality of each type of blood cell. The key values obtained from the CBC are:

1. White blood cell (WBC) count is a count of the actual number of white blood cells in a given volume of blood. Depending on the laboratory's reporting forms, the WBC is reported as thousands of cells in a microliter of blood (for example 5,000/ $\mu\text{L}$  or  $5.0 \times 10^3 / \mu\text{L}$ ) or as millions of cells in a liter of blood ( $5.0 \times 10^9 / \text{L}$ ).

2. White blood cell differential looks at the different types of white blood cells present in the sample. The differential classifies white blood cells into each type: neutrophils (also known as segs, PMNs, grans), lymphocytes, monocytes, eosinophils, and basophils.

3. Red blood cell (RBC) count is a count of the actual number of red blood cells in a given volume of blood. Depending on the laboratory's reporting forms, the RBC is reported as millions of cells in a microliter of blood ( $4,250,000 / \mu\text{L}$  or  $4.25 \times 10^6 / \mu\text{L}$ ) or as millions of cells in a liter of blood ( $4.25 \times 10^{12} / \text{L}$ ).

4. Hemoglobin measures the amount of oxygen-carrying protein in the red blood cells.

5. Hematocrit measures the percentage of the total blood volume that consists of red blood cells.

6. The platelet count is the number of platelets in a given volume of blood. Depending on the laboratory's reporting forms, platelets are reported as thousands in a microliter of blood ( $150,000 / \mu\text{L}$  or  $150.0 \times 10^3 / \mu\text{L}$ ) or as millions in a liter of blood ( $150.0 \times 10^9 / \text{L}$ ).

**Note:** Normal lab results involve a range rather than a single value. The table in this brochure displays the mean (average) values for different blood components. Normal values for an individual may be higher or lower, depending on age, sex, medications being taken, and other factors.

## WHITE BLOOD CELLS

White blood cells (WBCs) are part of the immune system, defending the body against invading bacteria and viruses that cause infection. They are produced and reside in the bone marrow and the lymphatic system.

WBCs also remove dead or injured cells in the body and may help remove abnormal cells originating within the body itself.

There are five main types of WBCs: neutrophils, eosinophils, basophils, monocytes, and lymphocytes. The neutrophils, eosinophils, and basophils are called

granulocytes because they have granules in their cells that contain digestive enzymes used to kill microorganisms and remove the resulting cell debris.

Neutrophils are the most numerous type of WBC, comprising about 55% of the total number of white blood cells in an adult. They kill bacteria by ingesting them in a process called phagocytosis. Neutrophils can phagocytize 5 to 20 bacteria in their lifetime. Neutrophils have a multi-lobed, segmented or polymorphonuclear nucleus and so are also called PMNs, polys or segs. Immature neutrophils are called bands or stabs. When a bacterial infection is present, an increase of neutrophils and bands are seen.

Eosinophils kill parasites and have a role in allergic reactions. They comprise about 1% to 4% of the total adult WBC count.

Basophils are not well understood, but they also function in allergic reactions. They release histamine (which causes blood vessels to leak and attract WBCs) and heparin (which prevents clotting in the infected area so that the WBCs can reach the bacteria). They usually comprise less than 1% of the total adult WBC count.

Monocytes are blood-borne phagocytes that participate in immune and inflammatory responses. These cells engulf and destroy old, damaged and dead cells in the body and are also major producers of cytokines.

Lymphocytes are the primary cells that direct the body's immune response. The majority of lymphocytes are produced in the lymph nodes and thymus gland, which means that the number of lymphocytes is generally not affected in a patient with aplastic anemia. However, if the patient is undergoing immunosuppressive therapy, the lymphocytes may be decreased. Lymphocytes are different from the other WBCs because they can recognize and remember invading bacteria and viruses. They usually comprise 33% to 50% of the total adult WBC count.

The absolute neutrophil count (ANC), which is usually included in a Complete Blood Count, is a measure of the actual number of WBCs that are mature neutrophils. This is a reliable measure of a body's susceptibility to infection: the higher the ANC, the greater the resistance to infection. The number of WBCs, the percentage of polys, and the percentage of bands must be known to calculate the ANC. To calculate the ANC, add the percentage of the polys and the bands together and multiply the sum by the WBC. Remember that the lab value of the WBC is usually in thousands of cells and one must move the decimal three places to the right for the actual ANC number.

## RED BLOOD CELLS

Red blood cells (RBCs), also known as **erythrocytes**, are the most abundant cells in the blood. They give the blood its red color and contain **hemoglobin**, the protein that carries oxygen to cells. The life span of each RBC is about 120 days.

A **reticulocyte** is a very young RBC. The number of reticulocytes in the blood is proportional to the rate at which they are produced and released by the bone marrow. A normal reticulocyte count is 1% to 2% of the total RBC count. An elevated reticulocyte count (**reticulocytosis**) usually indicates that the bone marrow is responding to an increase in the need for red blood cells as happens when aplastic anemia is present.

## PLATELETS

**Platelets (thrombocytes)** are the smallest blood cells. The main function of the platelet is to rush to an area of injury, such as a cut on your finger. The platelets will stick to a torn blood vessel wall and form a plug that temporarily seals off the leak. Eventually a clot forms at the same site to stop the bleeding.

Platelets are formed in the bone marrow from very large cells called **megakaryocytes**. The megakaryocytes break apart and each tiny fragment

forms a platelet. After platelets leave the bone marrow they are stored in the spleen and released as needed by the body. Platelets live for about 8 to 10 days.

When the body does not have enough platelets (**thrombocytopenia**) a person may bleed spontaneously and possibly uncontrollably. Bleeding into the tissue can become visible in the form of a bruise. Bleeding from capillaries causes pinpoint red dots called **petechiae**. When the platelet count falls below 5,000 per cubic millimeter, bleeding can occur spontaneously anywhere in the body even without an injury. Some patients experience spontaneous or increased bleeding at platelet levels up to 20,000 or 30,000.

Each patient will respond differently to low platelet counts. The trigger level at which a platelet transfusion may be required will differ with age, other health problems, the site of bleeding, the extent of bleeding, and the treatment for aplastic anemia agreed upon by the patient and the physician.

The **lymphocytes** include a special population of cells known as natural killer cells. The main function of the natural killer cell is to exert direct cytotoxic effects on targeted nonself cells. It appears that the

### NORMAL (Mean) ADULT BLOOD VALUES\*

mm<sup>3</sup> (cubic millimeter) — g/dL (grams per deciliter) —% (percentage)

	WBC (x10 <sup>3</sup> /mm <sup>3</sup> )	Neutrophils (x10 <sup>3</sup> /mm <sup>3</sup> )	Hgb	Hematocrit	Reticulocyte	Platelets (x10 <sup>3</sup> /mm <sup>3</sup> )
Male	7.4	4.4	15.5 g/dL	47%	0.8-2.5	150-350
Female	7.4	4.4	14.0 g/dL	41%	0.8-4.1	150-350

### NORMAL (Mean) CHILDREN'S BLOOD VALUES\*

mm<sup>3</sup> (cubic millimeter) — g/dL (grams per deciliter) —% (percentage)

	WBC (x10 <sup>3</sup> /mm <sup>3</sup> )	Neutrophils (x10 <sup>3</sup> /mm <sup>3</sup> )	Hgb	Hematocrit	Reticulocyte	Platelets (x10 <sup>3</sup> /mm <sup>3</sup> )
1 month	10.8	3.8	13.9 g/dL	44%	0.1-1.7	—
6 month	11.9	3.8	12.6 g/dL	36%	0.7-2.3	—
6 mo-2 yrs	10.6	3.5	12.0 g/dL	36%	—	150-350
2-6 yrs	8.5	3.8	12.5 g/dL	37%	0.5-1.0	150-350
6-12 yrs	8.1	4.4	13.5 g/dL	40%	0.5-1.0	150-350
12-18 years						
male	7.8	4.4	14.5 g/dL	43%	0.5-1.0	150-350
female	7.8	4.4	14.0 g/dL	41%	0.5-1.0	150-350

\* data from *Harriet Lane Handbook*, 15th Edition, ed. Siberry and Iannone, C.V. Mosby, 2002.

natural killer cells are also effective in destroying unhealthy or abnormal self cells. Natural killer cells participate in the destruction of “nonself” cells from other individuals or animals. Usually these actions are beneficial to the individual, but can also cause the rejection of grafts and transplanted organs.

## THE IMMUNE SYSTEM

The immune system of a normal adult is continually challenged by a wide variety of substances that it recognizes as being foreign. These foreign substances, called **antigens**, consist of proteins present on the surface of cells. Our immune systems are usually tolerant of the antigens on our own cells.

The body’s reaction to antigens is called the immune response. When this response occurs, the body activates two major types of lymphocytes—B cells and T cells—that can recognize and destroy antigens. B cells produce antibodies that incapacitate antigens; T cells attack the antigens directly. Once the B and T cells have been exposed to a particular antigen, some of these cells, called “memory cells”, become capable of remembering the antigen and can act faster if the antigen re-enters the body.

When a foreign cell enters the body, it will eventually reach a lymph node. There it will stimulate B cells to produce specific antibodies. This antigen-antibody pair acts as a specific lock and key because each antibody usually only fights against or binds to one type of antigen.

## Chapter 3: Transfusions

When blood—or one of its components, such as red blood cells or platelets—is delivered into a person’s bloodstream, it is called a blood **transfusion**. Transfusions are usually given through a tiny tube that is inserted into a vein in the hand or arm with a small needle.

### RED BLOOD CELL TRANSFUSIONS

Transfusions of red blood cells are often needed for the temporary relief of anemia. Usually, some of the plasma (the yellowish fluid surrounding blood cells) is removed to make the red blood cells easier to give; this more concentrated blood product is known as **packed RBCs** or **PRBCs**. Transfusions may relieve fatigue, allowing the heart to work at a slower rate. Before a transfusion is given, blood specimens must be obtained for cross-matching. Cross-matching is testing of donor’s blood and recipient’s plasma for compatibility. The patient’s **vital signs**, including temperature, must be checked before and during a

transfusion. A transfusion of one unit of PRBCs (450 milliliters or 1 pint) usually takes two to four hours to complete. If a serious transfusion reaction occurs, the signs are usually seen within the first 15 to 20 minutes. One unit of blood typically increases the hemoglobin by 1g/dl and the hematocrit by 2% to 3%.

One drawback to the use of repeated transfusions is related to our bodies’ inability to eliminate excess iron. Iron is carried by hemoglobin inside the red cells. When the red cells break down, iron is released and stored in critical organs such as the liver and the heart. Under normal conditions there are approximately 4-6 grams of iron in the body. Each unit of transfused blood contains approximately 200-250 milligrams of iron. This means that a patient receiving two units of blood per month could accumulate 5-6 grams of iron in one year. Over many months or years, frequent red cell transfusions result in the accumulation of iron known as **hemochromatosis** or “iron overload” eventually causing organ dysfunction and even death. Diagnosis involves measurement of the patient’s ferritin level, serum iron, and **transferrin** saturation. This can sometimes be obtained from a bone marrow aspirate or, for more accuracy, from a liver biopsy. An indirect measure of body iron can be obtained by measuring storage iron (serum ferritin) in the blood.

Excess iron can be removed from the body using a drug called desferrioxamine (Desferal), which is an **iron chelator**. Chelators bind with iron and eliminate it from the body through the urine and stool. Desferal, the only iron chelating agent approved in the United States, is usually given via a slow **subcutaneous** infusion by syringe pump, at least four to six days a week. Intravenous administration during blood transfusions is useful for patients who comply poorly with the subcutaneous treatment. Most hematologists agree that chelation therapy should be started before organ damage has a chance to occur, some suggesting treatment after as few as 15 transfusions, or when the serum ferritin level has reached 1000mg/ml (normal is 40-160mg/ml).

The most common side effect from subcutaneous infusion of Desferal is pain and swelling at the injection site, usually subsiding after 24 hours. Warm compresses applied to the site are often helpful. Ask your doctor about drugs that can decrease inflammation of the skin such as Dexamethasone or Methylprednisolone.

A recent alternative to continuous subcutaneous infusion of Desferal is a rapid (bolus) injection of the same drug twice daily. This treatment was found to

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be equally effective, does not induce serious side effects, and is better accepted by many patients. An oral chelator is undergoing testing in Europe.

## **IMPORTANCE OF IRRADIATED AND LEUKOCYTE-REDUCED BLOOD**

If a large number of lymphocytes are present in the blood used to transfuse a patient, those cells can trigger a graft-versus-host reaction. For this reason, many doctors recommend transfusions of irradiated blood. The irradiation process does not kill the lymphocytes, but it inactivates them to prevent them from mounting an immune response against the patient. For those patients that need them, platelet transfusions should also be irradiated.

The use of filters to reduce the number of lymphocytes (also called leukopor filters) is recommended by doctors for patients who receive frequent blood transfusions. When combined with irradiation of the blood, such filtering can help patients who are transfusion-dependent from building up antibodies against platelets, transplantation proteins, and other antigens. Leukocyte filters also reduce the risk of transmitting cytomegalovirus. Ideally, patients who have not been exposed to cytomegalovirus and are candidates for a bone marrow transplant should receive transfusion products that have been checked and found to be negative for cytomegalovirus.

## **PLATELET TRANSFUSIONS**

The normal life span of a platelet is quite short, only 8-10 days. Patients respond differently to very low platelet counts. Some may need regular platelet transfusions but some may elect to avoid platelet transfusions unless they have bleeding. Like blood transfusions, platelets transfusions can trigger an immune response in the patient because the platelets are recognized as foreign to the body. Such a response can rapidly destroy transfused platelets. In these patients, the response to platelet transfusions may be improved by giving platelets that are HLA-matched with the patient.

## **WHITE BLOOD CELL TRANSFUSIONS**

White blood cells are usually not transfused to patients. Their life span is extremely short (only a few hours) so their use is reserved for individuals with severe infections who do not respond to antibiotics.

## **TRANSFUSION REACTIONS**

Common transfusion reactions include fever, chills, and allergic reactions (itching, hives). Diphenhydramine (Benadryl) or acetaminophen (Tylenol) can be used to treat or to prevent recurrent transfusion reactions. Severe transfusion reactions, due to infusion of incompatible red blood cells, may cause shortness of breath, back pain, low blood pressure, and decreased urine output. Medical staff always monitors transfusions but patients should be aware of their own reactions during transfusions and ask for help if symptoms develop.

## **RISKS OF TRANSFUSION CONTAMINATION**

Contamination of blood products for transfusion is rare. Although it is not possible to completely eliminate all risk, recent advances in the testing of blood products have reduced the possibility of contamination from viruses such as HIV and hepatitis to a point where the risk to the patient is extremely low.

## **TOPICAL ANESTHETIC**

For patients who are very sensitive to pain, doctors may suggest a topical anesthetic called EMLA (lidocaine & prilocaine) to numb the site before needle insertion. EMLA is a prescription gel that comes with its own adhesive bandages. It is applied to the area of puncture at least one hour before needle insertion takes place and covered with the bandages for protection. The result is decreased discomfort. Caregivers should ask about the use of EMLA to reduce pain for pediatric patients.

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# Glossary

**Absolute Neutrophil Count**—A measure of the actual number of mature neutrophils present in the blood per unit volume.

**Allergen**—A substance that causes an allergic reaction.

**Anemia**—Any condition in which there are too few red blood cells in the bloodstream, resulting in insufficient oxygen to tissues and organs.

**Antigen**—Protein present on the surface of cells that can stimulate an immune reaction.

**Aplastic**—Involving the absence or defective development of a tissue or organ.

**Acquired**—Any condition that is not genetic (inherited) or congenital (present at birth); usually caused by environmental factors and/or physical conditions.

**Autologous**—Involving the patient serving as his/her own donor, especially in transfusions and bone marrow transplants.

**Band**—An immature neutrophil.

**Basophil**—A type of white blood cell that plays a role in allergic reactions.

**Blast Cells**—Immature cells that mature into the three types of blood cells.

**Bone Marrow**—Soft tissue occupying the inner cavities of bones responsible for blood cell production.

**Bone Marrow Aspiration**—A medical process in which a small amount of bone marrow is extracted through a needle inserted into the back of the hip.

**Bone Marrow Biopsy**—A medical process in which an intact piece of marrow is removed for study

**Cellularity**—The quantity, quality, or condition of cells present in the bone marrow.

**Cytokines**—Hormone-like proteins secreted by many different cell types to regulate cell proliferation and function.

**Cytomegalovirus**—A widespread opportunistic virus that can cause disease in an immunosuppressed person

**Cytopenia**—A deficiency of cells in the blood.

**Cytotoxic**—Destructive to cells.

**Differentiate**—To become distinct or specialized; acquire a different characteristic or function than the original.

**Engraftment**—When bone marrow infused during a bone marrow transplant is accepted by the patient's body and begins producing blood cells.

**Enzyme**—A protein that acts as a catalyst to induce chemical changes in other substances.

**Eosinophil**—A type of white blood cell that kills parasites and plays a role in allergic reactions.

**Erythrocyte**—A mature red blood cell.

**FAB criteria**—Criteria for classifying leukemia and myelodysplastic syndromes developed and agreed upon by a group of French, American and British scientists.

**Febrile**—Involving an elevated body temperature; feverish.

**Granulocyte**—Any one of these three types of white blood cells: neutrophils, eosinophils, and basophils; so called because they have granules that contain enzymes to help fight infection.

**Hematocrit**—The percentage of a volume of blood occupied by red blood cells.

**Hematologist**—A doctor who specializes in the study of blood and blood-producing organs

**Hematopoiesis**—The process of blood cell production.

**Hemochromatosis**—An excess of iron deposits in the body, also known as iron overload.

**Hemoglobin**—The red blood cell protein-iron compound responsible for transporting oxygen from the lungs to the cells, and carbon dioxide from the cells to the lungs.

**Hereditary**—Refers to any condition passed via genes from parent to child

**Hyperplastic**—Involving an increased number of cells.

**Hypersensitivity**—An abnormal sensitivity to a stimulus.

**Hypoplastic**—Involving a decreased number of cells.

**Idiopathic**—Refers to any condition with no known cause.

**Immunosuppressive**—Being capable of inhibiting immune responses.

**Iron Chelator**—A substance that binds iron and then eliminates it from the body in the urine and stool.

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**Leukocyte**—White blood cells, important in defending against infection and clearing the body of harmful material (see also granulocytes, monocytes and lymphocytes).

**Lymph**—A clear, transparent filtrate of plasma that is collected from tissues throughout the body and eventually flows to the lymphatic system.

**Lymph Node**—see Lymphatic System

**Lymphatic System**—The tissues and organs (including the bone marrow, spleen, thymus and lymph nodes) that produce and store cells that fight infection and the network of vessels that carry lymph.

**Lymphocyte**—A type of white blood cell that directs the body's immune response; divided into two forms, B cells and T cells.

**Megakaryocyte**—A large cell in the bone marrow from which platelets are formed.

**Monocyte**—A type of white blood cell that plays a role in immune and inflammatory responses

**Morphology**—The study of the structure and form of an organism or one of its parts

**Neutropenia**—A deficiency of neutrophils in the blood.

**Neutrophil**—The most numerous of the white blood cells, important for helping the body fight infections (see also bands and stabs).

**Packed RBCs**—A concentrated blood product in which plasma has been removed from the blood to make transfusions easier and faster (also called PRBCs).

**Pancytopenia**—A deficiency of all types of blood cells.

**Petechiae**—Pinpoint hemorrhagic spots in the skin.

**Pathophysiology**—Functional changes in the body that are associated with or result from disease or injury.

**Petechiae**—Small red or purplish spots on the skin or a mucous membrane, caused by very small hemorrhages

**Phagocytosis**—The process by which white blood cells (specifically neutrophils) engulf and destroy microorganisms or cells.

**Plasma**—The fluid (noncellular) portion of circulating blood.

**Platelet**—The smallest blood cell, essential for blood clotting. Also called thrombocyte.

**PMN**—A mature neutrophil.

**Poly**—A mature neutrophil.

**Proliferation**—Growth by reproduction of similar cells.

**Reticulocyte**—An immature red blood cell normally restricted to the bone marrow and present in the bloodstream only in very low numbers.

**Reticulocytosis**—A condition in which there is an increase in the number of circulating reticulocytes

**Seg**—A mature neutrophil.

**Stab**—An immature neutrophil.

**Stem Cells**—Cells that are produced in the bone marrow and differentiate into red cells, white cells, and platelets

**Subcutaneous**—Beneath the skin.

**Thrombocyte**—Platelet.

**Thrombocytopenia**—A decrease in the number of platelets in the blood, resulting in the potential for increased bleeding and decreased ability for clotting.

**T-lymphocyte**—A type of lymphocyte that is important in the immune response, but in aplastic anemia suppresses the stem cells; also known as a T cell lymphocyte.

**Transferrin**—A protein that binds with iron and thus regulates iron absorption and transports iron in the body.

**Transfusion**—The process by which blood or one of its components is delivered directly into the bloodstream

**Unrelated Donor**—A donor that is not a sibling or other familial relation of the patient (recipient).

**Vital Signs**—A person's temperature, pulse, respiration, and blood pressure

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## **HOW WE CAN HELP**

**Patients, families and health care professionals can benefit from these FREE services:**

- ◆ **Emotional Support** provided by toll-free hotline and email.
- ◆ **Educational materials** explain the disease, treatment options, research updates, clinical trials, patients rights, steps in making treatment decisions, and emotional management.
- ◆ **Patient Information Department** personally answers questions from patients and family members by a team of medical experts.
- ◆ **Clinical Trial Listings** includes doctor's name, phone number, hospital and protocol description.
- ◆ **Patient Travel Fund** pays a family up to \$500 for travel expenses to participate in a Clinical Trial.
- ◆ **Global network of volunteers** composed of patients and family members share treatment experiences and other information regarding the physical and emotional aspects of these diseases.
- ◆ **International support groups** in 50 countries provide local assistance, regional resources and personal contacts with other patients.
- ◆ **Quarterly newsletters** feature medical updates, research articles, victory stories, helpful resources and Foundation activities.
- ◆ **Annual international patient conferences** gather hundreds of patients and families with recognized medical researchers and health care experts to discuss research updates, advances in treatments options and other related issues.
- ◆ **AA& MDSIF Voluntary Patient Registry** collects patient statistics to help medical researchers better understand the disease.
- ◆ **Medical research** studies financially funded in hopes of finding a cure.
- ◆ **Medical Advisory Board** composed of distinguished medical experts who advise the Foundation on research funding, educational materials, and patient information.

*For more information on our services, please contact the AA&MDSIF.  
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**APLASTIC ANEMIA & MDS INTERNATIONAL FOUNDATION, INC.**

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