LEUKEMIA--ACUTE MYELOID (MYELOGENOUS)

What is cancer?

Cancer develops when cells in a part of the body begin to grow out of control. Although there are many kinds of cancer, they all start because of out-of-control growth of abnormal cells.

Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide more rapidly until the person becomes an adult. After that, cells in most parts of the body divide only to replace worn-out or dying cells and to repair injuries.

Because cancer cells continue to grow and divide, they are different from normal cells. Instead of dying, they outlive normal cells and continue to form new abnormal cells.

Cancer cells develop because of damage to DNA. This substance is in every cell and directs all its activities. Most of the time when DNA becomes damaged the body is able to repair it. In cancer cells, the damaged DNA is not repaired. People can inherit damaged DNA, which accounts for inherited cancers. Many times though, a person’s DNA becomes damaged by exposure to something in the environment, like smoking.

Cancer usually forms as a tumor. Some cancers, like leukemia, do not form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Often, cancer cells travel to other parts of the body, where they begin to grow and replace normal tissue. This process is called metastasis. Regardless of where a cancer may spread, however, it is always named for the place it began. For instance, breast cancer that spreads to the liver is still called breast cancer, not liver cancer.

Not all tumors are cancerous. Benign (non-cancerous) tumors do not spread (metastasize) to other parts of the body and, with very rare exceptions, are not life threatening.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Cancer is the second leading cause of death in the United States. Nearly half of all men and a little over one third of all women in the United States will develop cancer during their lifetimes. Today, millions of people are living with cancer or have had cancer. The risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking and eating a better diet. The sooner a cancer is found and treatment begins, the better are the chances for living for many years.

What Is Acute Myeloid Leukemia?

Acute myeloid leukemia (AML) goes by many names, including acute myelocytic leukemia, acute myelogenous leukemia, acute granulocytic leukemia, and acute non-lymphocytic leukemia. "Acute" means that the leukemia can progress quickly, and if not treated, would probably be fatal in a few months.

AML is a cancer that starts in cells that would normally develop into different types of blood cells. Most cases of AML develop from cells that would turn into white blood cells (other than lymphocytes), but some cases of AML develop in other types of blood-forming cells. (Acute leukemia that develops in lymphocytes is called acute lymphocytic leukemia (ALL). For more information on this type of leukemia, see the American Cancer Society document, *Leukemia--Acute Lymphocytic*.)

AML starts in the bone marrow (the soft inner part of the bones, where new blood cells are made), but in most cases it quickly moves into the blood. It can sometimes spread to other parts of the body including the lymph nodes, liver, spleen, central nervous system (brain and spinal cord), and testes.

Other types of cancer can start in these organs and then spread to the bone marrow. But these cancers that start elsewhere and then spread to the bone marrow are not leukemia.

Normal Bone Marrow, Blood, and Lymphoid Tissue

In order to understand the different types of leukemia, it is helpful to have some basic knowledge about the blood and lymph systems.

Bone Marrow

Bone marrow is the soft inner part of some bones such as the skull, shoulder blades, ribs, pelvis, and backbones. The bone marrow is made up of a small number of blood stem cells, more mature blood-forming cells, fat cells, and supporting tissues that help cells grow.

The blood-forming cells come from blood *stem cells*. These stem cells only make new blood-forming cells and not other kinds of cells. (This makes them different from embryonic stem cells, which are formed in a developing fetus and can grow into most other cell types in the body.)

Stem cells go through a series of changes. During this process, the cells develop into either *lymphocytes* (a kind of white blood cell) or other blood-forming cells. The other blood-forming cells can develop into 1 of the 3 main types of blood cell components: red blood cells, white blood cells (other than lymphocytes), or platelets.

Red Blood Cells

Red blood cells carry oxygen from the lungs to all other tissues in the body, and take carbon dioxide back to the lungs to be removed. Anemia (having too few red blood cells in the body) typically causes weakness, fatigue, and shortness of breath because the body tissues are not getting enough oxygen.

Platelets

Platelets are actually cell fragments made by a type of bone marrow cell called the megakaryocyte. Platelets are important in plugging up holes in blood vessels caused by cuts or bruises. A shortage of platelets is called thrombocytopenia. A person with thrombocytopenia may bleed and bruise easily.

White Blood Cells

White blood cells are important in defending the body against infections. Lymphocytes are one type of white blood cell. The other types of white blood cells are granulocytes (neutrophils, basophils, and eosinophils) and monocytes.

Lymphocytes are the main cells that make up lymphoid tissue, a major part of the immune system. Lymphoid tissue is found in lymph nodes, the thymus gland, the spleen, the tonsils and adenoids, and is scattered throughout the digestive and respiratory systems and the bone marrow.

Lymphocytes develop from cells called *lymphoblasts* to become mature, infection-fighting cells. The 2 types of lymphocytes are known as B lymphocytes (B cells) and T lymphocytes (T cells).

- *B lymphocytes* protect the body from invading germs by developing (maturing) into plasma cells, which make antibodies. These antibodies attach to the germs, such as bacteria, viruses, and fungi. Once the germ has been coated in this way, other white blood cells can recognize and destroy it.

- *T lymphocytes* can recognize cells infected by viruses and directly destroy these cells.

Granulocytes are white blood cells that have granules in them, which are spots that can be seen under the microscope. These granules contain enzymes and other substances that can destroy germs, such as bacteria. The 3 types of granulocytes - *neutrophils*, *basophils*, and *eosinophils* - are distinguished by the size and color of their granules. Granulocytes develop from blood-forming cells called *myeloblasts* to become mature, infection-fighting cells.

Monocytes, which are related to granulocytes, also are important in protecting the body against bacteria. They start in the bone marrow as blood-forming *monoblasts* and develop into mature monocytes. After circulating in the bloodstream for about a day, monocytes enter body tissues to become *macrophages*, which can destroy some germs by surrounding and digesting them. Macrophages are also important in helping lymphocytes to recognize germs and start making antibodies to fight them.

Any of the blood-forming or lymphoid cells from the bone marrow can turn into a leukemia cell. Once this change takes place, the leukemia cells fail to go through their normal process of maturing. Although leukemia cells may reproduce quickly, in most cases the problem is that they don't die when they should. They continue to survive and accumulate. Over time, these cells spill into the bloodstream and spread to other organs, where they can keep other cells in the body from functioning normally.

Types of Leukemia

Not all leukemias are the same. Leukemias are divided into 4 main types. Knowing the specific type of leukemia can help doctors better predict each patient's prognosis (outlook) and select the best treatment.

Acute leukemia versus chronic leukemia

The first factor to consider in classifying a patient's leukemia is if most of the abnormal cells are mature (look like normal white blood cells) or immature (look more like stem cells).

In *acute* leukemia, the bone marrow cells cannot mature properly. Immature leukemia cells continue to reproduce and build up. Without treatment, most patients with acute leukemia would live only a few months. Some types of acute leukemia respond well to treatment, and many patients can be cured.Other types of acute leukemia have a less favorable outlook.

In *chronic* leukemia, the cells can mature partly but not completely. These cells are not really normal. They generally do not fight infection as well as do normal white blood cells. And, of course, they survive longer, build up, and crowd out normal cells. Chronic leukemias tend to progress over a longer period of time, and most patients can live for many years. However, chronic leukemias are generally harder to cure than acute leukemias.

Myeloid leukemia versus lymphocytic leukemia

The second factor to consider in classifying leukemia is the type of bone marrow cells that are affected.

Leukemias that start in early forms of myeloid cells -- white blood cells (other than lymphocytes), red blood cells, or platelet-making cells (megakaryocytes) -- are *myeloid* leukemias (also known as *myelocytic, myelogenous, or non-lymphocytic* leukemias).

If the cancer starts in early forms of lymphocytes, it is called *lymphocytic* leukemia (also known as *lymphoid* leukemia). Lymphomas are also cancers of lymphocytes. But, unlike lymphocytic leukemias, which develop in the bone marrow, lymphomas develop from lymphocytes in lymph nodes or other organs.

By considering whether they are acute or chronic and whether they are myeloid or lymphocytic, leukemias can be divided into 4 main types:

- acute myeloid (or myelogenous) leukemia (AML)
- chronic myeloid (or myelogenous) leukemia (CML)
- acute lymphocytic (or lymphoblastic) leukemia (ALL)
- chronic lymphocytic leukemia (CLL)

The rest of this document contains information on acute myeloid leukemias of adults only. Chronic leukemias of adults and acute lymphocytic leukemia (ALL) of adults are discussed in other American Cancer Society documents. For information on AML in children, please see the separate document,Childhood Leukemias.

What Are the Key Statistics About Acute Myeloid Leukemia?

About 44,270 new cases of leukemia will be diagnosed in the United States during 2008. About 13,290 of those cases will be acute myeloid leukemia (AML),and most AML patients will be adults. About 8,820 deaths from AML will occur in the United States during 2008, and almost all will be in adults.

Acute myeloid leukemia is generally a disease of older people and is rare before the age of 40. The average age of a patient with AML is about 67 years.

AML is slightly more common among men than among women. The lifetime risk of getting AML for the average man is about 1 in 225; for the average woman the risk is about 1 in 300.

Information on treatment success rates for adult AML can be found in the section, "How Is Acute Myeloid Leukemia Treated?"

What Are the Risk Factors for Acute Myeloid Leukemia?

A risk factor is something that affects a person's chance of getting a disease, such as cancer. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for a number of cancers.

But having a risk factor, or even several risk factors, does not mean that you definitely will get the disease. And many people who get the disease may not have had any known risk factors.

There are a few known risk factors for acute myeloid leukemia (AML).

Smoking

The only proven lifestyle-related risk factor for AML is smoking. Although many people know that smoking is linked to cancers of the lungs, mouth, throat, and larynx (voice box), few realize that it can also affect cells that don't come into direct contact with smoke. Cancer-causing substances in tobacco smoke are absorbed by the lungs and spread through the bloodstream to many parts of the body. Scientists estimate that as many as 1 out of 5 cases of AML is caused by smoking.

Chemical Exposure

The risk of AML may be increased by exposure to certain chemicals. In the workplace, long-term exposure to high levels of benzene (an industrial solvent used in the cleaning industry and to produce drugs, plastics, synthetic rubber, and dyes) is a risk factor for AML.

Patients with other cancers who are treated with certain chemotherapy drugs are more likely to develop AML. Some of the drugs linked with these secondary (treatment-related) leukemias include mechlorethamine, procarbazine, chlorambucil, etoposide, teniposide and cyclophosphamide. Combining these drugs with radiation therapy further increases the risk.

Most secondary cases of AML occur within 10 years after treatment of Hodgkin disease, non-Hodgkin lymphoma, or childhood acute lymphocytic leukemia (ALL). Secondary leukemias also sometimes occur following treatment of breast, ovarian, or other cancers.

Radiation Exposure

High-dose radiation exposure (such as being a survivor of an atomic bomb blast or nuclear reactor accident) increases the risk of developing AML. Japanese atomic bomb survivors had a greatly increased risk of developing acute leukemia, usually within 6 to 8 years after exposure.

The possible risks of leukemia from exposure to lower levels of radiation, such as from radiation therapy, x-rays, or CT scans, is not well-defined. Exposure of a fetus to radiation within the first months of development may also carry an increased risk of leukemia, although the extent of the risk is not clear. If there is an increased risk it is likely to be small, but to be safe, most doctors try to limit a person's exposure to radiation as much as possible.

Certain Blood Disorders

Patients with certain blood disorders seem to be at increased risk for getting AML. These include chronic *myeloproliferative disorders* such as polycythemia vera, essential thrombocytopenia, and idiopathic myelofibrosis. Chronic myelogenous leukemia (CML) is another type of *myeloproliferative disorder*, and some patients with CML can later develop a form of AML. The risk of developing AML is increased further if treatment for these disorders includes some types of chemotherapy or radiation.

Some patients who have a *myelodysplastic syndrome* (preleukemic condition) may develop AML. These conditions cause defects in blood cell formation, and over a period of years may evolve into leukemia. Patients who develop AML after a preleukemic condition typically have a poor prognosis.

Inherited Syndromes

Acute myeloid leukemia does not appear to be an inherited disease. It does not seem to run in families, so a person's risk is not usually increased if a family member has the disease. But there are some inherited syndromes with genetic changes that seem to raise the risk of AML. These include:

- Down syndrome
- Fanconi anemia
- Bloom syndrome
- Ataxia-telangiectasia
- Blackfan-Diamond syndrome

Having An Identical Twin With AML: This risk is largely confined to the first year of life. As mentioned above, most cases of AML are not thought to have a strong genetic link. Many doctors feel the increased risk among identical twins may be due to leukemia cells being passed from one fetus to the other while still in the womb.

Gender

AML is more common in males than in females, although the reasons for this are not clear.

Uncertain, Unproven or Controversial Risk Factors

Other factors that have been studied for a possible link to AML include:

- exposure to electromagnetic fields (such as living near power lines)
- workplace exposure to diesel, gasoline, and certain other chemicals and solvents
- exposure to herbicides

So far, none of these factors has been linked conclusively to AML. Research in these areas is ongoing.

Do We Know What Causes Acute Myeloid Leukemia?

Although some people with acute myeloid leukemia (AML) have one or more of the known risk factors mentioned earlier, most do not. The cause of their cancer remains unknown at this time. Even when a patient has one or more risk factors, there is no way to tell whether it actually caused the cancer. And many people with one or more cancer risk factors never develop this disease.

During the past few years, scientists have made great progress in understanding how certain changes in DNA can cause normal bone marrow cells to become leukemia cells. Normal human cells grow and function based mainly on the information contained in each cell's chromosomes. Human DNA is packaged in 23 pairs of chromosomes, which are long molecules of DNA in each cell. DNA is the chemical that makes up our genes - the instructions for how our cells function. We resemble our parents because they are the source of our DNA. But our genes affect more than the way we look.

Some genes contain instructions for controlling when our cells grow and divide. Certain genes that promote cell division are called *oncogenes*. Others that slow down cell division or cause cells to die at the right time are called *tumor suppressor genes*.

Each time a cell prepares to divide into 2 new cells, it must make a new copy of the DNA in its chromosomes. This process is not perfect, and errors can occur that may affect genes within the DNA. Cancers can be caused by DNA mutations (changes) that turn on oncogenes or turn off tumor suppressor genes. For instance, changes in certain genes such as FLT3, c-KIT, and RAS are commonly found in AML cells.

While mutations within a single gene are found in many cases of AML, larger changes in one or more chromosomes are also common. Even though these changes involve larger pieces of DNA, their effects are still likely due to their effects on just one or a few genes. Several types of chromosome changes may be found in AML cells:

- *Translocations* are the most common type of DNA change that can lead to leukemia. A translocation means that a segment of DNA from one chromosome breaks off and becomes attached to a different chromosome. The point at which the break occurs can affect nearby genes - for example, it can turn on oncogenes or turn off genes that would normally help a cell to mature.

- *Deletions* occur when part of a chromosome is lost. This may result in the cell losing a gene that helped keep its growth in check (a tumor suppressor gene).

- *Inversions* occur when part of a chromosome gets turned around, so it is now in reverse order. This can result in the loss of a gene (or genes), because the cell can no longer read its instructions (much like trying to read a book backwards).

- *Addition* means that there is an extra chromosome or part of a chromosome. This can lead to too many copies of certain genes within the cell. This can be a problem if one or more of these genes are oncogenes.

Doctors are trying to figure out how each of these changes might lead to leukemia. Not all cases of AML have the same chromosome changes. Some changes are more common than others, and some seem to have more of an effect on a person's prognosis (outlook) than others. For instance, they may affect how quickly the leukemia cells grow, or how likely they are to respond to treatment. This is discussed in more detail in the section, How Is Acute Myeloid Leukemia Classified?

Some people with certain types of cancer have inherited DNA mutations from a parent. These changes increase their risk for the disease. But AML is very rarely caused by one of these inherited mutations.

Most DNA mutations related to AML occur during a person's lifetime, rather than having been inherited before birth. They may result from exposure to radiation, cancer-causing chemicals, but they often occur for no apparent reason.

Can Acute Myeloid Leukemia Be Prevented?

The cause of most cases of acute myeloid leukemia (AML) is unknown. Since most leukemia patients have no known risk factors, at the present time there is no way to prevent it from developing.

As many as 1 out of 5 adult AML cases is related to smoking. It is by far the most significant controllable risk factor, and quitting offers the greatest chance to prevent AML. Of course, non-smokers are also much less likely than smokers to develop many other cancers, as well as heart disease, stroke, and other diseases.

Treatment of other cancers with chemotherapy and radiation may cause secondary (post-treatment) leukemias (see *What Are the Risk Factors for Acute Myeloid Leukemia?*). Doctors are now studying ways to treat cancer patients that minimizes their risk of developing secondary leukemia. Of course, the obvious benefits of treating life-threatening cancers with chemotherapy and radiation therapy must be balanced against the small chance of getting leukemia years later.

Avoiding known cancer-causing industrial chemicals, such as benzene, can lower the risk of getting AML. But most experts agree that exposure to occupational and environmental chemicals accounts for only a small number of leukemia cases.

Can Acute Myeloid Leukemia Be Found Early?

For many types of cancers, diagnosis at the earliest possible stage makes treatment much more effective. The American Cancer Society recommends screening tests for early diagnosis of certain cancers in people without any symptoms.

But at the present time, there are no special tests recommended to detect acute myeloid leukemia early. The best way to find leukemia early is to report any possible symptoms of leukemia (described in the next section) to the doctor right away.

People who are known to have an increased risk of AML because they have one of the myelodysplastic syndromes, an inherited disorder such as Down syndrome, or were treated with certain chemotherapy drugs should receive careful, regular medical checkups. These people do not usually develop leukemia, but they and their doctors should be familiar with possible symptoms of AML.

How Is Acute Myeloid Leukemia Diagnosed?

Signs and Symptoms of Acute Myeloid Leukemia

Acute myeloid leukemia (AML) can cause many different signs and symptoms, but some occur more commonly with certain subtypes.

Generalized Symptoms

Patients with AML often have several non-specific (generalized) symptoms. These can include weight loss, fatigue, fever, and loss of appetite. Of course, these are not specific to AML, and more often are caused by something other than cancer.

Shortage of Blood Cells

Most signs and symptoms of AML result from a shortage of normal blood cells, which happens when the leukemia cells crowd out the normal blood-making cells in the bone marrow. As a result, people do not have enough normal red blood cells, white blood cells, and blood platelets. These shortages show up on blood tests, but they can also cause symptoms.

- *Anemia* is a shortage of red blood cells. It can cause tiredness (fatigue), weakness, headache, feeling cold, dizzy, or lightheaded, and shortness of breath.

- A shortage of normal white blood cells (leukopenia) increases the risk of infections. A common term you may hear is *neutropenia*, which refers specifically to low levels of neutrophils (a type of granulocyte). Although patients with AML may have high white blood cell counts due to excess numbers of leukemia cells, these cells do not protect against infection the way normal white blood cells do. Fevers and recurring infections are some of the most common symptoms of AML.

- A shortage of blood platelets (*thrombocytopenia*) can lead to excess bruising, bleeding, frequent or severe nosebleeds, and bleeding gums.

Bone or Joint Pain

Some patients have bone pain or joint pain caused by the buildup of leukemia cells in bones or joints.

Swelling In the Abdomen

Leukemia cells may collect in the liver and spleen, causing them to enlarge. This may be noticed as a fullness or swelling of the belly. The lower ribs usually cover these organs, but when they are enlarged the doctor can feel them.

Spread to the Skin

If leukemia cells spread to the skin, they can cause lumps or spots that may look like common rashes. A tumor-like collection of AML cells under the skin or other parts of the body is called a chloroma or granulocytic sarcoma.

Spread to the Gums

Certain types of AML may spread to the gums, causing swelling, pain, and bleeding.

Spread to Other Organs

Sometimes, leukemia cells may spread to other organs. Spread to central nervous system (brain and spinal cord) can cause headaches, weakness, seizures, vomiting, trouble with balance, facial numbness, and blurred vision. On rare occasions AML may spread to the eyes, testicles, kidneys, or other organs.

Enlarged Lymph Nodes

In rare cases, AML may spread to lymph nodes. Affected nodes in the neck, groin, underarm areas, or above the collarbone may appear swollen.
Most symptoms of AML can also be seen in other problems like infections. For this reason, an accurate diagnosis is crucial.

Medical History and Physical Exam

If signs or symptoms suggest the possibility of leukemia, the doctor will want to obtain a thorough medical history, including how long symptoms have been present and whether or not there is any history of exposure to risk factors.

A thorough physical exam will likely include evaluation of the eyes, mouth, skin, lymph nodes, liver and spleen, and the nervous system. It will also include looking for areas of bleeding or bruising, or possible signs of infection.

If there is reason to think there might be problems caused by abnormal blood cells (anemia, infections, bleeding or bruising, etc.), the doctor will likely test the patient's blood counts. If the results suggest leukemia may be the cause, the doctor may refer the patient to a cancer doctor, who may run one or more of the tests described below.

Types of Specimens Used to Test for Acute Myeloid Leukemia

If signs and symptoms suggest that a patient may have leukemia, the doctor will need to check samples of cells from the patient's blood and bone marrow to be sure of the diagnosis. Other tissue and cell samples may also be taken in order to help guide treatment.

Blood Samples

Blood samples for tests for AML are generally taken from a vein in the arm.

Bone Marrow Samples

Bone marrow samples are obtained from a bone marrow aspiration and biopsy - two tests that are usually done at the same time. The samples are usually taken from the back of the pelvic (hip) bone, although in some cases they may be taken from the sternum (breast bone) or other bones.

In bone marrow *aspiration*, you lie on a table (either on your side or on your belly). After cleaning the area, the skin over the hip and the surface of the bone are numbed with local

anesthetic, which may cause a brief stinging or burning sensation. A thin, hollow needle is then inserted into the bone and a syringe is used to suck out a small amount of liquid bone marrow (about 1 teaspoon). Even with the anesthetic, most patients still have some brief pain when the marrow is removed.

A bone marrow *biopsy* is usually done just after the aspiration. A small piece of bone and marrow (about 1/16 inch in diameter and 1/2 inch long) is removed with a slightly larger needle that is twisted as it is pushed down into the bone. The biopsy may also cause some brief pain. Once the biopsy is done, pressure will be applied to the site to help prevent bleeding.

These bone marrow tests are used to help diagnose leukemia. They may also be repeated later to tell if the leukemia is responding to therapy.

Lumbar Puncture (Spinal Tap)

This test looks for leukemia cells in the cerebrospinal fluid (CSF), which is the liquid that surrounds the brain and spinal cord.

For this test, the patient may lie on his side or sit up. The doctor first numbs an area in the lower part of the back near the spine. A small needle is then placed between the bones of the spine to withdraw some of the fluid.

A lumbar puncture is not often used to test for AML, unless the patient is having symptoms that could be caused by the spread of leukemia cells into the central nervous system (CNS).

A lumbar puncture is sometimes used to deliver chemotherapy drugs into the CSF to prevent or treat the spread of leukemia to the spinal cord and brain.

Lab Tests Used to Diagnose and Classify Acute Myeloid Leukemia

One or more of the following lab tests may be used to diagnose AML and/or to determine the specific subtype of AML.

Blood Cell Counts and Blood Cell Examination

These tests look at how the different types of blood cells appear under the microscope and how many of them there are. Changes in the numbers and the appearance of these cells often help diagnose leukemia. Most patients with AML have too many immature white cells in their blood, and not enough red blood cells or platelets. Many of the white blood cells may be myeloblasts ("blasts"), immature blood-forming cells that are not normally found in the bloodstream. These immature cells do not function like normal, mature white blood cells. Even though these findings may suggest leukemia, the disease usually is not diagnosed without looking at a sample of bone marrow cells.

Blood Chemistry and Coagulation Tests

These tests measure the amounts of certain chemicals and the ability of the blood to clot. These tests are not used to diagnose leukemia, but can detect liver or kidney problems, abnormal levels of certain minerals in the blood, or problems with the clotting ability of the blood.

Routine Microscopic Exam

Samples of blood, bone marrow, or CSF are looked at under a microscope by a pathologist (a doctor specializing in diagnosing diseases with lab tests) and may be reviewed by the patient's hematologist/oncologist (a doctor specializing in cancer and blood diseases).

Based on the cells' size, shape, and other traits, doctors can classify them into specific cell types. A key element of this classification is whether the cells look like normal cells of circulating blood (mature) or lack features of normal blood cells (immature). The most immature cells are called *blasts*.

The percentage of cells in the bone marrow or blood that are blasts is particularly important. Having at least 20% blasts in the marrow or blood is generally required for a diagnosis of acute myeloid leukemia. AML can also be diagnosed if the blasts have a chromosome change that occurs only in a specific type of AML, even though the blast percentage doesn't reach 20%. Sometimes the leukemic blasts look similar to normal immature cells in the bone marrow. However, under normal circumstances, blasts are never more than 5% of bone marrow cells. In order for a patient to be considered to be in remission after treatment, the blast percentage must be no higher than 5%.

These additional tests are used to confirm the diagnosis of AML.

Cytochemistry

Cytochemistry tests involve exposing cells to chemical stains (dyes) that react with only some types of leukemia cells. These stains cause color changes that can be seen under a microscope, which can help the doctor determine what types of cells are present. For instance, one stain can help distinguish AML cells from acute lymphocytic leukemia (ALL) cells. The stain causes the granules of most AML cells to appear as black spots under the microscope, but it does not cause ALL cells to change colors.

Flow Cytometry

This technique is often used to look at the cells from bone marrow and blood samples. It is very accurate in determining the exact type of leukemia.

The test looks for certain substances on the surface of cells that help identify what types of cells they are. A sample of cells is treated with special antibodies (man-made immune system proteins) that stick to the cells only if these substances are present on their surfaces. The cells are then passed in front of a laser beam. If the cells now have antibodies attached to them, the laser will cause them to give off light, which can be measured and analyzed by a computer. Groups of cells can be separated and counted by these methods.

Related tests, called immunohistochemistry tests, can be used to detect these substances when viewing cells under a microscope.

These tests are used for *immunophenotyping* -- classifying leukemia cells according to the substances (antigens) on their surfaces. Specific types of leukemia cells have different antigens depending on their cell of origin and how mature they are, and this information can be helpful in AML classification.

Cytogenetics

These tests examine a cell's chromosomes (long strands of DNA) under a microscope. Normal human cells contain 23 pairs of chromosomes, each of which is a certain size and stains a certain way. In some cases of AML, the cells have chromosome changes that can be seen under a microscope.

For instance, 2 chromosomes may swap some of their DNA, so that part of one chromosome becomes attached to part of a different chromosome. This change, called a translocation, can usually be seen under a microscope. Other changes in chromosomes, such as inversions, deletions, or additions, are also possible. Recognizing these changes can help identify certain types of AML and may be important in determining the outlook for the patient.

The testing usually takes about 2 to 3 weeks, because the leukemia cells must grow in lab dishes for a couple of weeks before their chromosomes are ready to be looked at under the microscope.

The results of cytogenetic testing are written in a shorthand form that describes which chromosome changes are present.

- A *translocation*, written as t(8;21), for example, means a part of chromosome 8 is now located on chromosome 21, and vice versa.

- An *inversion*, written as inv(16), for example, means that part of the chromosome 16 is upside down and is now in reverse order but is still attached to the chromosome it originated from.

- A *deletion*, written as del(7) or -7, for example, indicates part of chromosome 7 has been lost.

- An *addition*, +8, for example, means that all or part of chromosome 8 has been duplicated, and too many copies of it are found within the cell.

Fluorescent In Situ Hybridization

Fluorescent In Situ Hybridization (FISH) is similar to cytogenetic testing. It can find most chromosome changes (such as translocations) that are visible under a microscope in standard cytogenetic tests, as well as some changes too small to be seen with usual cytogenetic testing. It uses special fluorescent dyes that only attach to specific parts of particular chromosomes. FISH can be used to look for specific changes in chromosomes. It can be used on regular blood or bone marrow samples. It is very accurate and can usually provide results within a couple of days, which is why this test is now used in many medical centers.

Very sensitive DNA tests such as **polymerase chain reaction (PCR)** tests can also find translocations too small to be seen under a microscope, even if very few leukemia cells are present in a sample.

These tests may also be used after treatment to find small numbers of leukemia cells that may not be visible under a microscope.

Imaging Tests

Imaging tests produce pictures of the inside of the body. Because leukemia does not usually form visible tumors, imaging tests are of limited value. There are several imaging studies that might be done in people with AML, but they are done more often to look for infections or other problems, rather than to look for the leukemia itself. In some cases imaging studies may be done to help determine the extent of the disease, if it is thought it may have spread beyond the bone marrow and blood.

X-rays

Routine chest x-rays may be done if a lung infection is suspected.

Computed tomography scan

The computed tomography (CT) scan is a type of x-ray that produces detailed, cross-sectional images of your body. Unlike a regular x-ray, CT scans can show the detail in soft tissues (such as internal organs). This test can help tell if any lymph nodes or organs in your body are enlarged. It isn't usually needed to diagnose AML, but it may be done if your doctor suspects the leukemia is growing in an organ, like your spleen.

Instead of taking one picture, as does a regular x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into detailed images of the part of your body that is being studied.

Often after the first set of pictures is taken, you will receive an intravenous (IV) injection of a contrast dye, or you may be asked to drink a solution of contrast material, to better outline blood vessels and internal organs. A second set of pictures is then taken.

The IV injection of contrast dye can cause a feeling of flushing or warmth, in the face or elsewhere. Some people get hives or, rarely, more serious allergic reactions like trouble breathing and low blood pressure. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays. You need to lie still on a table while they are being done. During the test, the table moves in and out of the scanner, a ring-shaped machine that completely surrounds the table. You might feel a bit confined by the ring you have to lay in when the pictures are being taken.

In some cases, a CT can be used to guide a biopsy needle precisely into a suspected abnormality, such as an abscess. For this procedure, called a *CT-guided needle biopsy*, you remain on the CT scanning table while a radiologist moves a biopsy needle through the skin and toward the location of the mass. CT scans are repeated until the needle is within the mass. A fine needle biopsy sample (tiny fragment of tissue) or a core needle biopsy sample (a thin cylinder of tissue about ½-inch long and less than 1/8-inch in diameter) is then removed to be looked at under a microscope.

Magnetic resonance imaging scan

Magnetic resonance imaging (MRI) scan**:** MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body. Not only does this create images of cross-sectional slices of the body like a CT scanner, it can also produce images of slices that are parallel with the length of your body. A contrast material might be injected, just as with CT scans, but is used less often. MRI scans are very helpful in looking at the brain and spinal cord.

MRI scans take longer than CT scans -- often up to an hour. You may have to lie inside a narrow tube, which is confining and can upset people with a fear of enclosed spaces. Newer, "open" MRI machines can help with this if needed. The MRI machine makes loud buzzing noises that you may find disturbing. Some places provide headphones to block this out.

Ultrasound

Ultrasound uses sound waves and their echoes to produce a picture of internal organs or masses. For this test, a small, microphone-like instrument called a transducer is placed on the skin (which is first lubricated with oil). It emits sound waves and picks up the echoes as they bounce off the organs. The echoes are converted by a computer into an image that is displayed on a computer screen. Ultrasound can be used to look for enlarged organs inside your abdomen such as the kidneys, liver, and spleen.

This is an easy test to have done, and it uses no radiation. You simply lie on a table, and a technician moves the transducer over the part of your body being looked at.

Gallium scan and bone scan

One of these tests may be useful if a patient has bone pain that might be due to either bone infection or cancer involving bones.

For these tests, the radiologist injects a slightly radioactive chemical into the bloodstream, which collects in areas of cancer or infection in the body. These areas can then be viewed with a special type of camera. The images from these scans are seen as "hot spots" in the body, but they don't provide much detail. If an area lights up on the scan, x-rays, CTs, or MRIs of the affected area can be done to get a more detailed look. If leukemia is a possibility, a biopsy of the area may be needed to confirm this.

How Is Acute Myeloid Leukemia Classified?

Most types of cancers are assigned numbered stages, based on the size of the tumor and how far from the original site in the body the cancer has spread.

Acute myeloid leukemia (AML), on the other hand, does not usually form tumor masses. It generally involves all of the bone marrow in the body and, in some cases, may have spread to other organs, such as the liver and spleen. Therefore the outlook for the patient with AML depends on other information, such as the subtype of AML (determined by lab tests), the age of the patient, and other lab test results.

The French-American-British (FAB) Classification of Acute Myeloid Leukemias

In the 1970s, an international conference of leukemia experts was held to decide on the best system for classifying acute leukemias. This group of French, American, and British doctors divided acute myeloid leukemias into subtypes, M0 through M7, based on the type of cell from which the leukemia developed and how mature the cells are. This was based largely on how the leukemia cells looked under the microscope after routine staining.

French-American-British (FAB) Classification of AML

FAB subtype	Name	Approximate % of adult AML patients	Prognosis compared to average for AML
M0	Undifferentiated acute myeloblastic leukemia	5%	Worse
M1	Acute myeloblastic leukemia with minimal maturation	15%	Average
M2	Acute myeloblastic leukemia with maturation	25%	Better
M3	Acute promyelocytic leukemia	10%	Best
M4	Acute myelomonocytic leukemia	20%	Average
M4 eos	Acute myelomonocytic leukemia with eosinophilia	5%	Better
M5	Acute monocytic leukemia	10%	Average
M6	Acute erythroid leukemia	5%	Worse
M7	Acute megakaryoblastic leukemia	5%	Worse

Some subtypes of AML defined in the FAB system are linked with certain symptoms. For example, bleeding or blood clotting problems are often a problem for patients with the M3 subtype of AML, also known as acute promyelocytic leukemia (APL).

Identifying APL is very important for 2 reasons. First, certain complications of APL can often be prevented by appropriate treatment. Second, APL is treated differently from most other forms of AML -- it usually responds to retinoids (drugs related to vitamin A).

Prognostic Factors

As leukemia treatment has improved over the years, research has focused on why some patients have a better chance to be cured than others. The AML subtype certainly plays a role in this. Other differences among patients that affect response to treatment are called *prognostic factors.* They help doctors decide if people with a certain type of leukemia should receive more or less treatment.

These prognostic factors include the cytogenetic test results (showing chromosome or gene changes), the patient's age, and the white blood cell count. Other features considered are pre-existing blood disorders (such as a myelodysplastic syndrome), or a history of an earlier cancer that was treated with chemotherapy and/or radiation therapy.

Chromosome Abnormalities

Chromosome changes give one clue to prognosis. Not all patients have these abnormalities. Those listed below are the most common, but there are many others. Patients without any of these usually have an outlook that is between favorable and unfavorable.

Favorable abnormalities:

- translocation between chromosomes 8 and 21 (seen in patients with M2)
- inversion of chromosome 16 (seen in patients with M4 eos)
- translocation between chromosomes 15 and 17 (seen in patients with M3)

Unfavorable abnormalities:

- deletion (loss) of part of chromosome 5 or 7 (no specific AML type)
- translocation between chromosomes 9 and 11 (seen in patients with M5)
- extra chromosome 8 (no specific AML type)

Gene Mutations

Newer tests allow doctors to find changes within specific genes on chromosomes. People who have certain gene mutations may have a better or worse outlook.

For instance, about 1 patient out of 3 with AML has a mutation in the FLT3 gene. These people tend to have a poorer outcome, but new drugs that target this abnormal gene are now being studied, which may lead to better outcomes.

Age

Older patients (over 60) generally do not fare as well as younger patients. Some of this may be because it is harder to treat them with more intense chemotherapy regimens.

White Blood Cell Count

A high white blood cell count (>100,000) at the time of diagnosis is linked to a worse outlook.

Prior Blood Disorders or Cancers

Having a prior blood disorder such as a myelodysplastic syndrome or having AML that develops after treatment for another cancer tends to lead to a worse prognosis, as these types of AML are often harder to treat.

World Health Organization (WHO) Classification of AML

The FAB classification system is useful and is still the most commonly used way to group AML into subtypes. But it doesn't take into account many of the prognostic factors listed above. The World Health Organization (WHO) recently proposed a newer system that includes some of these factors to try to help better classify cases of AML based on a patient's outlook. Not all doctors use this new system, as it is not yet clear how accurate it is.

The WHO classification system divides AML into several broad groups:

AML with certain genetic abnormalities

- AML with a translocation between chromosomes 8 and 21
- AML with a translocation or inversion in chromosome 16
- AML with changes in chromosome 11
- APL (M3), which usually has translocation between chromosomes 15 and 17

AML with multilineage dysplasia (more than one abnormal myeloid cell type is involved)

AML related to previous chemotherapy or radiation

AML not otherwise specified (includes cases of AML that don't fall into one of the above groups; similar to the FAB classification)

- undifferentiated AML (M0)
- AML with minimal maturation (M1)
- AML with maturation (M2)
- acute myelomonocytic leukemia (M4)
- acute monocytic leukemia (M5)
- acute erythroid leukemia (M6)
- acute megakaryoblastic leukemia (M7)
- acute basophilic leukemia
- acute panmyelosis with fibrosis
- myeloid sarcoma (also known as granulocytic sarcoma or chloroma)

Undifferentiated or biphenotypic acute leukemias (leukemias that have both lymphocytic and myeloid features. Sometimes called ALL with myeloid markers, AML with lymphoid markers, or mixed lineage leukemias.)

In the coming years, doctors will use newer tests such as cytogenetic studies, flow cytometry, and molecular genetic studies to learn more about the underlying genetic defects that cause AML and how they can be used to predict a patient's prognosis. These genetic defects might also form the basis for treating the leukemias.

Status of Acute Myeloid Leukemia After Treatment

Not surprisingly, how well a leukemia responds to treatment also has an effect on long-term prognosis.

A *remission (complete remission)* is usually defined as having no evidence of disease after treatment. This means the bone marrow contains fewer than 5% blast cells, the blood cell counts are within normal limits, and there are no signs or symptoms of the disease. A *molecular complete remission* means there is no evidence of leukemia cells in the bone marrow, even when using very sensitive tests, such as PCR.

Minimal residual disease is a term used after treatment when leukemia cells can't be found in the bone marrow using standard tests (such as looking at cells under a microscope), but more sensitive tests (such as flow cytometry or PCR) find evidence that leukemia cells remain in the bone marrow.

Active disease means that either there is evidence that the leukemia is still present during treatment or that the disease has come back after treatment (relapsed). For a patient to be in relapse, they must have more than 5% blast cells present in the bone marrow.

How Is Acute Myeloid Leukemia 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.

This section starts with general comments about types of treatments used for acute myeloid leukemia (AML). This is followed by a discussion of the typical treatment approach for AML. The treatment of acute promyelocytic leukemia (APL) is different from other subtypes, and is discussed separately.

As noted earlier, adult AML is not a single disease. It is really a group of related diseases, and patients with different subtypes of AML vary in their outlook and response to treatment. Treatment options for each patient are based on the FAB subtype and cytogenetic studies of the leukemia cells, as well as certain other prognostic features (described in the previous section).

Several types of treatment may be used in people with AML. The major therapy is chemotherapy. Surgery and radiation therapy may be used in special circumstances.

Chemotherapy

Chemotherapy uses anti-cancer drugs that are injected into a vein, muscle, or into the cerebrospinal fluid (CSF), or are taken by mouth to destroy or control cancer cells. Except

when given into the CSF, these drugs enter the bloodstream and reach all areas of the body, making this treatment useful for cancers that spread widely, such as leukemia.

Chemotherapy for AML usually involves a combination of 2 or 3 anti-cancer drugs. The drugs used may include:

- cytarabine, also known as cytosine arabinoside or ara-C (Cytosar)
- daunorubicin, also known as daunomycin (Cerubidine)
- idarubicin (Idamycin)
- mitoxantrone (Novantrone)
- 6-thioguanine, also known as 6-TG
- 6-mercaptopurine, also known as 6-MP (Purinethol)
- fludarabine (Fludara)
- vincristine (Oncovin)
- etoposide (VePesid, others)
- prednisone (numerous brand names)

Chemotherapy drugs work by attacking cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow, the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemotherapy, which can lead to side effects.

The side effects of chemotherapy depend on the type and dose of drugs given and how long they are taken. These side effects may include:

- hair loss
- mouth sores
- loss of appetite
- nausea and vomiting
- lowered resistance to infection (due to low white blood cell counts)
- easy bruising or bleeding (due to low blood platelets)
- fatigue (due to low red blood cells)

These side effects are usually short-term and go away once treatment is finished.

Be sure to talk with your cancer care team about any side effects you have because there are often ways to lessen them. For example, drugs can be given to help prevent or reduce nausea and vomiting.

Drugs known as growth factors, such as G-CSF (filgrastim, Neupogen) and GM-CSF (sargramostim, Leukine), are sometimes given to increase the white blood cell counts after chemotherapy, to reduce the chance of infection. Because they may hasten the recovery of the white blood cell count and do not seem to cause any harm, they can be used during chemotherapy in patients with AML. They seem to have only a modest benefit, however.

If your white blood cell counts are very low during treatment, you can help reduce your risk of infection by carefully avoiding exposure to germs. During this time, your doctor may tell you to:

- Wash your hands often.
- Avoid fresh, uncooked fruits and vegetables and other foods that might carry germs.
- Avoid fresh flowers and plants because they may carry mold.
- Make sure other people wash their hands when they come in contact with you.
- Avoid large crowds and people who are sick (wearing a surgical mask offers protection in these situations).

Antibiotics may be given before there are signs of infection or at the earliest sign that an infection may be developing. The most commonly used drugs are a combination of trimethoprim and sulfamethoxazole (Bactrim or Septra), which help fight bacteria. Drugs that help prevent viral and fungal infections may also be given.

Because many of the side effects of chemotherapy are caused by low white blood cell counts, some people find it helpful to keep track of their counts. Also, decisions about when a patient can leave the hospital are often influenced by his or her counts. If you are interested in having this information, ask your doctor or nurse about your blood cell counts and what these numbers mean.

If your platelet counts are low, you may be given drugs or platelet transfusions to help prevent bleeding. Likewise, shortness of breath and extreme fatigue caused by low red blood cell counts may be treated with drugs or with red blood cell transfusions.

Tumor lysis syndrome is another possible side effect of chemotherapy. This syndrome can be seen in patients who had large numbers of leukemia cells in the body before treatment. When chemotherapy kills these cells, they break open and release their contents into the bloodstream, which may affect the kidneys, heart, and nervous system. This can be prevented by giving extra fluids during treatment and by giving certain drugs, such as bicarbonate, allopurinol, and rasburicase, which help the body get rid of these substances.

Some possible side effects are specific to certain drugs. For example, cytarabine (ara-C) can cause certain problems, especially when used at high doses. These can include dryness in the eyes and effects on certain parts of the brain, which can lead to coordination and balance problems. The drug dose may need to be reduced or stopped altogether if these side effects appear.

Other organs that could be directly damaged by chemotherapy drugs include the kidneys, liver, testes, ovaries, heart, and lungs. Because of careful monitoring, some of these side effects have become rare.

If serious side effects occur, the chemotherapy may have to be reduced or stopped, at least for a short time. Careful monitoring and adjustment of drug doses are important because some side effects affecting organs are permanent.

Monoclonal Antibodies

Monoclonal antibodies are man-made versions of immune system proteins (antibodies) that are designed to attach to specific targets (in this case, substances on the surface of leukemia cells). Some work by boosting the body's immune response against the leukemia cells. Other monoclonal antibodies have radioactive chemicals or cell poisons attached to them. When they are injected into the patient, the antibodies act like a homing beacon, bringing the radioactivity or poison directly to the leukemia cells, which kills them.

Gemtuzumab ozogamicin (Mylotarg) is a monoclonal antibody with a cell poison attached that is sometimes used to treat AML.. It targets a molecule on AML cells called CD33, and it can be used in older adults with AML who have relapsed after initial chemotherapy who might not be able to tolerate the side effects of other chemotherapy.

The most common side effects of Mylotarg are fever, chills, low blood pressure, and rashes during the injection. It can also cause low white blood cell and platelet counts because, like chemotherapy, it can kill normal blood-forming cells. Mylotarg may also affect the liver.

This drug is still being studied to see how it might best be used. Doctors are now testing it along with chemotherapy as the first treatment in patients with leukemia, and are testing it in younger patients as well.

Surgery

Because leukemia cells spread widely throughout the bone marrow and to many other organs, it is not possible to cure this type of cancer with surgery. Surgery rarely has any role even in the diagnosis, since a bone marrow aspirate and biopsy can usually diagnose leukemia. On rare occasions, an isolated tumor of leukemia cells (known as a granulocytic sarcoma or a chloroma) may be treated with surgery.

Often before treatment is about to start, surgery is needed to insert a small plastic tube, called a central venous catheter or venous access device (VAD), into a large vein. The end of the tube is just under the skin or sticks out in the chest area or upper arm. The VAD is left in place during treatment to take blood samples and give intravenous (IV) drugs, such as chemotherapy. This lowers the number of needle sticks needed during treatment. It is very important for the patient to learn how to care for the VAD to prevent it from getting infected.

Radiation Therapy

Radiation therapy uses high-energy radiation to kill cancer cells. External beam radiation therapy focuses high-energy beams on the cancer from a machine outside the body. Getting

radiation therapy is much like getting a regular x-ray, although it often takes longer. There are a few instances in which radiation therapy may be used to help treat leukemia:

- Radiation is sometimes used to treat leukemia that has spread to the brain and spinal fluid or to the testicles.
-
- Radiation to the whole body is often an important part of treatment before a bone marrow or peripheral blood stem cell transplant (see below).
-
- It is used (rarely) to help shrink a tumor if it is pressing on the trachea (windpipe) and causing breathing problems. But chemotherapy is often used instead, as it may work more quickly.
-
- Radiation can also be used to reduce pain in an area of bone that is invaded by leukemia, if chemotherapy hasn't helped.

Bone Marrow or Peripheral Blood Stem Cell Transplant

The usual doses of chemotherapy drugs can cause serious side effects to quickly dividing tissues such as the bone marrow. Even though higher doses of these drugs might be more effective, they are not given because the severe damage to bone marrow cells would cause lethal shortages of blood cells and damage to vital organs.

A stem cell transplant (SCT) allows doctors to use higher doses of chemotherapy and, sometimes, radiation therapy. After treatment is finished, the patient receives a transplant of blood-forming stem cells to restore the bone marrow.

Blood-forming stem cells used for a transplant are obtained either from the blood (for a peripheral blood stem cell transplant, or PBSCT) or from the bone marrow (for a bone marrow transplant, or BMT). Bone marrow transplant was more common in the past, but it has largely been replaced by PBSCT.

Types of Transplants

There are 2 main types of stem cell transplants. They differ with regard to the source of the blood-forming stem cells.

In an **allogeneic stem cell transplant**, the stem cells come from someone else - usually a donor whose tissue type is almost identical to the patient's. Tissue type is based on certain substances present on the surface of cells in the body. These substances can cause the immune system to react against the cells. Therefore, the closer a tissue "match" is between the donor and the recipient, the better the chance the transplanted cells will "take" and begin making new blood cells.

The donor may be a brother or sister or, less often, a matched unrelated donor (MUD). The stem cells from an unrelated donor come from volunteers whose tissue type has been stored in a central registry and matched with that of the patient. Sometimes umbilical cord stem cells are used. These stem cells come from blood drained from the umbilical cord and placenta after a baby is born and the umbilical cord is cut.

Although an allogeneic transplant is often the preferred type of transplant for AML when it is available, its use is limited by the need for a matched donor. It is also limited by its side effects, which are too severe for most people over 55 to 60 years old.

In an **autologous stem cell transplant**, a patient's own stem cells are removed from his or her bone marrow or peripheral blood. They are stored while the person gets treatment (high-dose chemotherapy and/or radiation) and then are reinfused into the patient's blood.

Autologous transplants are sometimes used for people with AML who are in remission after initial treatment. Some doctors feel that it is better than standard "consolidation" chemotherapy (see below) for these people, but not all doctors agree with this.

One problem with autologous transplants is that it is hard to separate normal stem cells from leukemia cells in the bone marrow or blood samples. Even after purging (treating the stem cells in the lab to try to kill or remove any remaining leukemia cells), there is the risk of returning some leukemia cells with the stem cell transplant. There is another important reason to use stem cells from someone else for transplantation. These cells seem to help in fighting any remaining leukemia cells through an immune reaction. This is called a "graft-versus-leukemia" reaction. Studies of this approach are still going on.

The Transplant Procedure

Blood-forming stem cells from the bone marrow or peripheral blood are collected, frozen, and stored. The patient receives high-dose chemotherapy and sometimes also radiation treatment to the entire body. (Radiation shields are used to protect the lungs, heart, and kidneys from damage during radiation therapy.)

The chemotherapy and radiation treatments are meant to destroy any remaining cancer cells. They also kill the normal cells of the bone marrow and the immune system. This prevents the stem cell transplant (graft) from being rejected. After these treatments, the frozen stem cells are thawed and given as a blood transfusion. The stem cells settle into the patient's bone marrow over the next several days and start to grow and make new blood cells.

In an allogeneic SCT, the person getting the transplant is given drugs such as prednisone and methotrexate or cyclosporine to prevent acute graft-versus-host disease (GVHD) .For the next few weeks the patient will get regular blood tests and supportive therapies as needed, which might include antibiotics, red blood cell or platelet transfusions, other medicines, and help with nutrition.

Usually within a couple of weeks after the stem cells have been infused, they begin making new white blood cells. This is followed by new platelet production and, several weeks later, new red blood cell production.

Patients usually stay in the hospital in protective isolation (guarding against exposure to germs) until their white blood cell count rises above 500. They may be able to leave the hospital when their white blood cell count is near 1,000. The patient is then examined in the outpatient clinic almost every day for several weeks. Because platelet counts take longer to return to a safe level, patients may receive platelet transfusions as an outpatient.

Practical Points

Bone marrow or peripheral blood SCT is a complex treatment. If the doctors think a patient may benefit from a transplant, it should be done at a hospital where the staff has experience with the procedure and with managing the recovery phase. Some bone marrow transplant programs may not have experience in certain types of transplants, especially transplants from unrelated donors.

SCT is very expensive (more than $100,000) and often requires a lengthy hospital stay. Because some insurance companies may view it as an experimental treatment, they may not pay for the procedure. It is important to find out what your insurer will cover and to have an idea of what you might have to pay before deciding on a transplant.

Side Effects

Side effects from SCT are generally divided into early and long-term effects.

The early complications and side effects are basically the same as those caused by any other type of high-dose chemotherapy (see the Chemotherapy section of this document), and are due to damage to the bone marrow and other quickly dividing tissues of the body. Complications can include low blood cell counts (with increased risk of infection and bleeding), nausea, vomiting, loss of appetite, mouth sores, and hair loss.

One of the most common and serious short-term effects is the increased risk for infection from bacteria, viruses, or fungi. Antibiotics are often given to try to prevent this from happening. Other side effects, like low red blood cell and platelet counts, may require blood product transfusions or other treatments.

Some complications and side effects can persist for a long time or may not occur until months or years after the transplant. These include:

- *Graft-versus-host disease* (GVHD), which can occur in allogeneic (donor) transplants. This happens when the donor immune system cells attack tissues of the patient's skin, liver, and digestive tract. Symptoms can include weakness, fatigue, dry mouth, rashes, nausea, diarrhea, yellowing of the skin and eyes (jaundice), and

muscle aches. In severe cases, GVHD can be fatal. GVHD is often described as either acute or chronic, based on how soon after the transplant it begins. Drugs that weaken the immune system are often given to try to keep GVHD under control.

- Damage to the lungs, causing shortness of breath
- Damage to the ovaries in women, causing infertility and loss of menstrual periods
- Damage to the thyroid gland that causes problems with metabolism
- *Cataracts* (damage to the lens of the eye that can affect vision)
- Bone damage called *aseptic necrosis* (the bone dies because of poor blood supply); if damage is severe, the patient will need to have part of the bone and the joint replaced.

Graft-versus-host disease is the most serious complication of allogeneic (donor) stem cell transplants. It occurs because the immune system of the patient is taken over by that of the donor. The donor immune system then begins reacting against the patient's other tissues and organs.

The most common symptoms are severe skin rashes and severe diarrhea. The liver and lungs may also be damaged. The patient may also become tired easily and have muscle aches. Sometimes the graft-versus-host disease becomes chronic and disabling and, if it is severe enough, can be fatal. Drugs that affect the immune system may be given to try to control it.

On the positive side, graft-versus-host disease also leads to "graft-versus-leukemia" activity. Any leukemia cells remaining after chemotherapy and radiation therapy may be killed by the immune reaction of the donor cells.

Non-myeloablative Transplant (Mini-transplant)

Most patients over the age of 55 can't tolerate a standard allogeneic transplant that uses high doses of chemotherapy. Some may be able to have a non-myeloablative transplant (also known as a mini-transplant or reduced-intensity transplant), where they receive lower doses of chemotherapy and radiation that do not completely destroy the cells in their bone marrow. They then receive the allogeneic (donor) stem cells. These cells enter the body and establish a new immune system, which sees the leukemia cells as foreign and attacks them (a "graft-versus-leukemia" effect).

Doctors have learned that if they use small doses of certain chemotherapy drugs and low doses of total body radiation, an allogeneic transplant can still work with much less toxicity. In fact, a patient can receive a non-myeloablative transplant as an outpatient. The major complication is graft-versus-host disease.

This procedure is still considered experimental, and is being studied to determine how useful it may be against AML.

For more information on stem cell transplants, see the American Cancer Society document, *Bone Marrow & Peripheral Blood Stem Cell Transplants*.

Clinical Trials

You have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is deciding which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you. Clinical trials are one way to get state-of-the art cancer care. Still, they are not right for everyone.

Here we will give you a brief review of clinical trials. Talking to your health care team, your family, and your friends can help you make the best treatment choice for you.

What Are Clinical Trials?

Clinical trials are carefully controlled research studies that are done with patients. These studies test whether a new treatment is safe and how well it works in patients, or they may test new ways to diagnose or prevent a disease. Clinical trials have led to many advances in cancer prevention, diagnosis, and treatment.

The Purpose of Clinical Trials

Clinical trials are done to get a closer look at promising new treatments or procedures in patients. A clinical trial is only done when there is good reason to believe that the treatment, test, or procedure being studied may be better than the one used now. Treatments used in clinical trials are often found to have real benefits and may go on to become tomorrow's standard treatment.

Clinical trials can focus on many things, such as:

- new uses of drugs that are already approved by the US Food and Drug Administration (FDA)
- new drugs that have not yet been approved by the FDA
- non-drug treatments (such as radiation therapy)
- medical procedures (such as types of surgery)
- herbs and vitamins
- tools to improve the ways medicines or diagnostic tests are used
- medicines or procedures to relieve symptoms or improve comfort
- combinations of treatments and procedures

Researchers conduct studies of new treatments to try to answer the following questions:

- Is the treatment helpful?
- What's the best way to give it?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Are there more or fewer side effects than the standard treatment used now?

- Do the benefits outweigh the side effects?
- In which patients is the treatment most likely to be helpful?

Phases of Clinical Trials

There are 4 phases of clinical trials, which are numbered I, II, III, and IV. We will use the example of testing a new cancer treatment drug to look at what each phase is like.

Phase I clinical trials: The purpose of a phase I study is to find the best way to give a new treatment safely to patients. The cancer care team closely watches patients for any harmful side effects.

For phase I studies, the drug has already been tested in lab and animal studies, but the side effects in patients are not fully known. Doctors start by giving very low doses of the drug to the first patients and increase the doses for later groups of patients until side effects appear or the desired effect is seen. Doctors are hoping to help patients, but the main purpose of a phase I trial is to test the safety of the drug.

Phase I clinical trials are often done in small groups of people with different cancers that have not responded to standard treatment, or that keep coming back (recurring) after treatment. If a drug is found to be reasonably safe in phase I studies, it can be tested in a phase II clinical trial.

Phase II clinical trials**:** These studies are designed to see if the drug works. Patients are given the best dose as determined from phase I studies. They are closely watched for an effect on the cancer. The cancer care team also looks for side effects.

Phase II trials are often done in larger groups of patients with a specific cancer type that has not responded to standard treatment. If a drug is found to be effective in phase II studies, it can be tested in a phase III clinical trial.

Phase III clinical trials**:** Phase III studies involve large numbers of patients -- most often those who have just been diagnosed with a specific type of cancer. Phase III clinical trials may enroll thousands of patients.

Often, these studies are randomized. This means that patients are randomly put in one of two (or more) groups. One group (called the control group) gets the standard, most accepted treatment. Another group (or more than one group) will get the new treatment being studied. All patients in phase III studies are closely watched. The study will be stopped early if the side effects of the new treatment are too severe or if one group has much better results than the others.

Phase III clinical trials are usually needed before the FDA will approve a treatment for use by the general public.

Phase IV clinical trials**:** Once a drug has been approved by the FDA and is available for all patients, it is still studied in other clinical trials (sometimes referred to as phase IV studies). This way more can be learned about short-term and long-term side effects and safety as the drug is used in larger numbers of patients with many types of diseases. Doctors can also learn more about how well the drug works, and if it might be helpful when used in other ways (such as in combination with other treatments).

What It Will Be Like to Be in a Clinical Trial

If you are in a clinical trial, you will have a team of experts taking care of you and watching your progress very carefully. Depending on the phase of the clinical trial, you may receive more attention (such as having more doctor visits and lab tests) than you would if you were treated outside of a clinical trials. Clinical trials are specially designed to pay close attention to you.

However, there are some risks. No one involved in the study knows in advance whether the treatment will work or exactly what side effects will occur. That is what the study is designed to find out. While most side effects go away in time, some may be long-lasting or even life threatening. Keep in mind, though, that even standard treatments have side effects. Depending on many factors, you may decide to enter (enroll in) a clinical trial.

Deciding to Enter a Clinical Trial

If you would like to take part in a clinical trial, you should begin by asking your doctor if your clinic or hospital conducts clinical trials. There are requirements you must meet to take part in any clinical trial. But whether or not you enter (enroll in) a clinical trial is completely up to you.

Your doctors and nurses will explain the study to you in detail. They will go over the possible risks and benefits and give you a form to read and sign. The form says that you understand the clinical trial and want to take part in it. This process is known as giving your informed consent. Even after reading and signing the form and after the clinical trial begins, you are free to leave the study at any time, for any reason.

Taking part in a clinical trial does not keep you from getting any other medical care you may need.

To find out more about clinical trials, talk to your cancer care team. Here are some questions you might ask:

- Is there a clinical trial that I could take part in?
- What is the purpose of the study?
- What kinds of tests and treatments does the study involve?
- What does this treatment do? Has it been used before?
- Will I know which treatment I receive?
- What is likely to happen in my case with, or without, this new treatment?

- What are my other choices and their pros and cons?
- How could the study affect my daily life?
- What side effects can I expect from the study? Can the side effects be controlled?
- Will I have to stay in the hospital? If so, how often and for how long?
- Will the study cost me anything? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment would I be entitled to?
- What type of long-term follow-up care is part of the study?
- Has the treatment been used to treat other types of cancers?

How Can I Find Out More About Clinical Trials That Might Be Right for Me?

The American Cancer Society offers a clinical trials matching service for patients, their family, and friends. You can reach this service at 1-800-303-5691 or on our Web site at http://clinicaltrials.cancer.org.

Based on the information you give about your cancer type, stage, and previous treatments, this service can put together a list of clinical trials that match your medical needs. The service will also ask where you live and whether you are willing to travel so that it can look for a treatment center that you can get to.

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.

For even more information on clinical trials, the American Cancer Society has a document called *Clinical Trials: What You Need to Know.* You can read this on the Web site, www.cancer.org, or have it sent to you by calling 1-800-ACS-2345.

Complementary and Alternative Therapies

When you have cancer you are likely to hear about many ways to treat your cancer or relieve symptoms that are different from mainstream (standard) medical treatment. These methods could include vitamins, herbs, and special diets; or methods such as acupuncture or massage—among many others. You may have a lot of questions about these treatments. Here are some you may have thought of already:

- How do I know if a non-standard treatment is safe?
- How do I know if it works?
- Should I try one or more of these treatments?
- How might my doctor react if I use one of these methods? Should I tell the doctor that I'm thinking about it?
- Will these treatments cause a problem with my standard medical treatment?
- What is the difference between "complementary" and "alternative" methods?
- Where can I find out more about these treatments?

The Terms Can Be Confusing

Not everyone uses these terms the same way, so it can be confusing. To make it easier, the American Cancer Society uses *complementary* to refer to medicines or methods that are used *along with* your regular medical care. *Alternative* medicine is used *instead of* standard medical treatment, often with serious results for the patient.

Complementary Methods

Complementary methods, for the most part, are not are not presented as cures for cancer. Most often they are used to help you feel better. Some examples of complementary methods are breathwork, meditation, homeopathy, dietary supplements, and aromatherapy. There are many others. Some of these methods are known to help, while others have not been tested. Some have been proven not be helpful. A few have even been found harmful. However, if one or more of these methods is carefully chosen and managed, it can often add to your comfort and well-being.

Alternative Methods

Alternative methods (those that are used instead of your regular medical care) may put you at great risk. Some of these methods are dangerous and may have life-threatening side effects. With others, the main danger is that you may lose the chance to benefit from standard treatment. Delays or interruptions of your standard medical treatment can give the cancer more time to grow. Many of these methods are also very costly and are not covered by insurance.

Deciding What to Do

It is easy to see why people with cancer consider complementary or alternative methods. You want to do all you can to fight the cancer or to relieve symptoms. Sometimes mainstream treatments such as chemotherapy can be hard to take. When someone you know is telling you that a certain treatment is "natural" and has no side effects, it may sound tempting. Sometimes people imply that their method can cure you or make you better, and it's normal to want to believe them. But the truth is that standard methods of treatment have been tested and scientifically proven to be effective for treating cancer.

Unlike complementary and alternative methods, mainstream treatments must be carefully tested in large groups of people before they are used. (This is done through the clinical trial process, which was described above.) Because there is so much interest in them, many of the non-standard methods have now been tested in animals or people. Even though the testing is usually limited, it is helpful to find a reliable source and learn the results of any such tests before you make a decision.

There are also many complementary methods that you can safely use right along with your medical treatment to help relieve symptoms or side effects, to ease pain, and to help you enjoy life more. For example, some people find methods such as aromatherapy, massage therapy, meditation, or yoga to be useful.

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

- Talk to your doctor or nurse about any method you are thinking about using.
- Check the list of "red flags" below.
- Contact the American Cancer Society at 1-800-ACS-2345 to learn more about complementary and alternative methods in general and learn more about the specific methods you are thinking about.

Red Flags

You can use the questions below to spot treatments or methods to avoid. A "yes" answer to any one of these questions should raise a "red flag."

- Does the treatment promise a cure for all or most cancers?
- Are you told not to use standard medical treatment?
- Is the treatment or drug a "secret" that only certain people can give?
- Does the treatment require you to travel to another country?
- Do the promoters attack the medical or scientific community?

The Decision Is Yours

Decisions about how to treat or manage your cancer are always yours to make. If you decide to use a complementary or alternative method without getting all the facts or without talking to your doctor, you may find out later that your treatment options have become more limited. With reliable information and input from your health care team, you should be able to safely use the methods that can help you while you avoid those that could be harmful.

Typical Treatment of Acute Myeloid Leukemia (Except Promyelocytic M3)

Treatment of AML is usually divided into 2 chemotherapy phases:

- remission induction
- post-remission therapy (consolidation)

Remission Induction

This first part of treatment is aimed at getting rid of all visible leukemia. It usually involves treatment with 2 chemotherapy drugs, cytarabine (ara-C) and an anthracycline drug such as daunorubicin (Daunomycin) or idarubicin (Idamycin). Sometimes a third drug, 6-

thioguanine, is added. This intensive therapy, which usually takes place in the hospital, typically lasts one week. How intense the treatment is may depend on the person's age and on other prognostic factors.

In rare cases where the leukemia has spread to the brain or spinal cord, chemotherapy may be given into the cerebrospinal fluid (CSF) as well.

Most of the normal bone marrow cells as well as the leukemia cells will be destroyed by the treatment. During chemotherapy and the following couple of weeks, the patient's blood cell counts will probably be dangerously low, and drugs to raise white blood cell counts, antibiotics, and blood product transfusions may be used to help protect against complications. Usually, the patient stays in the hospital during this time.

If induction is successful, no leukemia cells will be found in the blood, and the number of blast cells in the bone marrow will be less than 5% within a week or two. Normal bone marrow cells will return in a couple of weeks and start making new blood cells.

If one week of treatment does not induce remission, the process may be repeated.

Induction is successful in about 40% to 80% of all AML patients. This depends to a large part on a person's specific prognostic factors. For instance, older people are more likely to have unfavorable cytogenetic test results, are more likely to have a pre-existing blood disorder, and are less likely to be able to tolerate intensive therapy than younger patients, so generally they don't respond as well.

Remission induction usually does not destroy all the leukemia cells, and a small number often persist. Without more treatment, called consolidation, the leukemia is likely to return within several months.

Consolidation (Post-remission) Therapy

If remission induction is successful, further treatment may be given to try to destroy any remaining leukemia cells and help prevent a relapse. The options for AML consolidation therapy are:

- several courses of high-dose cytarabine (ara-C) chemotherapy
- allogeneic (donor) stem cell transplant
- autologous stem cell transplant

High-dose consolidation chemotherapy differs from induction therapy in that usually only cytarabine (ara-C) is used. The drug is given at very high doses, typically over 5 days. This process is repeated once or twice. When examined four years after this treatment, about 40% of young patients (younger than 60 years) will not show any signs of leukemia. In older adults, this number is around 15%.

Another approach after successful induction therapy is a stem cell transplant. Patients first receive very high doses of chemotherapy to destroy all bone marrow cells. This is followed by either an allogeneic (from a donor) or autologous (patient's own) stem cell transplant to restore blood cell production.

It is not clear which of the 3 treatment options (high-dose chemotherapy, allogeneic transplant, or autologous transplant) is best for consolidation. They each have their pros and cons. Doctors look at several different factors when recommending what type of post-remission therapy a patient should receive. These include:

- *How many courses (cycles) of chemotherapy it took to bring about a remission.* If it took more than one course, some doctors recommend that the patient receive a more intensive program, which would involve a stem cell transplant.

- *The availability of a brother, sister, or an unrelated donor who matches the patient's tissue type.* If a close enough tissue match is found then an allogeneic (donor) stem cell transplant may be offered for post-remission therapy.

- *The potential of collecting leukemia-free bone marrow cells from the patient.* If cytogenetic studies show that a patient is in remission, collecting stem cells from the patient's bone marrow or blood for an autologous stem cell transplant is an option for post-remission therapy. Stem cells collected from the patient would be purged (treated in the lab to try to remove or kill any remaining leukemia cells) to lower the chances of relapse.

- *The presence of one or more adverse prognostic factors,* such as certain chromosome changes, a very high initial white blood cell count, AML that develops from a myelodysplastic syndrome or after treatment for an earlier cancer, or spread to the central nervous system. These factors might lead doctors to recommend more aggressive therapy, such as a stem cell transplant. On the other hand, for people with good prognostic factors, such as favorable chromosome changes, many doctors might advise holding off on a stem cell transplant unless the disease recurs.

- *The age of the patient.* Older patients may not be able to tolerate some of the severe side effects that can occur with stem cell transplants. Therefore, this may not be as practical an option for them.

- *The patient's wishes.* There are many issues that revolve around quality of life that must be discussed. An important issue is the higher chance of early death from allogeneic transplant. This and other issues must be discussed between the patient and the doctor.

Stem cell transplants are intensive treatments with real risks of serious complications, including death, and their exact role in treating AML is not clear. Some doctors feel that if the patient is healthy enough to withstand the procedure and a compatible donor is available, an allogeneic transplant offers the best chance for survival. Others feel that studies have not

yet shown this conclusively, and that in some cases a transplant should be reserved in case the leukemia comes back after standard treatment. Because most studies of stem cell transplants have involved patients who tend to be younger and in better health, their improved survival might not be due to the procedure. That is, they might have done just as well with standard high-dose chemotherapy. Research in this area continues.

Treatment of Acute Promyelocytic (M3) Leukemia

The early diagnosis and treatment of the acute promyelocytic leukemia (APL) subtype of AML is important because patients with APL may develop serious blood-clotting or bleeding problems. This can often be prevented or treated with blood-thinning medicines. Other treatments might include transfusions of platelets or other blood products. With modern therapies, bleeding is often less of a problem once treatment of APL begins.

The treatment of most cases of APL differs from usual AML treatment. Initial treatment usually involves an anthracycline chemotherapy drug (daunorubicin or idarubicin) plus a non-chemotherapy drug, all-trans retinoic acid (ATRA), which is a relative of vitamin A.

Treatment with ATRA and chemotherapy induces remission in about 80% to 90% of patients. As with other subtypes of AML, these patients then receive post-remission treatment.

Consolidation therapy usually consists of 2 or more courses of chemotherapy (with an anthracycline), usually along with ATRA. This is often followed by maintenance therapy with ATRA for at least a year. Some doctors may also add low doses of chemotherapy, usually with the drugs 6-mercaptopurine (6-MP) and methotrexate.

The possible side effects from the chemotherapy part of this treatment are generally the same as those of standard AML induction chemotherapy. But ATRA can cause a problem called *retinoic acid syndrome*. Symptoms include breathing problems due to fluid buildup in the lungs, low blood pressure, kidney damage, and severe fluid buildup elsewhere in the body. It can often be treated by stopping the ATRA for a while and giving a steroid such as dexamethasone.

About 70% to 90% of patients with APL are cured with this treatment.

What If the Leukemia Doesn't Respond or Comes Back After Treatment?

If AML doesn't go away with the first treatment, newer or more intensive doses of chemotherapy drugs may be tried, if they can be tolerated. A stem cell transplant may be tried in younger patients if a suitable stem cell donor can be found. Clinical trials of new treatment approaches may also be an option.

If AML comes back (recurs) after treatment, it will most likely do so in the bone marrow and blood. The brain or cerebrospinal fluid (CSF) rarely will be the first place it recurs, but if it does, it is treated with chemotherapy given directly into the CSF.

If the leukemia went away and has now come back, the treatment options may depend on the patient's age, and on how long the leukemia was in remission. For those whose remission lasted longer than 6 months, it is sometimes possible to put the leukemia into remission again with more chemotherapy, although this is not likely to be long-lasting. For younger patients (generally those younger than 60), most doctors would advise a stem cell transplant if a suitable donor can be found. Gemtuzumab ozogamicin (Mylotarg) may also be an option, particularly in older patients. Clinical trials of new treatment approaches may also be considered.

If AML comes back sooner than 6 months, most doctors will advise a stem cell transplant for younger patients, if possible. Gemtuzumab ozogamicin (Mylotarg) has been used in some patients who have relapsed, particularly those who are older. It is now being studied in younger patients as well. Taking part in a clinical trial is another option.

For the 20% to 30% of patients with **acute promyelocytic leukemia (APL)** who don't respond to initial treatment or who relapse, a drug called arsenic trioxide (Trisenox) is often very effective at inducing a second remission. The most serious possible side effect of this drug is a change in heart rhythm. A stem cell transplant may be another option if a donor can be found.

If treatment with arsenic trioxide achieves a second remission, a stem cell transplant may be recommended, if possible. If a second remission is not achieved, treatment options may include Mylotarg, a stem cell transplant, or taking part in a clinical trial.

If the leukemia keeps coming back or doesn't go away, further chemotherapy treatment will probably not be very helpful. If a stem cell transplant is not an option, a patient may want to consider taking part in a clinical trial of newer treatments.

Those who want to continue treatment to fight the leukemia as long as they can need to consider the odds of more treatment having any benefit. In many cases, the doctor can estimate the response rate for the treatment being considered. Some people are tempted to try more chemotherapy, for example, even when their doctors say that the odds of benefit are less than 1%. In this situation, it is important to think about and understand the reasons for choosing this plan.

Palliative Treatment

If a clinical trial is not an option, it is important at this time to focus on relieving the symptoms of the leukemia. This is known as palliative treatment. The doctor may advise less intensive chemotherapy with the goal of slowing the leukemia growth instead of trying to cure it.

As the leukemia grows in the bone marrow it may cause pain. It is important to treat it with radiation or appropriate pain-killing medicines. If medicines such as aspirin and ibuprofen don't help with the pain, more potent opioid medicines such as morphine are likely to be helpful.

Other common symptoms from leukemia are low blood counts and fatigue. Medicines or blood transfusions may be needed to help correct these problems. Nausea and loss of appetite can be treated with medicines and high calorie food supplements. Infections that occur may be treated with antibiotics.

At some point, a patient may benefit from hospice care. Most of the time, this can be given at home. The leukemia may be causing symptoms or problems that need attention, and hospice focuses on the patient's comfort. Receiving hospice care doesn't mean you can't have treatment for the problems caused by the cancer or other health conditions. It just means that the focus of care is on living life as fully as possible and feeling as well as one can at this difficult stage.

Remember also that maintaining hope is important. The hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that can bring happiness and meaning. In a way, pausing at this time in your cancer treatment is an opportunity to refocus on the most important things in your life. This 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.

More Treatment Options

For more details on treatment options -- including some that may not be addressed in this document -- the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. Those are available on the NCCN Web site (www.nccn.org).

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

What Should You Ask Your Doctor About Acute Myeloid Leukemia?

It is important to have frank, open, and honest communications with your doctor about your condition. Your doctor and the rest of the cancer care team want to answer all of your questions. For instance, consider these questions:

- What kind of acute myeloid leukemia do I have?
- Are there any specific factors that might affect my prognosis?
- What treatment choices do I have?
- Which treatment do you recommend, and why?
- What side effects are there to the treatments that you recommend?
- What can I do to help reduce the side effects I may have from the chemotherapy?
- Should we consider a stem cell transplant? When?
- What are the chances that my leukemia will come back once I am in remission?
- What is the outlook for my survival?

Be sure to write down any questions you have that are not on this list. For instance, you might want specific information about expected recovery times so that you can plan your work schedule. Or you may want to ask about second opinions or about clinical trials for which you may qualify. Taking another person and/or a tape recorder to the appointment can be helpful.

What Will Happen After Treatment for Acute Myeloid Leukemia?

Completing treatment can be both stressful and exciting. You will be relieved to finish treatment, yet it is hard not to worry about cancer coming back. (When cancer returns, it is called recurrence.) This is a very common concern among those who have had cancer.

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 cancer learn to live with uncertainty.

Follow-up Care

You will need frequent follow-up exams -- likely every few months for several years after the treatment for acute myeloid leukemia (AML) is finished. It is very important to keep all follow-up appointments. During these visits, your doctor will likely ask about symptoms, do physical exams, and order blood tests or bone marrow exams. Follow-up is needed to check for cancer recurrence or spread, as well as possible side effects of certain treatments. This is a good time for you to ask your health care team any questions you need answered and to discuss any concerns you might have.

Almost any cancer treatment can have side effects. Some may last for a few weeks to several months, but others can be permanent. Don't hesitate to tell your cancer care team about any symptoms or side effects that bother you so they can help you manage them.

If a relapse occurs, it is usually while the patient is being treated or shortly after they have finished chemotherapy. If this happens, treatment would be as described in the section, *What if the Leukemia Doesn't Respond or Comes Back After Treatment?* It is unusual for AML to return if there are still no signs of the disease within a few years after treatment.

Seeing a New Doctor

At some point after your cancer diagnosis and treatment, you may find yourself in the office of a new doctor. Your original doctor may have moved or retired, or you may have moved or changed doctors for some reason. It is important that you be able to give your new doctor the exact details of your diagnosis and treatment. Make sure you have the following information handy:

- a copy of your pathology report from any biopsy or surgery
- if you had surgery, a copy of your operative report
- if you were hospitalized, a copy of the discharge summary that every doctor must prepare when patients are sent home from the hospital
- finally, since some drugs can have long-term side effects, a list of your drugs, drug doses, and when you took them

Lifestyle Changes to Consider During and After Treatment

Having cancer and dealing with treatment can be time-consuming and emotionally draining, but it can also 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 begin this process during cancer treatment.

Make Healthier Choices

Think about your life before you learned you had cancer. Were there things you did that might have made you less healthy? Maybe you drank too much alcohol, or ate more than you needed, or smoked, or didn’t exercise very often. Emotionally, maybe you kept your feelings bottled up, or maybe you let stressful situations go on too long.

Now is not the time to feel guilty or to blame yourself. However, you can start making changes *today* that can have positive effects for the rest of your life. Not only will you feel better but you will also be healthier. What better time than now to take advantage of the motivation you have as a result of going through a life-changing experience like having cancer?

You can start by working on those things that you feel most concerned about. 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 Quitline ® tobacco cessation program at 1-800-ACS-2345.

Diet and Nutrition

Eating right can be a challenge for anyone, but it can get even tougher during and after cancer treatment. For instance, treatment often may change your sense of taste. Nausea can be a problem. You may lose your appetite for a while and lose weight when you don't want to. On the other hand, some people gain weight even without eating more. This can be frustrating, too.

If you are losing weight or have taste problems during treatment, do the best you can with eating and remember that these problems usually improve over time. You may want to ask your cancer team for a referral to a dietitian, an expert in nutrition who can give you ideas on how to fight some of the side effects of your treatment. You may also find it helps to eat small portions every 2 to 3 hours until you feel better and can go back to a more normal schedule.

One of the best things you can do after treatment is to put healthy eating habits into place. You will be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Try to eat 5 or more servings of vegetables and fruits each day. Choose whole grain foods instead of white flour and sugars. Try to limit meats that are high in fat. Cut back on processed meats like hot dogs, bologna, and bacon. Get rid of them altogether if you can. If you drink alcohol, limit yourself to 1 or 2 drinks a day at the most. And don't forget to get some type of regular exercise. The combination of a good diet and regular exercise will help you maintain a healthy weight and keep you feeling more energetic.

Rest, Fatigue, Work, and Exercise

Fatigue is a very common symptom in people being treated for cancer. This is often not an ordinary type of tiredness but a "bone-weary" exhaustion that doesn't get better with rest. For some, this fatigue lasts a long time after treatment, and can discourage them from physical activity.

However, exercise can actually help you reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel physically and emotionally improved and can cope better.

If you are ill and need to be on bed rest during treatment, it is normal to expect your fitness, endurance, and muscle strength to decline. Physical therapy can help you maintain strength and range of motion in your muscles, which can help fight fatigue and the sense of depression that sometimes comes with feeling so tired.

Any program of 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 3 times a week. If you haven't exercised in a few years but can still get around, you may want to think about taking short walks.

Talk with your health care team before starting, and get their opinion about your exercise plans. Then, try to get an exercise buddy so that 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, though, you will need to balance activity with rest. It is okay to rest when you need to. It is really hard for some people to allow themselves to do that when they are used to working all day or taking care of a household. (For more information about fatigue, please see the publication, *Cancer Related Fatigue and Anemia Treatment Guidelines for Patients.)*

Exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- It strengthens your muscles.
- It reduces fatigue.
- It lowers anxiety and depression.
- It makes you feel generally happier.
- It helps you feel better about yourself.

And long term, we know that exercise plays a role in preventing some cancers. The American Cancer Society, in its guidelines on physical activity for cancer prevention, recommends that adults take part in at least 1 physical activity for 30 minutes or more on 5 days or more of the week. Children and teens are encouraged to try for at least 60 minutes a day of energetic physical activity on at least 5 days a week.

How About Your Emotional Health?

Once your treatment ends, you may find yourself overwhelmed by 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 your treatment.

Now you may find that you think about the possibility of your own death, or the effect of your cancer on your family, friends, and career. You may also begin to re-evaluate your relationship with your spouse or partner. Unexpected issues may also cause concern -- for instance, as you become healthier and have fewer doctor visits, you will see your health care team less often. That can be a source of anxiety for some.

This is an ideal time to seek out emotional and social support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or individual counselors.

Almost everyone who has been through cancer can benefit from getting some type of support. 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.

The cancer journey can feel very lonely. It is not necessary or realistic to go it all by yourself. And your friends and family may feel shut out if you decide 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-ACS-2345 and we can put you in touch with an appropriate group or resource.

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life -- making healthy choices and feeling as well as possible, physically and emotionally.

What's New in Acute Myeloid Leukemia Research and Treatment?

Researchers are now studying the causes, diagnosis, supportive care, and treatment of acute myeloid leukemia (AML) at many medical centers, university hospitals, and other institutions.

Genetics of Leukemia
Scientists are making progress in understanding how changes in a person's DNA can cause normal bone marrow cells to develop into leukemia. A greater understanding of the genes (regions of the DNA) involved in certain translocations or other chromosomal changes that often occur in AML is providing insight into why these cells become abnormal.

As this information unfolds, it may be used in developing newer targeted therapies against AML (see below).

Gene Expression Profiling
This new lab technique is being studied to help identify and classify different cancers. Instead of looking at single genes, this test uses microarrays to look at the patterns of many different genes in the cancer cells at the same time. This type of test is now being looked at to

help classify cases of AML into different risk categories. This may add to the information that comes from the standard molecular genetic studies.

Detection of Minimal Residual Disease
Progress in understanding DNA changes in AML has already provided a highly sensitive test for detecting the smallest amount of disease left after treatment (minimal residual disease), even when so few leukemia cells are present that they cannot be found by routine bone marrow tests.

The polymerase chain reaction (PCR) test can identify AML cells based on their gene translocations or rearrangements. This test can find one leukemia cell among a million normal cells. A PCR test can be useful in determining how completely the treatment has destroyed the AML cells.

Doctors are now trying to determine what effect minimal residual disease has on a patient's outlook, and how this might affect the need for further or more intensive treatment.

Improving Chemotherapy
Studies are being done to find the most effective combination of chemotherapy drugs while still avoiding unwanted side effects.

Newer chemotherapy drugs such as clofarabine (Clolar) and decitabine (Dacogen) have shown some promising results in early studies when combined with other chemotherapy drugs. Tipifarnib, a newer type of drug known as a farnesyl transferase inhibitor, has also shown promise in early studies. Farnesyl transferase inhibitors are drugs that keep a protein that is very active in cancer from functioning. These drugs are now being tested in larger clinical trials.

The effectiveness of chemotherapy may be limited in some cases because the leukemia cells become resistant to it. Researchers are now looking at ways to prevent or reverse this resistance by using other drugs along with chemotherapy.

Studies are also under way to determine whether patients with certain unfavorable prognostic features benefit from more intensive chemotherapy, and whether some patients with favorable prognostic factors might not need as much treatment.

Stem Cell Transplants
Researchers continue to refine stem cell transplants to increase effectiveness, reduce complications and determine which patients are likely to be helped by this treatment. Many studies are under way to try to help determine exactly when autologous, allogeneic, and mini-transplants might best be used.

Targeted Therapies
New targeted drugs that specifically attack some of the genetic changes seen in AML are now being developed..

About 1 person out of 3 with AML has a mutation in the FLT3 gene. Several new drugs, called FLT3 inhibitors, target this gene. They have shown activity against AML in early studies, especially when combined with chemotherapy. So far, they are only available in clinical trials.

Other gene mutations, such as changes in the c-KIT gene, also appear to be important in some cases of AML, and may become important targets for new therapies. Drugs that target this gene, such as imatinib (Gleevec) and dasatinib (Sprycel) are already used against other types of leukemia, and are now being studied against AML.

Gemtuzumab ozogamicin (Mylotarg) is a monoclonal antibody that is often used in older patients if AML doesn't respond to chemotherapy or comes back after treatment. Doctors are now studying whether this drug might be useful if given with chemotherapy earlier in the course of the disease.

Additional Resources

More Information From Your American Cancer Society

The following information may also be helpful to you. These materials may be ordered from our toll-free number.

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

Bone Marrow & Peripheral Blood Stem Cell Transplants

Cancer-Related Fatigue and Anemia Treatment Guidelines for Patients

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

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

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

The following books are available from the American Cancer Society. Call us at 1-800-ACS-2345 to ask about costs or to place your order.

American Cancer Society's Guide to Pain Control

Cancer in the Family: Helping Children Cope with a Parent's Illness

Caregiving: A Step-By-Step Resource for Caring for the Person with Cancer at Home

Coming to Terms with Cancer: A Glossary of Cancer-Related Terms

Consumers Guide to Cancer Drugs

Informed Decisions, Second Edition: The Complete Book of Cancer Diagnosis, Treatment, and Recovery

When the Focus Is on Care: Palliative Care and Cancer

National Organizations and Web Sites*

In addition to the American Cancer Society, other sources of patient information and support include:

Caitlin Raymond International Registry (for unrelated bone marrow transplants)
Telephone: 1-800-726-2824
Internet Address: www.crir.org

Leukemia & Lymphoma Society
Telephone: 1-800-955-4572
Internet Address: www.lls.org

Leukemia Links
Internet Address: www.acor.org/leukemia

National Bone Marrow Transplant Link (nbmtLINK)
Telephone: 1-800-LINK-BMT (1-800-546-5268)
Internet Address: www.nbmtlink.org

National Cancer Institute
Telephone: 1-800-4-CANCER (1-800-422-6237)
Internet Address: www.cancer.gov

National Marrow Donor Program
Telephone: 1-800-MARROW-2 (1-800-627-7692)

Internet Address: www.marrow.org

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

The American Cancer Society is happy to address almost any cancer-related topic. If you have any more questions, please call us at 1-800-ACS-2345 any time, 24 hours a day.

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Last Medical Review: 8/3/2007

Last Revised: 3/22/2008